Sharon Kimble
(S.E.N.,R.G.N.)

Hormones 2016

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Contents

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Preface

Disclaimer

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The author takes no responsibilities for any problems, damages, or loss of sanity resulting from improper usage of hormones. If you are in any doubt, do NOT take the tablets, or whatever but post a question to your relevant newsgroup or refer to a competent medical doctor or endocrinologist. Messing about with something you do not understand may seriously damage your health. YOU HAVE BEEN WARNED.

Introduction

Very little information, if any, is given to us when we are prescribed these drugs, or when they are dispensed at the pharmacy. We are not told the benefits that we should expect from these drugs or of what to be aware of with regard to any side effects. I am concerned about the scarcity of reliable information for transsexuals in any public forum, or in any easily read,

understandable format. This then, is the primary reason for the existence of this ebook - to hopefully help to remedy that situation. Also, these medications are licensed for use in specific circumstances, which generally do not include usage on or for transsexuals.

All of the drugs mentioned are ones that I have heard about. I make no recommendations as to which is best, it is up to the individual prescriber and their knowledge of the drugs action and also their knowledge of their patient. It is inadvisable also, to take any medication that has been prescribed for someone else.

This document

This document has a long history, having had several previous incarnations, first in December 1999, then in December 2001, and next in August 2005, and then a long gap until March 2015. On each occasion it seemed to be well received, but it was just for transsexuals within the United Kingdom utilising the National Health Service and the private medical sector. Since then things have moved on and more information is available on the internet, so its time for a revision and update. As I now have more information available, I've decided to use information which is applicable to folk all over the world. And I've found that as people seem to be confused over the title, its now just called "Hormones 2016".

This is written to be read online, or offline with your favourite PDF reader. If you were to print it out you would lose access to all the cross-references, and other stuff too.

Previous versions

Title	Version	When published
UK Hormone FAQ	v3.6	December 1999
UK Hormones FAQ	v4.0	December 2001
UK Hormones 2005		August 2005
Universal Hormones 2015	v1.0	March 2015

Table 1.1 – Previous versions of this document

Please note

In some places you may see **on a word or two**, these show that they are a common side-effect.

You may also see this **which shows a moderately common** side-effect.

This a warning that something is amiss and needs attending to.

Shows a dangerous side-effect which should be notified extremely soon, if not now, to your local General Practitioner, a community-based doctor (GP), Doctor, Endocrinologist, or Hospital.

Shows an overdose. Speak to your local GP, Doctor, Endocrinologist, or Hospital As Soon As Possible, if not sooner!

Possible **other side-effects** are shown like this one.

I have placed various sections in what I consider to be a logical order, but also in alphabetical order within the chapters.

Acknowledgements

Thanks to all the people, too many to list individually, who contributed to my research for this book. Any errors or omissions are nobodies fault except my own, but I would also refer you back to the disclaimer.

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About the author

My name is Sharon Kimble, and I am a former Registered General Nurse and a State Enrolled Nurse, living and working in the United Kingdom.

I have approached this subject with the idea and question of - "What information would I want to know about this drug if I were going to start taking it?"

Some people have wondered why I have used such old documents and references? My reasoning is that yes, some are old, like Richard Doll with his ground-breaking research into smoking sixty years ago. But, just because they are old does not diminish from the strength of their message, which is still vibrant and worth listening to. So the first time that someone says something that is important and relevant, and it is published in some format, is the time that I record it.

Sharon Kimble
✉ My email address
1st May 2016

Changes

These are the changes between version 1.0, and this version 2.0.

Removed

- Chapter 5 - Herbal Hormones - now superseded by its own document.
- Individual prices in the individual drugs, as the prices are out of date by the time that its published.
- Blood donating,
- the legal situation in the UK.

Added

- Sleep at page 542,
- Stretch marks at page 566,
- Infection? at page 485,
- Sitting down? at page 535,
- Pelvic examination at page 515,
- Sexually transmitted infections - STI's at page 308,
- Getting a urine sample at page 474,
- Getting older at page 475,
- Grapefruit Juice at page 476,
- Depression at page 465,

- Free prescriptions at page 520,
- Blood tests and their results at page 245,
- Urine tests and their results at page 299,
- Other infections that can be caused by an STI at page 385,
- Skin care at page 535,
- Deprecated Drugs at page 194,
- README FIRST at page 15,
- Stress management at page 551,
- Renewed Confidence in HRT at page 483,
- Accessing your health records at page 411,
- Treatment aims at page 588,
- Breast Screening at page 456,
- Expiry dates at page 468,
- Removed all coloured boxes and replaced them with coloured text, hopefully it will be easier to read?

Chapter 2

README FIRST

This chapter gives a quick introduction to the most important parts of *"Hormones"*. The rest of the book is basically a verbose version of this chapter. You should start by reading this chapter, as it summarises all the hormones, giving their name, uses, and common side-effects. For more detailed information you can read their main entries. It's arranged in alphabetical order to make it easier to find things.

If you want to know more about endocrinology, you can read Preamble and also Endocrinology. Or you can jump right in and read your favourite hormone in this chapter and then click on the hormones name at the end of its section to jump straight to its main entry.

If you want to know more about the different colour of the side-effects, then jump to Please note.

Whatever, I hope you read it and enjoy what you're learning. If you have any questions you can email me on my email address at the end of Chapter 1, and I'll endeavour to help.

Ametop

Used as a topical anaesthetic for skin anaesthesia.

Also known as

Tetracaine, Amethocaine.

Common side-effects

Skin

- **Erythema**, (skyscape, 2014).

Further information

This can be found at Ametop.

Bicalutamide

What is it?

Anti-androgen.

Also known as

Casodex, Bicalutamid (German), Bicalutamida (Spanish)

Common side-effects

General

- **Back pain**,
- **pelvic pain**,
- **general body pain**,
- **headache**,
- **weakness**,
- **asthenia**.

Gastrointestinal

- **constipation**,
- **diarrhoea**,
- **flatulence**,
- **nausea**, (Abramovitz, 2016).

Cardiovascular

- **hot flashes**.

Genitourinary

- **nocturia**,
- **impotence** (Abramovitz, 2016).

Metabolic

- **Peripheral oedema**,
- **hyperglycaemia**, and
- **weight loss**, (Abramovitz, 2016).

Nervous system

- **insomnia**,
- **dizziness**, (Abramovitz, 2016).

Dermatological

- **sweating**, (Abramovitz, 2016).

Other

- **breast tenderness**,
- **breast swelling**,
- **hot flashes**, (unknown, 2014a).

- **breast pain**,
- **gynaecomastia**,
- **generalized pain**,
- **hot flashes**,
- **pelvic pain**,
- **libido decrease**,
- **impotence**, (unknown, 2014a).

Further information

This can be found at Bicalutamide.

Cyproterone Acetate

What is it?

Cyproterone acetate, sometimes abbreviated as CPA, and sold under brand names such as Androcur and Cyprostat, is a synthetic steroidal antiandrogen drug with additional progestogen and antigonadotropic properties (Neumann and Topert, 1986).

Also known as

Androcur, Cyprostat, Dianette, Siterone in USA, Diane-35 in Canada, and Dixi-35 in Chile.

Common side-effects

Respiratory

- **Breathlessness**. (BNF, 2016a),
- **shortness of breath**, (emc, 2016).

Gastrointestinal

- **Weight changes**, (BNF, 2016a).

Genitourinary

- **Breast swelling**,
- **decreased sex drive**,
- **impotence**,
- **reduced sperm count**,
- **reduced volume of ejaculate**, (emc, 2016)

Other

- **Tiredness**,
- **lassitude**,
- **Hot flushes**,
- **sweating**,
- **depressed mood**,
- **restlessness**, (emc, 2016).

Further information

This can be found at Cyproterone Acetate.

Dutasteride

What is it?

dihydrotestosterone (DHT)-blocker.

Also known as

Avodart, Dutasterid (German), Dutasterida (Spanish).

Common side-effects

- **Gynaecomastia**, (Abramovitz, 2016).

Further information

This can be found at Dutasteride.

Dydrogesterone

A synthetic progestational hormone with no androgenic or oestrogenic properties (drugbank, 2014b).

Also known as

Duphaston, Duphaston Hormone Replacement Therapy (HRT).

Common side-effects

Central Nervous System

- **Headache**,
- **dizziness**,
- **insomnia**,
- **drowsiness**,
- **depression**, (BNF, 2016a).

Gastrointestinal

- **Weight gain**,
- **nausea**, (BNF, 2016a).

Skin

- **Skin reactions** (including urticaria, pruritis, rash, and acne),
- **urticaria**,
- **hirsutism**, and
- **alopecia**, (BNF, 2016a).

Metabolism

- **Bloating**,
- **fluid retention**,
- **weight gain**,
- **nausea**, (BNF, 2016a).

Genitourinary

- **Breast tenderness**, (BNF, 2016a).

Further information

This can be found at Dydrogesterone.

Emla Cream

EMLA stands for 'eutectic mixture of local anaesthetic'.

Common side-effects

None known.

Further information

This can be found at Emla Cream.

Estradiol Valerate

Estradiol Valerate is a naturally occurring oestrogen given in the form of Estradiol Valerate or one of its semisynthetic esters as oestrogen replacement therapy in menopausal women (TGC, 2015a).

Also known as

Climaval, Estraderm MX, Estraderm TTS, Estradiol implant, Evorel, Progynova, Progynova TS, Zumenon, Estradiol (USA), Estradiol (German), Estradiol (French), Estradiol (Spanish).

Common side-effects

Central Nervous System

- **headache**, (Abramovitz, 2016).

Cardiovascular

- **oedema**, (Abramovitz, 2016).

Eyes

- **Myopia/astigmatism worsens**,
- **contact lens intolerance**, (Abramovitz, 2016).

Gastrointestinal

- **Nausea**,
- **vomiting**,
- **abdominal cramps**,
- **bloating**, (Abramovitz, 2016).

Genito-urinary

- **Testicular atrophy**,
- **erectile dysfunction**, (Abramovitz, 2016).

Metabolic

- **Weight changes**, (Abramovitz, 2016).

Skin

- **Melasma**,
- **hair loss**, (Abramovitz, 2016).

Other

- **gynaecomastia**,
- **hot flashes**,
- **breast tenderness**,
- **breast enlargement**, (Abramovitz, 2016).

Further information

This can be found at Estradiol Valerate.

Finasteride

What is it?

DHT-blocker

Also known as

Proscar, Propecia, Finasterid (German), Finastéride (French), Finasterida (Spanish).

Common side-effects

Central Nervous System

- **Dizziness**.

Cardiovascular

- **orthostatic hypotension**.

Other

- **Gynaecomastia**, (Abramovitz, 2016).

Further information

This can be found at Finasteride.

Flutamide

What is it?

Anti-androgen.

Also known as

Flutamid (German), Flutamida (Spanish).

Common side-effects

Gastrointestinal

- **Diarrhoea**,
- **nausea**,
- **vomiting**, (Abramovitz, 2016)

Genitourinary

- **Erectile dysfunction**, (Abramovitz, 2016).

Further information

This can be found at Flutamide.

Goserelin

Used for the treatment of advanced prostate cancer, endometriosis, advanced breast cancer, endometrial thinning (Abramovitz, 2016).

Also known as

Zoladex, Zoladex LA, Goséréline (French), Goserelina (Spanish).

Common side-effects

Central Nervous System

- **headache**, (Abramovitz, 2016).
- **Hot flushes** (drugs.com, 2014c).

Cardiovascular

- **hot flashes**, (Abramovitz, 2016)

Genitourinary

- **Sexual dysfunction**,
- **vaginitis**, (Abramovitz, 2016).
- **amenorrhoea**,
- **PSA increased**,
- **decreased libido**, (rxisk, 2016d).

Other

- **Changes in breast size**,
- **changes in libido**,
- **breast swelling**, (Abramovitz, 2016).

Further information

This can be found at Goserelin.

Leuprorelin Acetate

Anti-androgen

Also known as

Prostap SR, and Prostap 3.

Common side-effects

Central Nervous system

- **Headache**, (Macmillan, 2014).

Genitourinary

- **Hot flushes**,
- **impotence**,
- ↓ **libido**,
- **gynaecomastia**, (Macmillan, 2014).

Further information

This can be found at Leuprorelin Acetate

Minoxidil

Applied to the scalp in the treatment of male-pattern baldness.

Also known as

Regaine, Rogaine.

Common side-effects

None known.

Further information

This can be found at Minoxidil.

Oestrogel

Applied to the skin as an alternative route for administering oestrogen.

Also known as

Estrodose, divigel, elestrin, EstroGel.

Common side-effects

Skin

- **Irritation**,
- **reddening of the skin**,
- **mild and transient erythema** at the site of application (emc, 2016).

Further information

This can be found at Oestrogel.

Progesterone

A pharmaceutical-grade progesterone.

Also known as

Cyclogest, Gestone, Utrogestan, Prometrium (USA and Canada), Crinone.

Common side-effects

Central Nervous System

- **headache**,
- **fever**, (WebMD, 2014e)
- **chills**,
- **cold or flu-like symptoms**, (drugs.com, 2014c).
- **dizziness**, (Medscape, 2014).

Gastrointestinal

- **cough**, (drugs.com, 2014c).

Genitourinary

- **Breast tenderness**,
- **breast discomfort** or
- **enlargement**, (WebMD, 2014e).
- **problems with urination**, (drugs.com, 2014c).
- **breast pain**, (Medscape, 2014).

Further information

This can be found at Progesterone.

Sandrena

Hormone replacement therapy for oestrogen deficiency symptoms in postmenopausal women.

Common side-effects

Central Nervous System

- **headache**, (Abramovitz, 2016).

Cardiovascular

- **oedema**, (Abramovitz, 2016).
- **hot flushes**, (rxisk, 2016e).

Eyes

- **myopia/astigmatism worsens**,
- **contact lens intolerance**, (Abramovitz, 2016).

Gastrointestinal

- **Nausea**,
- **vomiting**,
- **abdominal cramps**,
- **bloating**, (Abramovitz, 2016).

Genito-urinary

- **Testicular atrophy**,
- **erectile dysfunction**, (Abramovitz, 2016).

Metabolic

- **Weight changes**, (Abramovitz, 2016)

Skin

- **Melasma**,
- **hair loss**, (Abramovitz, 2016)

Other

- **Gynaecomastia**,
- **breast tenderness**,
- **breast enlargement**, (Abramovitz, 2016)

Further information

This can be found at Sandrena.

Testosterone

Administration is by deep muscular injection, in the form of a gel, or as a patch.

Also known as

Sustanon 100, Sustanon 250, Testogel, Andropatch, Restandol, Testosteron (German), Testostérone (French), Testosterona (Spanish).

Common side-effects

Gastrointestinal

- **gum or mouth irritation**,
- **gum pain**,
- **gum tenderness**, or
- **gum oedema**, (Abramovitz, 2016).

Haematologic

- **haematocrit** [1] increased,
- **polycythaemia** [2].

Genitourinary

- **decreased libido**,
- **PSA increased**, (rxisk, 2016f).

Other

- **gynaecomastia**, (Abramovitz, 2016).

Further information

This can be found at Testosterone.

Triptorelin

Triptorelin is a synthetic analogue of gonadotropin-releasing hormone (gonadotropin-releasing hormone (GnRH)) agonist. It works by decreasing the production of certain hormones, which reduces testosterone levels in the body (drugs.com, 2016).

---

[1] a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells

[2] having a high concentration of red blood cells in your blood

Common side-effects

Gastrointestinal disorders

- **Nausea** (emc, 2009)

General disorders

- **asthenia**,
- **hyperhidrosis**,
- **fatigue**,
- **injection site erythema**,
- **injection site inflammation**,
- **injection site pain**,
- **injection site reaction**,
- **oedema** (emc, 2009).

Musculoskeletal disorders

- **back pain**,
- **musculoskeletal pain**,
- **pain in extremity** (emc, 2009).

Nervous system

- **paraesthesia in lower limbs**,
- **dizziness**,
- **headache** (emc, 2009).

Psychiatric disorders

- **depression**,
- **mood changes** (emc, 2009).

Reproductive system

- **erectile dysfunction**,
- **loss of libido** (emc, 2009).

Skin disorders

- **hyperhidrosis** (emc, 2009).

Vascular disorders

- **hot flush** (emc, 2009).

Further Information

This can be found at Triptorelin.

Vaniqa

Eflornithine, an antiprotozoal drug, inhibits the enzyme ornithine decarboxylase in hair follicles and topical application can reduce the growth of unwanted facial hair (BNF, 2016a).

Common side-effects

None known.

Further information

This can be found at Vaniqa.

Chapter 3

Preamble

What are hormones?

Hormones are the body's way of carrying messages from organs in a person's body through the bloodstream to its cells where homeostasis is achieved. Some of the glands, from about a dozen, in the endocrine system responsible for secreting hormones are the pancreas, thyroid, adrenals, and the pituitary. These glands play a large part in keeping a natural balance in the body.

Possible Health Risks

Some health risks are involved and should be fully researched and considered before beginning HRT. Pre-existing health problems could also disqualify a person for HRT.

One of the most troublesome aspects of HRT is that such little research has been performed to find out what health risks are involved. There could possibly be serious long-term health risks involved that still have not been uncovered. One serious risk that is definitely correlated with HRT is thromboembolic disease, which is a disease that causes blood clots. The risk for this can be decreased by regular exercise. Transwomen[3] can experience extreme mood swings on oestrogen and severe depression and loss of energy can result. The mortality rate in transwomen is 6 times higher than the general population. This is primarily due to suicide and unknown causes. Oestrogen can also cause transwomen to be a higher risk for benign pituitary tumors, gallbladder disease, and hypertension.

[3] is someone who was labelled male at birth but has a female gender identity, and therefore transitions to live completely and permanently as a woman (LGBT, 2014b)

Transmen[4] can develop serious acne problems, and weight gain of greater than 10% is fairly common. Transmen face higher risks of breast cancer, diabetes, high cholesterol, hypertension, heart attacks, and liver disease. Smoking tobacco makes these risks even greater, so a person pursuing HRT should be or become a non-smoker.

The most obvious risk with HRT is that once changes begin to occur, many of the changes are irreversible. **Sterility** results in both transwomen and transmen after prolonged treatment. If an transwoman thinks she would eventually like to father a child, she should seriously consider storing sperm in a sperm bank prior to starting HRT. (Also see Sperm banking) If an transman would like to have a child, it is sometimes possible to become pregnant after being on testosterone for a period of time, though pregnancy would require cessation of hormone treatment. It is possible to freeze eggs, but the technology has not sufficiently developed yet for this to be a long-term feasible solution for most people (University, 2014).

Side effects

Most drugs have some side-effects, and it is essential that the side-effects do not outweigh the benefits to you, the user. Because, if they do, then compliance with your regime will be scanty and full benefit will not be obtained. However, as with all medications, some people react differently to others. It is important for you to understand that there are side-effects to hormones, some side-effects may be acceptable, after all, you have come this far and a few slight adverse reactions are not going to slow you down now! These are the details you need to know however, to make an informed choice and to gain the maximum benefit from your hormone regime with the safest possible level of self-care. Side-effects are potential, NOT inevitable (unknown, 2005).

Taking Progynova as an example; some people may experience problems with their "cardiovascular" system (heart and circulation). There may be some evidence of fluid build-up in the body and blood clotting, oedema or thromboembolism[5] - the latter can be quite a serious side-effect so you need to understand the symptoms of this. (See Deep Vein Thrombosis for more information). Taking oral medication also carries a slight risk of liver problems, so watch out for symptoms such as jaundice. You may also experience nausea and vomiting (some women report that this is only in the early stages), as well as abdominal cramps and bloating. A common side effect is weight gain, generally through fluid or sodium retention in the tissues. So attention to diet becomes even more important if you

[4] is someone who was labelled female at birth but has a male gender identity, and therefore transitions to live completely and permanently as a man (LGBT, 2014b)

[5] Blockage of a blood vessel caused by a blood clot carried by the bloodstream from its point of origin

want to keep your weight down! Your breasts may become tender and enlarge slightly, called gynaecomastia, (so that's the good news!). Some people report headaches, and changes in their vision. If you're short-sighted it may worsen, and if you use contact lenses you may find them more uncomfortable. Remember, some side effects are temporary, but some are a continuing characteristic of the medication. Your GP[6] and/or endocrinologist will be able to advise you as to the most effective regime for you and will monitor your reactions to the hormones. Your own observations of the side effects are also very important so that you can take an active part in the medication that assists your transition. It will help if you keep a "hormone diary" where you record how you feel and what changes you see.

This is a considerably simplified overview, but I have tried to list the side effects in terms of increasing risk/discomfort to you, but people's experiences do differ.

You may feel more prepared for side effects and symptoms if you know about them in advance, which is one of the reasons for writing this document. Discuss the possible side effects of a drug with your doctor before starting treatment. Once you start treatment, make sure you talk to your doctor about side effects or symptoms you are experiencing. It's helpful to take notes so you can describe them accurately to your doctor. Side effects often improve over time. Knowing that can make it easier to stick with a drug until you see whether the side effects really do improve.

Remember that many things could be causing the problem you are having. Get a full diagnosis from your doctor. Yes, it could be a drug side effect - but maybe it's a problem with what you are eating, or an infection or a result of Getting older. There are options for dealing with symptoms and side effects.

- If the problem isn't too serious, wait and see if it improves on its own.
- If it's clear which drug is causing the side effect, your doctor may decide to switch you to another drug that doesn't cause this side effect.
- Perhaps it is not a drug that is causing the problem. Maybe it is something else that is causing it. In this case, your doctor will try to diagnose and treat this problem.
- You and your doctor may be able to find some way to deal with the problem, so you can live with it.

[6] General Practitioner, a community-based doctor

Where do hormones come from?

In both sexes, the adrenal cortex secretes significant amounts of both oestrogens (female hormones) and androgens[7]. In the female, the ovaries produce oestrogens and progesterone; oestrogen from the graafian follicles and progesterone from a temporary structure known as the corpus luteum. In the male, testosterone is secreted by the testes (TGC, 2015a).

Long-term treatment

Any long-term treatment should only be prescribed on the basis of "informed consent", see also Consent and Informed Consent hence another reason for this ebook. You should be aware that you will continue to take one form or other of hormones for the rest of your natural life.

Research has found that compliance for drug regimes can be increased by keeping the regime simple (sounds obvious, doesn't it), which in most cases means you take your medication only once or twice a day (Lynn, 1995). This means that you're less likely to forget to take a dose, and less likely to get muddled and to take too much dosage.

What will hormones do to me?

The following physiological effects are normally observed -

1. They are not a magic pill. You won't "become a woman" taking them.
2. Hormonal-induced changes are generally quite subtle.
3. Do not depend on them alone to make you passable, because they will not.
4. They will have an effect on body hair eventually (especially androgen blockers, which, strictly speaking, are not hormones but rather "hormone blockers").
5. Androgen blockers can help to reduce the doses of hormones needed, but only if taken concurrently.
6. Androgen blockers may have a use for assisting with and helping to halt scalp hair loss, but this is debatable.
7. You will see changes in your complexion and fat redistribution.
8. They had a wonderful calming effect for me and took the edge off my sex drive

[7] a male sex hormone, such as testosterone

9 You can hide the effects of hormones from others for as long as you want in virtually every case. Those who say they can't seem to want people to notice.
10 Hormones are potentially dangerous.
11 I do not recommend herbals or care about them, since their potency and safety are not regulated. Those serious about a safe, successful transition should be taking prescription hormones under a physician's care.
12 Getting a prescription and doing it supervised is often cheaper, safer, and more effective than black market options (James, 2014).

What changes will I see?

Male-to-Female (MTF) also known as 'transwomen'

Irreversible changes

- breast development,
- enlarged nipples and areolae
- stretch marks (for some) (unknown, 2015e)

Reversible changes

- decreased libido,
- redistribution of body fat,
- reduced muscle development,
- various skin changes,
- significantly reduced body hair
- change in body odour and sweat production,
- less prominence of veins,
- ocular changes,
- gonadal size (unknown, 2015e)

Typical changes from anti-androgens	
Average timeline	**Effect of blocking testosterone**
1–3 months after starting anti-androgens	Testosterone blocking changes, decrease in sex drive, fewer instances of waking up with an erection or spontaneously having an erection, some M→Fs also have difficulty getting an erection even when they are sexually aroused, decreased ability to make sperm and ejaculatory fluid

Typical changes from anti-androgens	
Average timeline	**Effect of blocking testosterone**
Gradual changes (usually at least 2 years)	Gradual changes, slower growth of facial and body hair, slowed or stopped "male"-pattern balding, slight breast growth (reversible in some cases, not in others)(Ashbee and Goldberg, 2006b)
Anti-androgens affect the entire body	
It's not possible to pick some changes and not others	

Table 3.1 – Taking anti-androgens alone (without oestrogen) which may vary from person to person

Typical changes from oestrogen	
Average timeline	**Effect of oestrogen**
1–3 months after starting oestrogen	Oestrogenic changes - softening of skin, decrease in muscle mass and increase in body fat, redistribution of body fat to a more "feminine" pattern, decrease in sex drive, fewer instances of waking up with an erection or spontaneously having an erection; some M→Fs also find their erections are less firm during sex, or can't get erect at all, decreased ability to make sperm and ejaculatory fluid
Gradual changes (maximum change after 1–2 years on Oestrogen)	Gradual changes, nipple and breast growth, slower growth of facial and body hair, slowed or stopped "male"-pattern balding, decrease in testicular size (Ashbee and Goldberg, 2006b)
Oestrogen affects the entire body	
It's not possible to pick some changes and not others	

Table 3.2 – Typical changes from using oestrogen (which may vary from person to person)

Changes to expect	**Traits that won't change**
Softer skin and body appearance	Voice
Breast growth	Height
Lessening of body hair	Size of hands and feet
Loss of strength	Presence of facial hair, (may grow more fine)

Changes to expect	Traits that won't change
Increased emotional sensitivity, especially to stress - depression not uncommon	Hair loss stops, but what has been lost won't grow back
Diminished ability to achieve erections and to ejaculate	Adam's apple
Redistribution of body fat from stomach to breasts, hips, and thighs	(University, 2014)

Table 3.3 – Things that might, or might not, change

Effect	Notes
Breast development	Usually starts in 3–6 months, Breasts reach full size in 2–3 years, Size varies. A or B cup-size is typical, This is a permanent change
Body fat redistribution	Usually starts in 3–6 months, Reaches maximum effect in 2–5 years, Less fat on abdomen, More fat on buttocks, hips and thighs, Usually not a permanent change if you stop taking hormones
Reduced muscle mass and strength	Usually starts in 3–6 months Reaches maximum effect in 1–2 years Reduced muscle and strength in upper body Usually not a permanent change if you stop taking hormones
Softening of skin	Usually starts in 3–6 months Skin will be softer and less oily Usually not a permanent change if you stop taking hormones
Less body and facial hair	Usually starts in 6–12 months Maximum effect in more than 3 years Body hair will appear less noticeable Body hair will grow more slowly Beard and mustache may grow more slowly and appear less noticeable, but will not go away If you have male pattern baldness, it may slow down Hair that has already been lost likely will not grow back This is usually not a permanent change if you stop taking hormones

Effect	**Notes**
Reduced sex drive	Usually starts in 1–3 months Reaches maximum effect in 1–2 years Fewer morning erections Fewer spontaneous erections Usually not a permanent change if you stop taking hormones
Fertility	Timeline varies Sperm may no longer reach maturity Won't produce as much semen May not be able to get hard enough for penetrative sex May become permanently unable to make someone pregnant (but birth control is still recommended)
Smaller testes	Usually starts in 3–6 months Maximum effect in 2–3 years May shrink down to half their initial size This may or may not be a permanent change if you stop taking hormones
Emotional changes	Your overall emotional state may or may not change; this varies from person to person. You may find that you experience a narrower range of emotions or feelings (Transhealth, 2015a).

Table 3.4 – Expected effects of feminizing hormone therapies

Risk level	**Feminizing hormones**
Likely increased risk	Serious blood clots (Venous thromboembolic disease) Gallstones Elevated liver enzymes Weight gain Hypertriglyceridemia (risk factor for heart disease and pancreas problems)
Likely increased risk with presence of additional risk factors	Cardiovascular disease
Possible increased risk	High Blood Pressure (Hypertension) Hyperprolactinemia or prolactinoma
Possible increased risk with presence of additional risk factors	Type 2 Diabetes
No increased risk or inconclusive research	Breast cancer (Transhealth, 2015a)

Table 3.5 – Risks associated with feminizing hormone therapies

Female-to-Male (FTM) also known as 'transmen'

Irreversible changes

- deepening of the voice,
- growth of facial and body hair,
- male pattern baldness (in some individuals),
- an enlargement of the clitoris,
- growth spurt and closure of growth plates if given before the end of puberty, and
- possible shrinking and/or softening of breasts, although this is due to changes in fat tissue (unknown, 2012).

Reversible changes

- increased libido,
- redistribution of body fat,
- cessation of ovulation and menstruation,
- further muscle development (especially upper body),
- increased sweat and changes in body odour,
- prominence of veins and coarser skin,
- acne (especially in the first few years of therapy),
- alterations in blood lipids (cholesterol and triglycerides), and
- increased red blood cell count (unknown, 2012).

Typical changes from testosterone	
Average timeline	**Effect of testosterone**
1–3 months after starting testosterone	Toestrogenic changes - increased sex drive, vaginal dryness, growth of your clitoris (typically 1–3 cm), increased growth, coarseness, and thickness of hairs on arms, legs, chest, back, plus abdomen oilier skin and increased acne, increased muscle mass and upper body strength, redistribution of body fat to a more "masculine" pattern (more fat around the waist, less around the hips)
1–6 months after starting testosterone	menstrual periods stop
3–6 months after starting testosterone	voice starts to crack and drop within first 3–6 months, but can take a year to finish changing
1 year or more after starting testosterone	gradual growth of facial hair (usually 1–4 years to reach full growth), possible "male"-pattern balding (Ashbee and Goldberg, 2006a)
Testosterone affects the entire body	

Typical changes from testosterone	
Average timeline	**Effect of testosterone**
It's not possible to pick some changes and not others	

Table 3.6 – Typical changes from using testosterone (which may vary from person to person)

Effect	Expected onset	Expected maximum effect
Skin oiliness/acne	1–6 months	1–2 years
Facial/body hair growth	3–6 months	3–5 years
Scalp hair loss	>12 months	Variable
Increased muscle mass/strength	6–12 months	2–5 years
Body fat redistribution	3–6 months	2–5 years
Cessation of menses	2–6 months	n/a
Clitoral enlargement	3–6 months	1–2 years
Vaginal atrophy	3–6 months	1–2 years
Deepened voice	3–12 months	1–2 years

Table 3.7 – Effects and expected time course of masculinizing hormones

Changes to expect	Traits that won't change
Growth of facial hair (slow process)	Height (unless starting treatment at a young age)
A lower voice	Size of hands (though feet may grow a few sizes)
Distribution of body fat from breasts, hips, and thighs to stomach	Breast growth (though they may shrink a little)
Increased strength and muscle development	
Enlargement of the clitoris	
Increased body hair	
Masculinization of facial features	
Male-pattern hairline and baldness	
Increased aggression, heightened libido	
Cessation of menstruation	(University, 2014)

Changes to expect	Traits that won't change

Table 3.8 – Things that will, and won't, change

Option	What is it?	Advantages	Disadvantages
Injectable Testosterone (e.g.testosterone cypionate or testosterone enanthate)	A medication you inject once a week or once every two weeks	It's lower cost. It's widely available	May create highs and lows in energy and mood in between doses
Testosterone Patch (e.g.Androderm)	A patch you wear every day on your back, upper arm, thigh or stomach	It's administered at a constant rate, eliminating the highs and lows in energy and mood associated with injectable testosterone	It's relatively expensive. Some people have a skin reaction to the adhesive
Testosterone Gel (e.g.Androgel, or compounded testosterone gel/cream)	A gel or cream applied to your skin at the same time each day	It's administered at a constant rate, eliminating the highs and lows in energy and mood associated with injectable testosterone	Androgel is relatively expensive. When you are in intimate contact with someone, it can be challenging to avoid exposing them to the gel
Oral Testosterone (e.g. testosterone undecanoate)	A pill you take once a day	It's administered at a constant rate, eliminating the highs and lows in energy and mood associated with injectable testosterone	Not commonly used because it is less effective at stopping monthly bleeding (Transhealth, 2015b).

Table 3.9 – Common masculinizing therapies

Name	Safety
Testosterone cypionate	Good
Testosterone enanthate	good
Testosterone	good

Table 3.10 – Popular androgens

Name	Safety and Efficacy
Goserelin	Excellent
Leuprorelin Acetate	Fair

Table 3.11 – Anti-hormones

Effect	Notes
Increased sex drive	Usually starts in 1–3 months
Monthly bleeding stops	Usually happens within 2–6 months You may still be able to get pregnant even when your monthly bleeding stops (note: it is not safe to take testosterone while pregnant) Reversible change, if you stop taking testosterone
Bigger clitoris	Usually starts in 3–6 months Reaches full size in 1–2 years Size typically ranges from 1–3cm Likely permanent, even if you stop taking testosterone
More facial and body hair	Usually starts in 3–6 months Maximum effect in 3–5 years Gradual growth of mustache and beard More, thicker and coarser hairs on abdomen, arms, chest, back and legs Likely permanent, even if you stop taking testosterone
Male pattern baldness	Usually starts in less than 12 months Hair loss at temples and along the crown of head Possibility of becoming completely bald Likely permanent, even if you stop taking testosterone You can take medications to minimize this
Oily skin and acne	Usually starts in 1–6 months Maximum effect in 1–2 years More acne. May permanently scar You can take medications to minimize this Not a permanent change if you stop taking testosterone
Increased muscle mass and strength	Usually starts in 6–12 months Maximum effect in 2–5 years This is not a permanent change if you stop taking testosterone

Effect	**Notes**
Body fat redistribution	Usually starts in 3–6 months Maximum effect in 2–5 years More abdominal fat Less fat around buttocks, hips and thighs Not a permanent change if you stop taking testosterone
Deepened voice	Usually starts in 3–12 months Maximum effect in 1–2 years While your voice may deepen, other aspects of the way you speak may not sound "manlier". You can work with a speech therapist to achieve this, if desired. Permanent change
Changes to lining of the vagina	Usually starts in 3–6 months Maximum effect in 1–2 years Thinning and drying of the lining of the vagina May make penetration uncomfortable (treatments are available)
Emotional changes	Your overall emotional state may or may not change; this varies from person to person. You may find that you have access to a narrower range of emotions or feelings. You may find that you become irritable, frustrated or angry more easily. (If you are injecting testosterone every two weeks, your emotional changes may be the result of your fluctuating testosterone level. You may want to talk to your doctor about switching to weekly injections) (Transhealth, 2015b).

Table 3.12 – The expected effects of masculinizing hormone therapy

Effect	**Notes**
Likely increased risk	Polycythemia (blood disorder) Weight gain Acne Androgenic alopecia (balding) Sleep apnoea
Possible increased risk	Elevated liver enzymes Hyperlipidemia
Possible increased risk with presence of additional risk factors	Destabilization of certain psychiatric disorders (bipolar disorder, psychotic disorders) Cardiovascular disease Hypertension (high blood pressure) Type 2 Diabetes

Effect	Notes
No increased risk or inconclusive research	Loss of bone density Breast cancer Cervical cancer Ovarian cancer Uterine cancer (Transhealth, 2015b).

Table 3.13 – The risks associated with masculinizing hormone therapy

Common therapies

Oestrogens

Option	What is it?	Advantages	Disadvantages
Oral Oestrogen (e.g. Estrace)	A pill you swallow or dissolve under your tongue each day	Less expensive	Higher cardiovascular risk for people over 40, or people with other risk factors
Oestrogen Patch (e.g. Estradot, Estraderm)	A patch you wear on your skin that gets changed twice a week	Lower cardiovascular risk for people over 40, or people with other risk factors	More expensive. Some people have a skin reaction to the adhesive in the patch
Injectable Oestrogen (e.g. estradiol valerate)	A substance you inject every two weeks	Lower cardiovascular risk for people over 40, or people with other risk factors	More expensive. Less widely available. Some people find injections to be painful. Improper injection can be dangerous (Transhealth, 2015a)

Name	Safety & Efficacy	Source
Estradiol Valerate	excellent	synthetic (plant-based ?)
Ethinylestradiol *Deprecated*	fair	synthetic

Oestrogens, conjugated *Deprecated*	fair	Live animals or synthetic

Table 3.15 – Popular Oestrogens

Testosterone Blockers

Option	What is it?	Advantages	Disadvantages
Cyproterone (e.g.Androcur)	A pill that you swallow once a day	Potent testosterone blocker	More expensive. May cause liver inflammation and depression
Finasteride (e.g.Proscar)	A pill that you put under your tongue once a day or every other day. Usually used with one of the above anti-androgen therapies	Can help stop hereditary hair loss	(Transhealth, 2015a)

Name	Safety	Efficacy	Action
Spironolactone *Deprecated*	excellent	good	DHT blocker
Finasteride	excellent	good	Type II 5-androgen receptor (AR) inhibitor
Dutasteride	excellent	excellent	Type I & II 5-AR inhibitor
Cyproterone Acetate	fair	excellent	testosterone blocker
Flutamide	fair	excellent	testosterone blocker
Bicalutamide	fair	good	testosterone blocker

Table 3.17 – Popular anti-androgens

Progesterone

Option	What is it?	Advantages	Disadvantages

Micronized Progesterone (e.g.Prometrium)	A pill you take daily	Thought to be lower risk	Not as widely available (Transhealth, 2015a)

Name	Safety	Efficacy	Source
Progesterone	excellent	highly variable	Yams or Soy Beans
Dydrogesterone	good	variable	synthetic
Medroxyprogesterone Acetate *Deprecated*	fair	variable	synthetic

Table 3.19 – Popular progesteronic drugs

GnRH Agonists

Name	Safety & Efficacy
Goserelin	excellent
Leuprorelin Acetate	fair

Table 3.20 – Popular GnRH agonists

Drugs used in Male to Female transitioning

- Cyproterone Acetate - Androcur, Cyprostat.
- Dydrogesterone - Duphaston, Duphaston HRT.
- Estradiol Valerate - Climaval, Estraderm MX, Estradiol implant, Progynova, Progynova TS, Progynova TS forte, Zumenon.
- Finasteride - Proscar.
- Flutamide - Drogenil.
- Goserelin - Zoladex, Zoladex LA.
- Leuprorelin Acetate - Prostap SR, Prostap 3.
- Minoxidil - Regaine.
- Oestrogel - Oestrogel.
- Progesterone - Cyclogest, Gestone.

These are listed in alphabetical order. Some are hormones, some are anti-androgens, some are DHT-blockers, and some are progesterones, and so they are dealt with in separate chapters.

Drugs used in Female to Male transitioning

Testosterone - Sustanon 100, Sustanon 250.

How oestrogen works

Oestrogen drug products act by regulating the transcription[8] of a limited number of genes. Oestrogens diffuse through cell membranes, distribute themselves throughout the cell, and bind to and activate the nuclear oestrogen receptor, a deoxyribonucleic acid (DNA)-binding protein which is found in oestrogen-receptive tissues. The activated oestrogen receptor binds to specific DNA sequences, or hormone response elements, which enhances the transcription of adjacent genes and in turn lead to the observed effects. Oestrogen receptors have been identified in tissues of the reproductive tract, breast, pituitary, hypothalamus, liver, and bone of women (unknown, 2004a). Oestrogens are important in the development and maintenance of the female reproductive system and secondary sex characteristics. With other hormones, such as pituitary hormones and progesterone, they cause enlargement of the breasts, through promotion of ductal growth, stromal development, and the accretion of fat. Oestrogens occur naturally in several forms. The primary source of oestrogen in normally cycling adult women is the ovarian follicle, which secretes 70–500 micrograms of estradiol daily, dependant on the phase of the menstrual cycle. This is converted primarily to estrone, which circulates in roughly equal proportion to estradiol, and to small amounts of estriol. After the menopause, most endogenous oestrogen is produced by conversion of androstenedione, secreted by the adrenal cortex, to estrone by peripheral tissues. Thus, estrone - especially in it's sulphate ester form - is the most abundant circulating oestrogen on postmenopausal women. Although circulating oestrogens exist in a dynamic equilibrium of metabolic interconversions, estradiol is the principle intercellular human oestrogen and is substantially more potent than estrone or estriol at the receptor. Oestrogens used in therapy are well absorbed through the skin, mucous membranes, and gastrointestinal tract. When applied for a local action, absorption is usually sufficient to cause systemic effects. When conjugated with aryl and alkyl groups for parenteral administration, the rate of absorption of oily preparations is slowed with a prolonged duration of action, such that a singular injection of estradiol valerate or estradiol cypionate is absorbed over several weeks. Administered oestrogens and their esters are handled within the body essentially the same as the endogenous hormones. Metabolic conversion of oestrogens occurs primarily in the liver (first pass effect), but also at local target

[8]The natural process by which a molecule of RNA is synthsized on the model of a DNA template carrying the necessary genetic information

tissue sites. Complex metabolic processes result in a dynamic equilibrium of circulating conjugated and unconjugated oestrogenic forms which are continually interconverted, especially between estrone and estradiol and between esterified and nonesterified forms. Although naturally-occurring oestrogens circulate in the blood largely bound to sex hormone-binding globulin and albumin, only unbound oestrogens enter target tissue cells. A significant proportion of the circulating oestrogen exists as sulphate conjugates, especially estrone sulphate, which serves as a circulating reservoir for the formation of more active oestrogenic species. A certain proportion of the oestrogen is excreted into the bile and then reabsorbed from the intestine. During this enterohepatic recirculation, oestrogens are desulphated and resulphated and undergo degradation through conversion to less active oestrogens (estriol and other oestrogens), oxidation to nonoestrogenic substances (catecholoestrogens, which interact with catelcholamine metabolism, especially in the central nervous system), and conjugation with glucoronic acids (which are then rapidly excreted in the urine). When given orally, naturally-occurring oestrogens and their esters are extensively metabolised (first pass effect) and circulate primarily as estrone sulphate, with smaller amounts of conjugated and unconjugated oestrogenic species. This results in limited oral potency. By contrast, synthetic oestrogens, such as ethinylestradiol and the nonsteroidal oestrogens, are degraded very slowly in the liver and other tissues, which results in their high intrinsic potency. Oestrogen drug products administered by non-oral routes (i.e. transdermally) are not subject to first-pass metabolism, but also undergo significant hepatic[9] uptake, metabolism, and enterohepatic[10] recycling (unknown, 2004a).

Natural hormones, such as the oestrogen called 17-β-estradiol (pink), travel through the bloodstream and enter cells (cyan), where they may find matching hormone receptors, such as oestrogen receptors (purple). Not all cells have a hormone's compatible receptor. The ones that do are called target cells.

Once inside a target cell, the hormone (pink) binds to a receptor (purple) - similar to a hand sliding in a glove or mitten - and forms what is known as a hormone-receptor complex between the ligand and receptor. A ligand is any molecule that binds to a specific site on a protein or other molecule. In this case, the oestrogen hormone 17-β-estradiol is the ligand, and the oestrogen receptor is the protein.

Binding turns on, or activates, a hormone receptor. Activation sets in motion cell signaling systems that trigger gene expression and lead to responses typical of a particular hormone. First, the activated receptor attaches to a specific region of the DNA[11] in the nucleus where it interacts with other activating molecules to turn on a specific gene or suite of genes. Then, the

[9] Relating to the liver

[10] Circulation of substances which are absorbed from the intestine and carried to the liver where they are secreted into the bile and again enter the intestine

[11] deoxyribonucleic acid

DNA's genetic code is copied to make a complimentary messenger RNA (mRNA) through a process called gene transcription. The mRNA moves from the nucleus to the cytoplasm, where it is transcribed by ribosomes to make the proteins (enzymes, other receptors, etc.) that directly guide cell and body responses. In the case of oestrogen hormones, these responses can include uterine growth to prepare for pregnancy, or to maintaining systems to prevent bone loss.

Its been found that a more fluid and less structured molecular process allows for related natural hormones, such as the oestrogens 17-β-oestradiol, estrone, and estriol to dock with the same receptor, such as ER-α. Likewise, a single hormone, such as 17-β-oestradiol, can bind with multiple related receptors, such as ER-α and ER-β.

Unexpectedly, other, nonhormone molecules were found to exploit the system, too.

Many, vastly different natural compounds and synthetic chemicals do bind to hormone receptors. Nonylphenols, some PolyChlorinated Biphenyls, are industrial products or chemicals (PCB's)[12], some chemicals used to make plastics (bisphenol-A), and many plant flavonoids, also known as phytoestrogens, are examples.

Generally, these, and other plant and fungal compounds, drugs, pesticides, industrial agents, and metals known to interfere with natural hormones are collectively called endocrine disrupters endocrine disruptor (ED)[13]. More is understood about how EDs interfere with receptor binding than with the other ways, or mechanisms, that these foreigners employ to disrupt endocrine-related functions. But whether the binding causes any long-term, adverse health conditions in humans is still debated (tulane.edu, 2014).

[12] PolyChlorinated Biphenyls, are industrial products or chemicals

[13] endocrine disruptor

Hormone effects in male→female

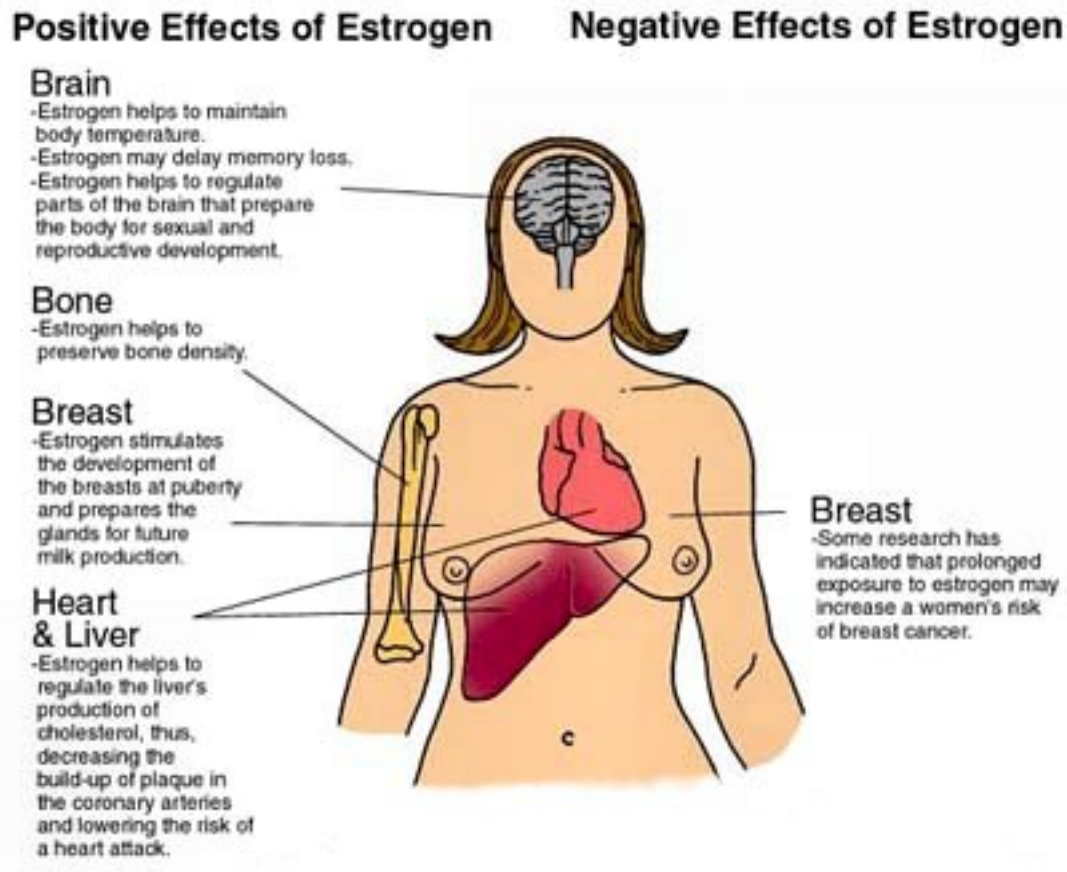

Figure 3.1 – Positive and negative effects of oestrogen

Cardiovascular

- The most significant cardiovascular risk for transgender women is the pro-thrombotic effect of oestrogens (Increased blood clotting.) This manifests most significantly as an increased risk for thromboembolic disease: deep venous thrombosis (deep venous thrombosis (DVT)[14]) and pulmonary embolism (pulmonary embolism (PE)[15]) which occurs when DVTs break off and migrate through the venous system to the lungs. It is important for any person on female hormones to immediately seek medical care if she develops pain or swelling of one leg (especially calf) as this is the predominant symptom of a DVT, or if she develops symptoms of PE - chest pain, shortness of breath, fainting, or palpitations (even without leg pain or swelling). See also Deep Vein Thrombosis.

[14] deep venous thrombosis

[15] pulmonary embolism

- In practice this becomes very important to transgender women undergoing surgery. Hormones should be withheld for a week before, and until two weeks after surgery. Also see what your surgeon says.
- DVTs occur more frequently in the first year of treatment with oestrogens. However this may represent a 'screening by treatment' of patients who may have genetic predispositions to thromboembolic disease, with those who are more likely to develop DVTs doing so early on in therapy. However, if patients have a family history of thromboembolic disease, screening for known disease may be appropriate.
- DVT risk is greater with oral rather than transdermal or injectable oestrogens.
- DVT risk also increases with age and with smoking, so many clinicians advise using the safer transdermal formulations in patients who smoke or are older than age 40.
- If screening is undertaken for known pro-thrombotic mutations such as Factor V-Leiden, antithrombin III, and protein C or S deficiency, it should be done so to increase the safety of hormonal therapy and not as a screen for who may undertake hormonal therapy. Given that the risk of warfarin treatment in a relatively young, well-informed, and otherwise healthy population is quite low and that the risk of adverse physical and psychological outcome for untreated transgender patients is high, a prothrombotic mutation is not an absolute contraindication for hormonal therapy (Levy, Crown, and Reid, 2003).
- The antiandrogen bicalutamide is associated with an increased risk of heart failure when used as monotherapy (without any other drugs). A study (Iversen et al., 2004) of prostate cancer patients also showed an increased number of deaths unrelated to cancer among patients taking 150mg/day bicalutamide. This prompted Health Canada to withdraw its approval (Borkowski, 2003) for 150mg bicalutamide as monotherapy. The increased death rate has not been observed where bicalutamide was combined with a method of reducing androgen production. The exact reasons for the heart failure and deaths have not been completely determined, however a likely cause is acute adrenal insufficiency due to the action of DHT (Rossi et al., 1998) during episodes of bicalutamide withdrawal. Because bicalutamide is extremely lipophilic[16], it is difficult to avoid periods of low serum concentration due to the uptake of bicalutamide into fat cells (unknown, 2015e).

[16] the ability to dissolve or attach to lipids

Hair

- Current facial hair is only slightly affected (some reduction in density, coverage, and slower growth) by anti-androgens. Those who are less than a decade past puberty and/or whose ethnicity generally lacks a significant amount of facial hair will have better results with anti-androgens. Those taking anti-androgens will have better results with electrolysis/laser hair removal than those who are not. If one is still in their teens or early twenties, there will be prevention of new facial hairs from developing if testosterone levels are within the female range.
- Body hair (chest, periareolar, shoulders, back, abdomen, rear, thighs, tops of hands, tops of feet) will, over time, turn from terminal hairs[17] to vellus hairs[18]. Hair on the arms, perianal, and perineal will reduce but may not turn to vellus hair on the latter two regions (some natal females also have some hair in these areas). Underarm hair will slightly change in texture and length, pubic hair becomes more typically female in pattern. Lower leg hair becomes less dense in concentration. All depend upon genetics.
- Head hair may slightly change in texture, curl, and colour (new hairs that is, not hair that has already formed and reached the surface prior to HRT), this is especially likely with hair growth from previously bald areas.
- Eyebrow hair becomes less "bushy" or scattered (unknown, 2015e).

Urogynaecological effects

- Transgender women report a sometimes significant reduction in libido all depending upon the dosage of anti-androgens. A small number of post-operative transsexual women may take small amounts of testosterone to boost the libido. Many pre-operative transsexual women simply wait until after sex-reassignment surgery to begin an active sex life (due to how they feel towards their genitals and/or, for heterosexual or bisexual transsexual women, an aversion to anal sex) and for post-operative transsexual women how satisfied they are with the results. Raising oestrogen dosage or adding a progestogen has also raised the libido of some transwomen.
- Spontaneous and morning erections decrease in frequency significantly, however some who have had an orchiectomy still experience morning erections. Voluntary erections can be maintained since the brain is the most important sex organ, a developed repertoire of fantasies and good visualization is a must. It also depends on how one views their own genitals (disgust, strong aversion to, tolerable, etc.).

[17] normal hairs

[18] very tiny, blonde "baby" hairs

- Testicular volume is reduced by about 25% with typical dosages and as much as 50% in higher dosages, especially after a year of HRT. This is in response to the decrease in Leydig cells[19], Sertoli cells[20], and interstitial tissue, which produce both sperm and testosterone. When testosterone is dramatically reduced spermatogenesis[21] is halted almost completely, when the cells that are involved in these processes go unused they atrophy[22].
- The prostate shrinks
- The bladder shrinks
- The line that runs down the underside of the penis and down the middle of the scrotum, the peno-scrotal raphe (where the urogenital folds fused early in the womb), will darken.
- Minor water retention is likely (unknown, 2015e).

Childbearing

- Childbearing, as experienced by cisgender[23] women, is impossible with today's technology. Pre-operative sperm banking can be done, however, allowing artificial insemination to be used to produce genetic offspring with someone else at a later date. See also Sperm banking. Medical advances in the near future may one day make this possible by using a donor uterus long enough to carry a child to term as anti-rejection drugs do not seem to affect the foetus. The DNA in a donated ovum can be removed and replaced with the DNA of the receiver. Further in the future stem cell biotechnology may also make this possible, with no need for anti-rejection drugs (unknown, 2015e). See also Male pregnancy.

[19]Leydig cells, also known as interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicle. They can secrete testosterone and are often closely related to nerves

[20]A Sertoli cell is a kind of sustentacular cell, and is a 'nurse' cell of the testes which is part of a seminiferous tubule. It is activated by follicle-stimulating hormone, and has FSH-receptor on its membranes

[21]Spermatogenesis is the process by which male spermatogonia develop into mature spermatozoa. Spermatozoa are the mature male gametes in many sexually reproducing organisms. Thus, spermatogenesis is the male version of gametogenesis. In mammals it occurs in the male testes and epididymis in a stepwise fashion, and for humans takes approximately 64 days

[22]shrink

[23]Denoting or relating to a person whose self-identity conforms with the gender that corresponds to their biological sex; not transgender (unknown, 2015a)

Bone

- Both oestrogens and androgens are necessary in both biological males and females for healthy bone. (Young healthy women produce about 10 mg of testosterone monthly. Higher bone mineral density in males is associated with higher serum oestrogen.)
- Bone is not static. It is constantly being reabsorbed and created. Osteoporosis results when bone formation occurs at a rate less than bone reabsorption.
- Oestrogen is the predominant sex hormone that slows bone loss (even in men.)
- Both oestrogen and testosterone help stimulate bone formation (T, especially at puberty.)
- The hips will rotate slightly forward due to changes in the tendons so hip discomfort is not uncommon (unknown, 2015e).

Skin

- The uppermost layer of skin, the *stratum corneum*, becomes thinner and therefore more translucent and pinkish (spider veins may appear or be more noticeable), less collagen, more suscepitable to tearing and irritation from scratching or shaving, increased tactile sensation, and slightly lighter in colour due to a slight decrease in melanin (pigment).
- Skin becomes softer
- Sebaceous gland activity (which is triggered by androgens) lessens which lowers the amount of sebum (oil) production on the skin and scalp, consequently the skin becomes less prone to the formation of acne due to the lesser quantity of oil that is produced. Dry skin becomes a problem and lotions and oils may be necessary.
- The skin's pores become smaller due to the low quantities of sebum produced.
- Body odour (skin, sweat, and urine) will become less "metallic", "sharp", or "acrid" and more "sweet" and "musky".
- Many apocrine glands (type of sweat glands) become inactive and body odour decreases. Sebum also contributes to body odour, the production of which is reduced by anti-androgens (as described above).
- More subcutaneous[24] adipose[25] tissue accumulates. This gives a more puffy/softer appearance. Consequently dimpling, or cellulite, will be more apparent on the thighs and buttocks due to this along with the thinness of the skin.
- Susceptibility to sunburn increases possibly due to the thinner skin and/or less skin pigment.

[24] under the skin

[25] fat

- Because of the increase in adipose tissue in the hips, thighs, and rear, stretch marks (*striae distensae*) may appear on the skin in these areas (unknown, 2015e). See also Stretch marks.

Eye changes

- The lens of the eyes changes in curvature.
- Due to decreased androgens, the meibomian glands[26] produce less oil (oil that makes up the lipid layer of tear film which prevents the evaporation of the watery layer beneath) and a tendency for dry eyes may be a problem (unknown, 2015e).

Senses

- Sensitivity to male body odour(s) (including male pheromones) may be positively correlated with elevated oestrogen levels. Overall, olefactory senses may increase. Progestogens, however, often lowers the sensitivity to male pheromones (unknown, 2015e).

Breast development

- Breast, nipple, and areolar development takes 4–6 years to complete depending upon genetics, and sometimes as long as 10 years. It is normal for there to be a "stall" in breast growth during feminization, or for the size of one breast to be a little bigger than the other. Transwomen who undergo HRT often experience breast development which is below the comparable natal female norm (many seek breast augmentation); it is rare for a HRT patient to opt for breast reduction. The size of the rib cage and shoulder width also play a role in the perceivable "size" of the breasts; both characteristics are usually smaller than in natal females, i.e., if a natal female and a transsexual female were to have the same cup size, the transsexual female's breasts would most likely appear smaller. Thus when a transsexual female opts to have breast augmentation, the implants used, are on the average, larger than those commonly used by natal females.
- The nipples will become more sensitive to stimulation (unknown, 2015e).

[26] also known as tarsal, palpebral, or tarsoconjunctival glands. A type of sebaceous gland on the upper and lower eyelids that open at the edges of the lids

Fat distribution

- Fat distribution in the body slowly changes over months and years. The body will now tend to accumulate new adipose tissue in a typically female pattern. This includes the hips, thighs, rear, pubis, upper arms, and breasts. The body will now tend to use/burn the old adipose tissue in the waist making the waist appear smaller as well as on the shoulders and back.
- Subcutaneous adipose tissue increases in the face (cheeks and lips) making the face appear puffier, appears to "round out" the face, and the face appears less "drawn" or "hollow" with slightly less emphasis on the jaw due to the lower portion of the cheeks having filled in (unknown, 2015e).

Gastrointestinal

- Oestrogens may predispose to gallbladder disease - especially in older and obese people.
- Oestrogens (especially oral forms) may cause elevations in transaminases (liver function tests) indicating liver toxicity. LFTs should therefore be periodically monitored in transgender women (unknown, 2015e).

Neurological/Psychiatric

- Mood changes can occur - including the development of depression, particularly in those who take progestins.
- Migraines can be made worse or unmasked by oestrogen therapy
- Oestrogens can induce the development of prolactinomas, which is why prolactin levels should periodically be monitored in transgender women. Milk discharge from the nipples can be a sign of elevated prolactin levels. If a prolactinoma becomes large enough, it can cause visual changes (especially decreased peripheral vision), headaches, mood changes, depression, dizziness, nausea, vomiting, and symptoms of pituitary failure like hypothyroidism.
- An article from 2006 indicates that cross-hormone therapy in transwomen may result in a reduction in brain volume towards female proportions (Pol et al., 2006) (unknown, 2015e).

Metabolic

- Oestrogen therapy causes decreased insulin sensitivity which places transgender women at increased risk of developing type II diabetes.

- One's metabolism slows down and one tends to gain weight, lose energy, need more sleep, and become cold more easily. Due to androgen deprivation a loss of muscle tone, a slower metabolism, and physical weakness becomes more evident. Building muscle will take twice as much work than before. However, the addition of a progestogen may increase energy although an increase in appetite may be seen as well (unknown, 2015e).

Hormone effects in female→male

Cardiovascular

- In biological men, testosterone levels that are either significantly above or below normal are associated with increase cardiovascular risk. This may be causative or simply a correlation.
- A single retrospective study in the medical literature of 293 transmen treated with testosterone (range of 2 months to 41 years) by the Amsterdam Gender Dysphoria Clinic from 1975 to 1994 showed no increase in cardiovascular mortality or morbidity when compared with the general female Dutch population. (As with all scientific studies, this does not conclusively prove that no causal link exists. A small to moderate detrimental effect remains a possibility, though a very large effect is more unlikely.)
- Androgen therapy does adversely affect the blood lipid profile by causing decreases in High-density lipoprotein (HDL) (good) cholesterol, increases in LDL (bad) cholesterol, and increases in triglycerides.
- Androgen therapy redistributes the fat toward abdominal obesity, which is associated with increased cardiovascular risk rather than fat carried on the buttocks and hips.
- Androgen therapy can cause weight gain and decreased insulin sensitivity (perhaps worsening a predisposition to develop Type II diabetes.)
- Androgen therapy effects are not all negative, however. Acutely it causes dilation of the coronary arteries, and in men with testosterone levels within the normal physiological range, higher levels are actually associated with a slight decrease in cardiovascular disease.
- Supra-physiological levels of androgens (generally due to abuse) are associated with significantly increased risks of strokes and heart attacks (even in the young.) More is not better!
- Cardiovascular risk factors are more than additive. (If high blood pressure is worth 10 and smoking is worth 10, together they are worth more than 20.) So for transgendered men, the addition of risk with androgen therapy makes improving modifiable risk factors more important.

- The most important modifiable risk factor for many men is smoking (unknown, 2012).

Hair

- The action of testosterone on hair follicles is mainly due to the more potent androgen, dihydrotestosterone, DHT.
- With androgen therapy, genetics primarily determines how much hair will develop (and where) as well as whether male pattern baldness will develop.
- Testosterone is converted (within the cells of the hair follicle's dermal papilla) by 5-alpha reductase to DHT. There are two forms of this enzyme: type 1 and 2. However, type 2 is the form that is important to the development of male pattern baldness. Male pseudohermaphrodites with congenital deficiency of type 2 5-alpha reductase (but functional Type 1) never develop male pattern baldness.
- Propecia (Finasteride) and Avodart (Dutasteride) are Type-2, 5-a-Reductase inhibitors that work by blocking the conversion of testosterone to DHT. While they will not make facial hair growth that has occurred regress, they may slow or prevent further development of new facial hair. Finasteride is sold as 5mg tablets as Proscar which is used to treat prostate enlargement and Propecia as 1 mg tablet to treat baldness. The cost of Propecia per mg is significantly higher than Proscar so some patients split tablets into quarters. At the 1-1.25mg/day dose it may also decrease libido.
- Rogaine (Minoxidil) available without a prescription in the US) is a topical preparation of a potent blood pressure medicine. It is sold as 2% and 5% solutions. The 5% solution is not recommended for use by women because it may cause the adverse effect of unwanted facial hair growth in a small percentage of women. It may also cause skin irritation and itching. One ml is applied twice daily to the scalp (predominantly in the areas where hair loss is greatest.) It may take several months to show effects and may cause a slight paradoxical[27] worsening of hair loss initially (that does eventually recover.)

With either minoxidil or finasteride the beneficial effect will be lost within months upon ceasing use of product. With either, best results occur when they are started before significant hair loss has occurred (unknown, 2012).

Gynaecological effects

- Menses should cease within 5 months of testosterone therapy (often sooner.) If bleeding continues past 5 months, transmen must see a gynaecologist.

[27] not being the normal or usual kind

- Clitoromegaly occurs, and frequently reaches its apex within 2–3 years of therapy. Sizes generally range from 3–8 cm with 4–5 cm being about average. This is genetically determined, but some physicians advocate topical clitoral testosterone as an adjunct to growth before metaidioplasty. However, this testosterone is absorbed and should be calculated into your total regimen.
- After long-term androgen therapy, ovaries may develop polycystic ovary syndrome (PCOS) morphology. (In both PCOS and transgender men there is an up-regulation of testosterone receptors in the ovaries.)
- Untreated PCOS is associated with a possibly increased risk of endometrial cancer as well as decreased fertility.
- It is unknown whether the risk of ovarian cancer is increased, decreased or unchanged in transgender men compared to women. It is unlikely to be determined in the near future because ovarian cancer is a relatively rare disease and the population of transgender men is too small to do the appropriate study. However, it has been recommended by some physicians that transgender men have an oophorectomy within 2–5 years of starting androgen therapy due to the possible increased risk. (Note: Testosterone dose can frequently be decreased after oophorectomy.)
- The risk of endometrial cancer is similarly unknown. However, a high prevalence of endometrial hyperplasia[28] has been noted in a small study of transgender men undergoing hysterectomy (Futterweit and Deligdisch, 1986).

Frequently the first sign of endometrial cancer is bleeding in post-menopausal women. Transgender men who have any bleeding after the cessation of menses with androgen therapy should have an endometrial biopsy (and possibly an ultrasound) done to rule-out endometrial cancer.

- Some sources recommend endometrial ultrasounds every two years. Testosterone usually causes atrophy of the endometrium. Any transgender man with an endometrium that is not thinned on ultrasound should have a biopsy to evaluate for endometrial cancer and possibly use progesterone to cause sloughing of the endometrium. Vaginal bleeding from progesterone may be emotionally uncomfortable for a transman, but it is preferable to developing endometrial cancer.
- Until recently, any adult with a uterus/cervix was advised to have a Pap smear yearly. This interval might be increased to every 2–3 years for certain people on the advice of a gynaecologist. However, recent research has linked cervical cancer to a sexually transmitted virus; transmen who have never had vaginal sex may not be at risk. However, since the long-term effects of testosterone on cervical tissues are not well understood, Pap smears may be considered a general precaution.

[28] This is an abnormal proliferation of the endometrium (ie greater than the normal proliferation that occurs during the menstrual cycle). It is a risk factor for the development of endometrial carcinoma (Tidy, 2014)

- Some transgender men report a decrease in breast size with androgen therapy. However, no morphological changes were found when this was studied and likely it is due to loss of fat in the breasts.
- Androgen therapy (and suppression of oestrogen production) may cause vaginal atrophy and dryness, which may result in dyspareunia (painful vaginal intercourse.) This can be alleviated with topical oestrogen cream.
- Most transgender men report a significantly increased libido. Some report that this decreases somewhat after several years on testosterone. (Natural testosterone levels peak in women just before ovulation which may account for the mid-cycle increase in libido many women experience.) (unknown, 2012)

Childbearing

- As the age at which transgender people begin therapy decreases, retention of reproductive potential becomes more important.
- If a transgender man has not undergone hysterectomy and oophorectomy, he may regain fertility on cessation of testosterone. With the ovarian changes of long-term androgen therapy, however it may require months of cessation of testosterone and possibly assistive reproductive technology to become pregnant. Testosterone must be withheld for the duration of pregnancy.
- If a transgender man is planning on having a hysterectomy/oophorectomy, future reproduction may still be preserved by -
  - ⋆ **Oocyte banking** hormonal stimulation to 'hyper-ovulate' with transvaginal oocyte harvest for freezing. Very poor survival of banked oocytes.
  - ⋆ **Embryo banking** oocyte harvest as above with immediate fertilization and banking of the embryo. Much better survival, but the sperm donor must be chosen before oophorectomy.
  - ⋆ **Ovarian tissue banking** probably the best option. Ovarian tissue is frozen after oophorectomy. Even after long term androgen therapy, ovaries usually retain usable follicles. Eventual use of frozen ovaries will require replantation into the transgender man for stimulation and harvest, but may eventually be possible in a lab as techniques for tissue culture improve (unknown, 2012).

Bone

- Both oestrogens and androgens are necessary in both biological males and females for healthy bone. (Young healthy women produce about 10 mg of testosterone monthly. Higher bone mineral density in males is associated with higher serum oestrogen.)

- Bone is not static. It is constantly being reabsorbed and created. Osteoporosis results when bone formation occurs at a rate less than bone reabsorption.
- Oestrogen is the predominant sex hormone that slows bone loss (even in men.)
- Both oestrogen and testosterone help stimulate bone formation (T, especially at puberty.)
- Testosterone may cause an increase in cortical bone thickness in transgender men (however this does not necessarily translate to a greater mechanical stability.)
- Transgender men who have been oophorectomized must continue androgen therapy to avoid premature osteoporosis. Oestrogen supplementation is theoretically not usually necessary, as some of the injected testosterone will be aromatized into oestrogen sufficient to maintain bone (as it does in biological men.) However, a single small study of transmen after oophorectomy demonstrated that androgens alone may be insufficient to retard bone loss (van Kesteren et al., 1998). It is likely the case that pre-oophorectomy, residual oestrogen production is protective. However, after oophorectomy, some transmen may have insufficient oestrogen to retard bone loss.
- Some physicians advocate a Dexa (bone density) scan at the time of oophorectomy and every year or two thereafter to diagnose osteoporosis before it becomes severe enough to be symptomatic. This is important because treatment of osteoporosis is most effective if done early.
- Daily calcium supplementation and possibly Vitamin D is probably a good idea for most transgender men, but it is even more important after removal of the ovaries (unknown, 2012).

Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is a condition where the walls of the throat relax and narrow during sleep, interrupting normal breathing and you have many periods when your breathing stops for 10 seconds or more whilst you're asleep. You wake up briefly after each episode of stopped breathing to start breathing again. You do not usually remember the times you briefly wake up, but you have a disturbed night's sleep. As a result, you feel sleepy during the day. A typical person with this condition is overweight, male, and middle-aged, and snores loudly. However, it can affect anyone.

- OSA may be worsened or unmasked by androgen therapy.
- Risk is greater in transgender men who are obese, smoke, or have COPD (Chronic Obstructive Pulmonary Disease.)
- Untreated OSA may have significant adverse effects on the heart, blood pressure, mood, and may cause headaches and worsen seizure disorders.

- Symptoms of OSA are noisy sleeping (snoring,) excessive daytime sleepiness, morning headache, personality changes, and problems with judgment, memory, and attention (unknown, 2012).

Polycythemia

Polycythemia is a condition that results in an increased level of circulating red blood cells in the bloodstream. People with polycythemia have an increase in haematocrit, haemoglobin, or red blood cell count above the normal limits (Nabili, 2014).

- Increased red blood cell mass usually from overproduction by the bone marrow.
- Testosterone (frequently in large doses) was previously used to treat anaemia from bone marrow failure.
- A transgender man's haematocrit (the percentage of whole blood made up of red blood cells) should be judged against normal age adjusted values for men.
- Therapy is via phlebotomy (periodic therapeutic blood draws similar to blood donation.)
- Tendency to become polycythemic worsens with age.
- Worse with injected testosterone (especially with longer intervals between doses) than with oral, transdermal, or Testopel. (Increase in RBCs occurs with the very high peaks from injection. So decreasing dose and interval to 7–10 days instead of 14 may help.)
- Severe polycythemia predisposes to both venous and arterial thrombosis (blood clots) such as: deep venous thrombosis, pulmonary embolism, heart attack, and stroke. See also Deep Vein Thrombosis, and Cardiovascular.
- Aspirin may decrease the risk (unknown, 2012).

Skin

- Increased activity of oil and sweat glands.
- Change in body odour less sweet and musky, more metallic and acrid.
- If severe odour is a problem, an antibacterial soap like chlorhexidine may be used in the armpits when showering. After 1–2 weeks of daily use, a noticeable decrease in odour should occur.
- **Acne** - generally worse the first few years of testosterone therapy (mimicking a second puberty.) Can be treated with standard acne therapy. Initial treatment is with increased cleansing (at least twice daily) with an anti-acne or oil reducing scrub. If this doesnt work, additional therapy may be prescribed by a physician.
- Some physicians see acne as a contraindication to increasing testosterone dose (unknown, 2012).

Gastrointestinal

- There is a risk of liver damage and liver cancer with all testosterone formulations, but this is minimal with all forms except oral or unless very high levels are administered. However, as with any drug that carries even a small risk of liver damage, liver function tests (or at least Alanine Transaminase (ALT)) should be periodically monitored (unknown, 2012). Maybe have Aspartate Transaminase (AST) tested as well. See also Alanine aminotransferase - ALT, and also Aspartate aminotransferase - AST

Neurological/Psychiatric

- **Headaches** - Pre-existing migraine headaches can be significantly worsened with androgen therapy. Headaches can also become problematic in men without prior headache disorders.
- **Epilepsy** - some seizure disorders are androgen-dependent. These may be worsened or (very rarely) unmasked with androgen therapy.
- Sleep deprivation worsens almost all seizure disorders, so concurrent obstructive sleep apnoea caused or worsened by androgen therapy may also be responsible.
- Some transgender men report mood swings, increased anger, and increased aggressiveness after starting androgen therapy (similarly to the effects reported with body builders who abuse androgens.) This is much less severe however than the "roid rage" experienced by body-builders because with transgender men significantly supraphysiologic levels are not present.
- Many transgender men, however, report improved mood, decreased emotional lability, and a lessening of anger and aggression. Likely this is not a physiologic effect but rather the alleviation of emotional distress from long-standing gender dysphoria.
- An article from 2006 indicates that cross-hormone therapy in transmen may result in an increase in brain volume towards male proportions (Pol et al., 2006) (unknown, 2012).

Metabolic

- Testosterone increases body weight (and increases appetite.) The form that this weight gain will take depends on diet and exercise as well as genetic factors. Since testosterone has anabolic effects, gain of lean muscle mass will be easier than it previously was for transgender men. Moderate amounts of exercise will cause greater gains and will ameliorate some of the adverse effects of testosterone.
- Many transgender men report an increased energy level, decreased need for sleep, and increased alertness after testosterone therapy.

- In biological men, abnormally high or low levels of testosterone are both associated with insulin resistance (which eventually can result in Type II diabetes.) So mid-normal levels of testosterone are the target for androgen therapy.
- In women, increased levels of either oestrogen or androgens are associated with decreased insulin sensitivity (which may predispose to diabetes.) In a study of transgender males and females, decreased insulin sensitivity was found in both populations after four months of hormonal treatment (Polderman et al., 1994) (unknown, 2012).

Desired characteristic	**Effects of hormone treatment**	**Possible or additional treatments**
Female type skull shape and facial features	None	Feminisation of jaw, brow ridges and skull possible via surgery
Softer, clearer skin with no acne or spots	Considerable improvement	Deep chemical skin peel
Smaller teeth	None	Dental surgery to improve teeth
Smaller nose	None	Rhinoplasty surgery
Smaller hands and feet	None	None
Reduce height	None	None
Broader pelvis	None	None
Stop facial beard hair growth	Little or no effect	Electrolysis and laser treatment
Thick female type scalp hair and forehead hairline	Hair loss ceases, slight reversal of balding	Wig, hair implants, some medications may help
Develop female pubic hair pattern. Hairless trunk and limbs	Substantial improvement after prolonged treatment	Electrolysis and laser treatment
Higher pitched feminine voice	None	Voice training, voice change surgery
Reduction of "Adams Apple"	None	"Tracheal Shave" (thyroid cartilage reduction) surgery
Slimmer neck	Little effect not ascribable to dieting	None
Breast development	Variable from slight to substantial breast development [29]	Mammoplasty (breast implants)

[29] Breast development will vary considerably depending on the individuals genetic make-up and the time from puberty. Early hormone treatment (by age 18) will typically result in breasts about one bra-cup size less than the girl's mother and sisters.

Desired characteristic	**Effects of hormone treatment**	**Possible or additional treatments**
Female type subcutaneous fat deposits (particularly thickening of hips, buttocks & thighs) and body shape	Variable, slight to substantial fat redistribution after prolonged treatment	Fat transfer, implants
Reduced weight	Weight increase [30]	Liposuction, diet and exercise
Small waist	May actually increase unless supported by dieting and exercise	Liposuction, lower rib removal, diet and exercise
Reduced muscular development	Some reduction	None
Reduce size of penis and testes	Moderate to significant reduction (not necessarily good if SRS is planned)	Surgery
Positive mental attitude	Depression may occur	Therapy, support of friends and family, anti-depressants
Menstrual cycle	premenstrual syndrome (PMS) and Hot Flushes only [31]	None (Richards, 2013).

Table 3.21 – The effects of female hormone treatment begun after male puberty has completed (i.e. after about age 17)

[30] Oestrogen hormones help to deposit fat. On a male type skeleton this can result in weight gain and a larger rather than reduced waist line. Sensible dieting and suitable exercising (e.g. aerobics, not power lifting!) is essential for developing a female type figure and body shape.

[31] Periods and menstruation are impossible even for a post-SRS transwomen. However most transwomen will suffer from Pre Menstrual Syndrome (PMS) and Hot Flushes if they choose to stop taking oestrogen for 1 week in every 4 week period. These unpleasant effects can be avoided by maintaining a continuous hormone dosage (Richards, 2013)

Chapter 4

Endocrinology

An overview of the endocrine system

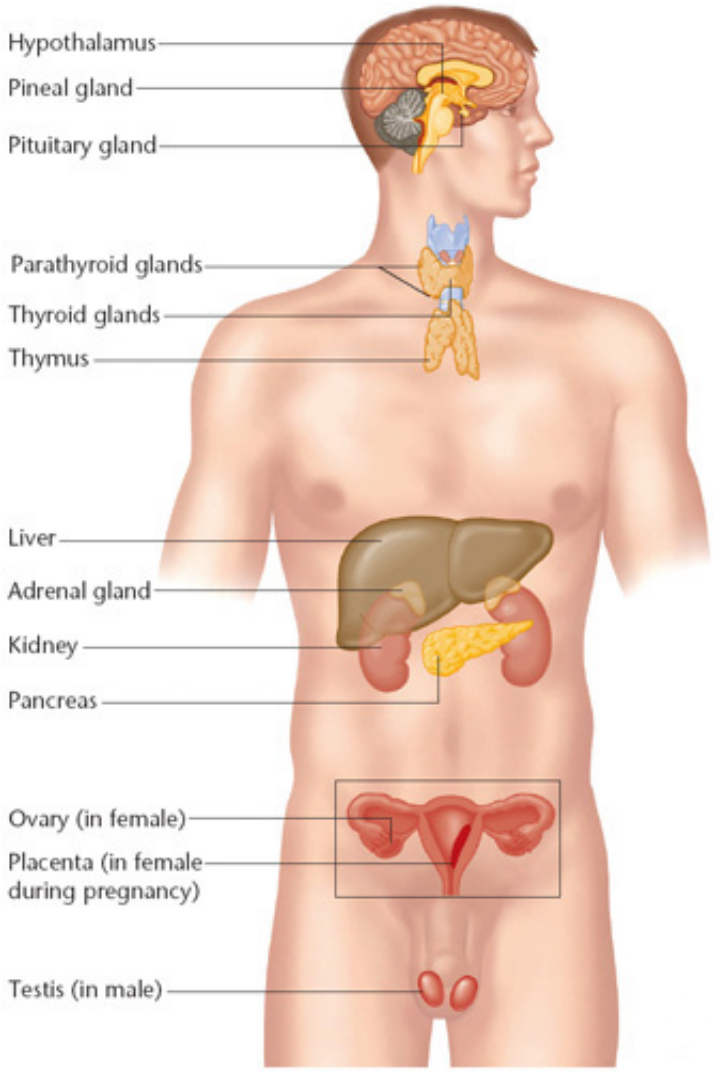

Figure 4.1 – The human body, showing all the endocrine sites

The endocrine system is a group of ductless glands that regulate the body processes by their secretion of chemical substances called hormones, which are carried to specific target organs and tissues by the bloodstream. Hormones are necessary for normal growth and development, for reproduction, and for homoeostasis[32]. They stimulate or inhibit various biochemical processes by combining with specific receptors on the membranes of target organs. Thus, although a hormone circulates throughout the body in the bloodstream, it does not affect every cell with which it comes into contact but only those cells that contain a specific receptor site. The major endocrine glands in the human body are the hypothalamus, the pituitary, the thyroid, the Islets of Langerhans in the pancreas (these produce insulin), the adrenals, the parathyroids, the ovaries and the testes. Almost every organ or tissue of the body (including the intestinal tract, the stomach, and the heart) has been found to be involved in endocrine secretions (unknown, 2014d). It has also been found that the ovaries produce small amounts of testosterone, and the testicles produce small amounts of oestrogen (unknown, 2014g).

Hormonal secretions are generally regulated by negative-feedback loops. In the simple loops, the concentration of another hormone or a metabolite (i.e. calcium) influences sensitive regulators in an endocrine gland to inhibit or stimulate hormonal secretions in the target organ. The complex loops involve a mechanism called the hypothalamo-pituitary-target-organ axis, in which the hypothalamus secretes releasing hormones that stimulate the pituitary to secrete a target hormone, which then enters the circulation and binds with the receptors of the target organ (unknown, 2014d). The hypothalamus produces gonadotropin-releasing hormone GnRH[33], which stimulates the anterior pituitary gland to synthesize and release luteinizing hormone luteinizing hormone (LH)[34]. To a lesser degree, GnRH also triggers the synthesis and release of follicle stimulating hormone follicle stimulating hormone (FSH)[35]. Subsequently, LH and FSH stimulate the gonads (ovaries in females, testes in males) to synthesize and release hormones that cause differentiation of the body tissue into female or male form: oestrogen, progesterone, and testosterone. A small quantity of testosterone is also produced by the adrenal gland. Proportionally, females have more oestrogen and progesterone than males; males have more testosterone (J. V. Turner, Agatonovic-Kustrin, and Glass, 2007).

Two body systems control all physiologic processes in the human body via a process of messaging — the **nervous system** with its electrical point-to-point control via nerves, and our system of interest — the **endocrine system**.

[32] Automatic self-regulation to maintain the normal or standard state of the body under variations in the environment i.e. the body producing sweat to help cool it down on a hot day

[33] gonadotropin-releasing hormone

[34] luteinizing hormone

[35] follicle stimulating hormone

In addition to gender based characteristics, hormones control and regulate a wide range of bodily activity necessary for our good health.

The major endocrine glands

Pituitary Gland

The pituitary gland is a pea-sized structure located at the base of the brain and consists of two lobes. The pituitary gland is often portrayed as the master gland of the body. This reference is justified in the sense that the anterior and posterior pituitary lobes secrete a whole shed-load of hormones that collectively influence all cells and affect virtually all physiologic processes.

But the power behind these processes is the brain's hypothalamus, crucial in the regulation of body temperature, certain metabolic processes, and other autonomic activities. The hypothalamus and its releasing and inhibiting hormones directly influences the anterior pituitary hormones.

The following table summarizes the major hormones synthesized and secreted by the pituitary gland. Contained within the table are the gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

Hormone	Target organs	Physiologic Effects
Anterior Pituitary		
Adrenocorticotropic hormone	Adrenal gland (cortex)	Stimulates secretion of glucocorticoids
Follicle stimulating hormone (FSH)	Ovary and testis	Control of reproductive function
Growth hormone	Liver, adipose tissue	Indirectly promotes growth, control of protein, lipid and carbohydrate metabolism
Luteinizing hormone (LH)	Ovary and testis	Control of reproductive function
Prolactin	Mammary gland	Milk production
Thyroid-stimulating hormone	Thyroid gland	Stimulates secretion of thyroid hormones
Posterior Pituitary		
Antidiuretic hormone	Kidney	Conservation of body water
Oxytocin	Ovary and testis	Stimulates milk ejection and uterine contractions (TGC, 2015b)

Table 4.1 – The major hormones synthesized and secreted by the pituitary gland

Parathyroid Gland

The parathyroid gland is any of four small endocrine glands lying near the thyroid and producing hormones that regulate calcium and phosphorus metabolism. The parathyroid glands affect skeletal development.

Thyroid Gland

The thyroid gland is located in the neck, close to the Adam's apple. This gland has an influence upon metabolism, growth and maintenance of body tissues, and aspects of reproduction in the genetic female.

Thymus Gland

The thymus gland is located in the upper chest under the breastbone. This gland is the central control organ for the immune system. When it is functioning properly, the thymus gland acts like a thermostat to provide the right balance of immunity. It turns up to help the body fight infection or tumour and down to prevent autoimmune disease.

Adrenal Glands

The adrenal glands are two in number and are located on the top of each kidney. These glands are responsible for glucose metabolism, water and electrolyte balance, and produce small amounts of the sex hormones, oestrogen and testosterone, in both genders.

Pancreas Gland

The pancreas is a long, tapered gland which lies across and behind the stomach. This gland secretes digestive juices which break down fats, carbohydrates, proteins and acids. Some cells in the pancreas secrete hormones which regulate the level of glucose in the blood.

Ovarian Glands

The ovary (plural - ovaries) is either of two organs found in the female reproductive tract in which ova form and which is responsible for the production of the hormones, oestrogen and progesterone. These hormones cause the genetic female's secondary sexual characteristics to develop. The ovaries are responsible for ova (plural - ovum) production, the female reproductive cell or egg.

Testicular Glands

The testis (also, testicle; plural - testes, testicles) is either of two primary male reproductive organs that produce both sperm cells and the male's major sex hormone, testosterone. The testes are located in a sac called the scrotum, which is located below the penis (TGC, 2015b).

The Biochemistry of Sex Hormones

All steroids in the body are formed from acetate, which is a 2-carbon compound. Steroids display a characteristic four-ring system. This steroid carbon skeleton, often referred to as the *steroid nucleus*, is found in all the steroids described here.

The first step in its conversion to a variety of steroids is the formation of **cholesterol**, which is a 27-carbon steroid. The formation of cholesterol occurs through a complex, eleven step series of reactions. Cholesterol is by far the most common steroid. It is found in most animal tissue, with the greatest amount in the tissues of the central nervous system, that being the brain and spinal cord.

With any introduction to the essential nature and importance of cholesterol, it should be noted that the common concern with cholesterol is derived from its excess, whereby it contributes to vascular and heart disease. Cholesterol, in of itself, is absolutely not unhealthy, but essential to life.

The Degradation of Cholesterol

In the next phase, the cholesterol degrades, and in the ensuing process, creates all sex steroids (sex hormones) and corticosteroids.

The variety of steroids created occur from a stepwise degradation of cholesterol: Pregnenolone, progesterone, 17-hydroxypregnenolone, 17-hydroxyprogesterone, and corticosteroids, having 21 carbon atoms, followed by androgens (testosterone and Androstenedione), having 19 carbon atoms, and natural oestrogens having 18 carbon atoms.

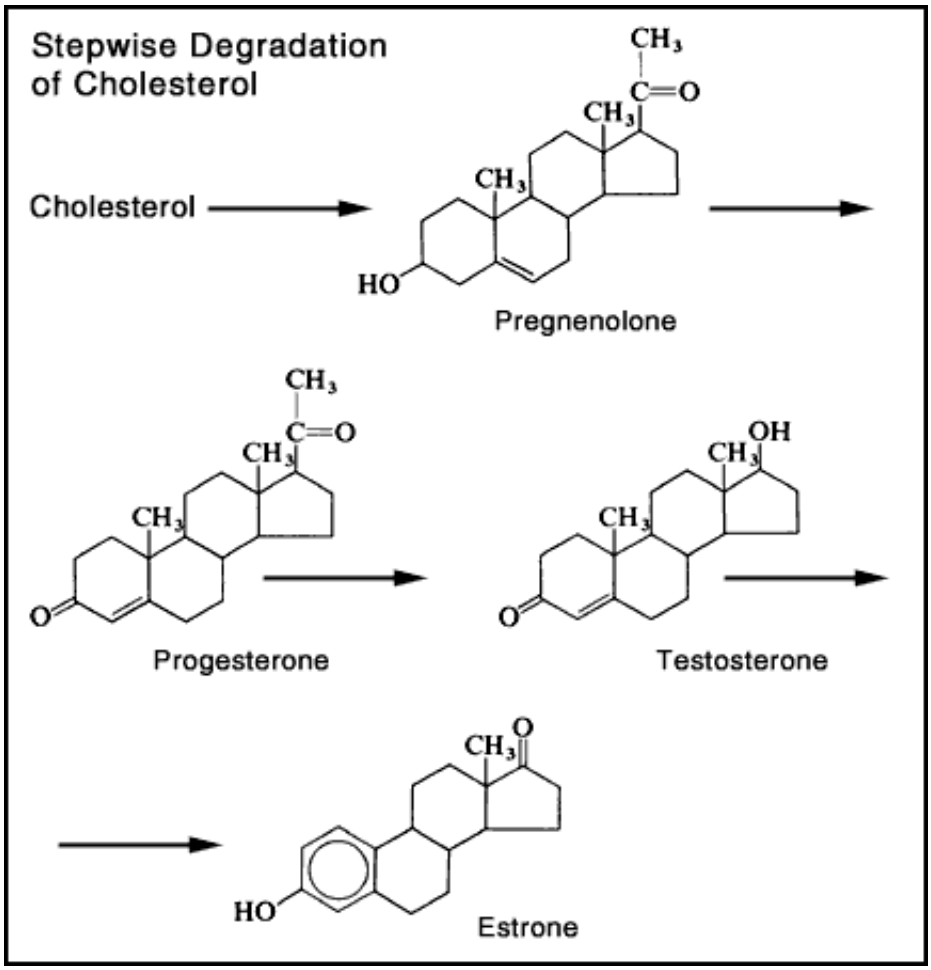

Figure 4.2 – The cholesterol degradation

Pregnenolone plays a vital role in the production of all other human sex hormones. It is converted to androgens (male sex hormones), progestins (hormones involved in pregnancy), and oestrogens (female sex hormones).

All three of these hormones are in the bloodstream of males and females at all times; the differing concentrations of testosterone, progesterone, and oestrogen contribute to the gender characteristics specific to males and females. These hormones are largely produced by the ovaries or the testes, as well as the adrenal glands of both sexes. As mentioned earlier, the pituitary controls the production of these hormones.

Progesterone is the most important pregnancy hormone. It is produced in the ovaries by the enzymatic oxidation of cholesterol and is responsible for both the successful initiation of a pregnancy and the successful completion of pregnancy. Its initial role is to prepare the uterine mucosa (lining) for reception of a fertilized ovum. When the fertilized ovum is successfully attached to the uterine wall, the progesterone continues to be produced, aiding in the successful development of the foetus and at the same time suppressing further ovulation. The role of steroids in pregnancy had led to research into the uses of these compounds as birth control agents. Initially progesterone itself was studied in this regard, but it was found that the dose required to prevent ovulation is much too large.

Progesterone in turn can be biochemically converted to testosterone, which is found in the testes, and finally to estrone (an oestrogen), which incidentally was first isolated from the urine of pregnant women. Both of these steroids play a major role in the development of male and female characteristics. Progesterone can also be converted to cortisone (a corticosteroid found in the adrenal gland), which is responsible for regulating a variety of metabolic processes.

Hormonal Breakdown

The liver plays an important role in hormonal modification and inactivation through its metabolism of both oestrogen and testosterone, the latter being largely broken down at its target cells.

Nearly all drugs are modified or degraded in some way in the liver. Oral medications are first absorbed by the gut and transported via portal circulation (a certain amount of blood from the intestine is collected into the portal vein and carried to the liver). At that point, drugs are modified, activated, or inactivated before they enter systemic circulation (the normal blood nourishment that is the major part of the circulatory system). The body's circuitous path to the administration of oral medication lends this process to be described as "requiring a first pass" through the liver versus the rapid access to systemic circulation when drugs are administered parenterally (into the muscle, into a vein, under the skin).

These hormones are effectively handled by the various cells of the body, of particular importance, the cells of the liver, without harm to the individual. But long term, as well as short term, administration of hormone therapies require careful administration and periodic monitoring to assure good health is maintained. The healthy liver will manage these processes very well. However, a damaged liver, whether related to substance abuse or infection, does not easily facilitate the necessary breakdown process (TGC, 2015b).

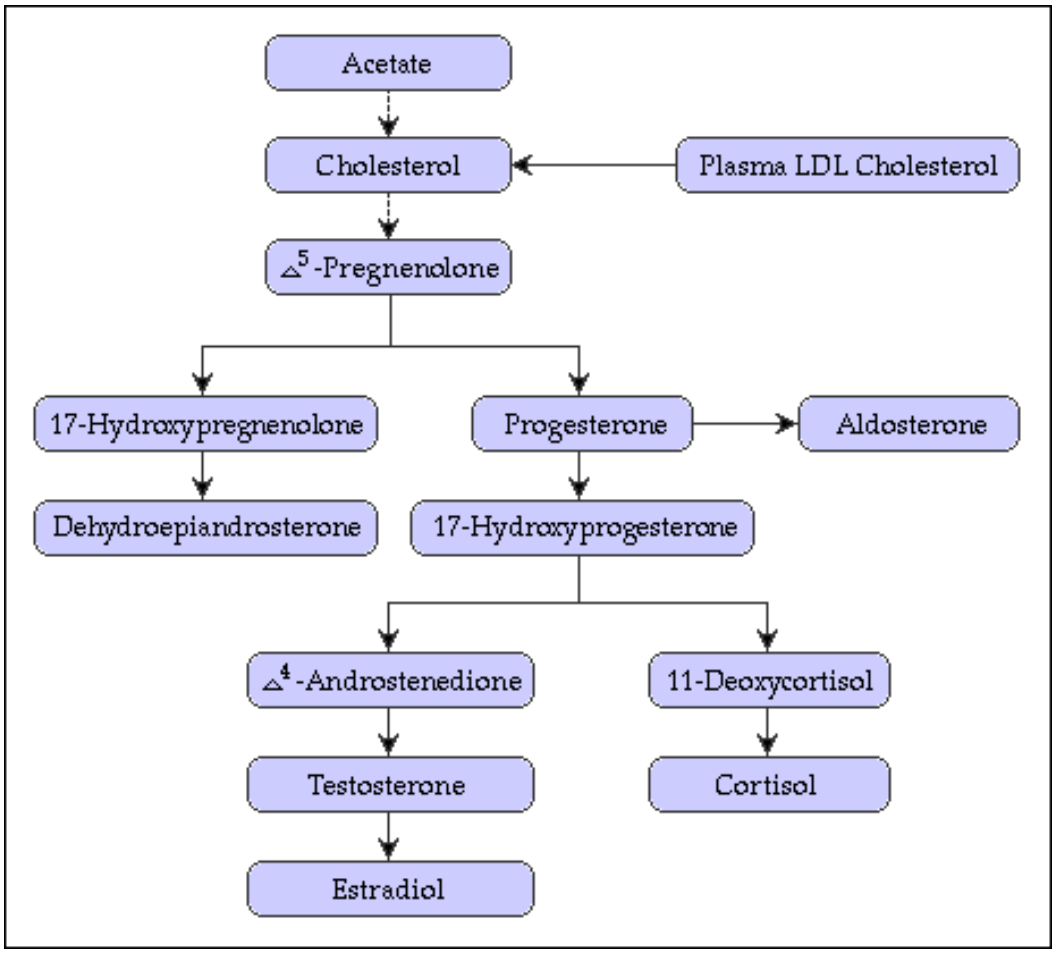

Figure 4.3 – The overall process of hormonal biosynthesis

Chapter 5

Human anatomy

Male Genital Anatomy

External

- **Penis** - The glans, or head, of the penis is covered with very thin skin that contains numerous nerve-endings and is therefore very sensitive to touch. At birth the foreskin covers the glans and on its lower side it is tethered to the inner surface by the frenulum. The frenulum is the small piece of skin on the underside of the penis where the glans meets the shaft. It is also a very sensitive area.
  The foreskin may be removed in a procedure known as circumcision. Circumcision is usually performed at a young age, for religious or hygiene reasons. The skin of the penis is thin and stretchy and loosely attached to the underlying tissues.
  The penis itself is composed of erectile tissue and is richly supplied with sensory nerves. It is filled with a rich network of blood vessels and three cylindrical areas of spongy tissue. The spongy tissue remains empty when the penis is flaccid and it fills during erection.
- **Scrotum** - The scrotum is the pouch of skin at the root of the penis that holds the testes. For healthy sperm to be produced the testes need to be kept at a temperature lower than the rest of the body. Under the skin of the scrotum is a muscle that contracts in response to cold or exercise, in order to maintain the ideal temperature.

Internal

- **Testicles** - The testicles have two functions -
  - ⋆ To produce sperm,
  - ⋆ To produce male hormones, primarily testosterone. Production of sperm continues throughout a man's life, unless there is a problem with infertility.

- **Epididymis** - When the sperm have been produced they move to a large tube called the Epididymis, where they continue to mature for six weeks.
- **Vas Deferens** - The Vas Deferens are the tubes that carry sperm from the epididymis to the urethra and penis.
- **Bladder** - The bladder holds urine. There is a valve at the base of the bladder that closes when the penis is erect to prevent urination.
- **Seminal Vesicles** - The seminal vesicles produce and store semen. The sperm are supported and nourished by this sticky fluid that forms part of the ejaculate.
- **Prostate Gland** - The prostate gland is situated just below the neck of the bladder. It produces secretions that form part of the seminal fluid during ejaculation, and pushes the ejaculate (semen and sperm) out of the penis during male orgasm.
- **Cowpers' Gland** - These glands are on either side of the urethra. They contain a clear alkaline fluid that cleans the urethra of any urine before ejaculation. This fluid also acts as a lubricant. This fluid is called pre-ejaculate (pre-cum) but may also contain a few sperm. This gland is responsible for the small amount of clear fluid ejaculate that may occur after hormonal therapy is under-way. Any pre-ejaculate produced will still continue after gender reassignment surgery. In the post-operative patient, this is experienced during orgasm as a small discharge from the newly constructed female urethra.
- **Urethra** - The urethra is the tube that runs from the bladder and seminal vesicles to the opening at the head of the penis. Semen, urine and pre-ejaculate pass down the urethra.

Female Genital Anatomy

Anatomy & Physiology

Anatomically, the female reproductive system consists of essential and accessory organs. The ovaries are essential to the production of eggs and hormones that initiate female secondary sexual characteristics and maintain normal reproductive function. The Fallopian tubes conduct the egg or (fertilized egg, the zygote) from the ovary to the uterus that is monthly changed into a habitable place for a fertilized egg. The cervix (narrowest portion of the uterus) serves as a gatekeeper to the body of the uterus. The vagina opens to the exterior in association with the external genitalia. Accessory glands participate in normal reproductive function. These include glands that produce mucus to lubricate the vagina and urethral opening.

- **Ovaries** - These small oval-shaped glands are located on either side of the uterus supported by several ligaments. The ovary consists of 3 areas

  - ⋆ cortex,
  - ⋆ medulla, and
  - ⋆ hilum.

  The cortex contains supportive cells, blood vessels, and developing follicles. The medulla contains connective tissue, smooth muscle, blood and lymph vessels and nerves. Nerves, blood vessels and connective tissue are found in the innermost portion, the hilum. The ovaries produce eggs (ova) and hormones.
- **Uterus** - The pear-shaped uterus opens to the vagina at the cervix and then widens toward the top where the Fallopian tubes enter the uterus. The uterus is a very muscular organ containing 3 layers of tissues. The interior layer, the endometrium, changes in thickness and secretory capability due to the influence of ovarian hormones over the course of the menstrual cycle. The myometrium, or muscle, is composed of 4 poorly defined layers of smooth muscle that is thickest at the top of the uterus. This makes for greater force during labour and delivery. The exterior of the uterus is covered with connective tissue. During pregnancy the baby (foetus) develops inside the uterus causing it to expand tremendously.
- **Fallopian Tubes** - These narrow muscular tubes are attached to the upper outer angles of the uterus and serve as tunnels for the egg (ova) to travel from the ovaries to the uterus. Ova are captured by the infundibulum which has a wide webbed finger-like appearance, called fimbriae, near the ovary. Wave-like contractions create a current that moves the ovulated egg towards the tubular opening. Conception normally occurs in the tubes, with the fertilized egg then propelled to the uterus by the peristaltic contractions of the tubes and ciliary beating of the tubular epithelium to the uterus for implantation. Sometimes implantation will occur in the Fallopian tubes. Such an ectopic pregnancy is undesirable and must be treated immediately before the growing embryo causes rupture of the tube.
- **Vagina** - This muscular canal extends from the midpoint of the cervix to its opening located between the urethra and rectum. The mucous membrane lining the vagina and musculature are continuous with the uterus. The epithelium lining the vagina thickens and produces lubricating substances in response to oestrogen. These secretions aid in sexual intercourse.
- **Mammary Glands** - The breasts are milk producing glands located over the pectoral muscles consisting of a nipple, lobes, ducts and fibrous and fatty tissue. The nipple is surrounded by a pigmented, circular area (areola) and contains ductal openings. Nipple erection is produced with stimulation. The 15 to 25 lobes of each breast are further divided in lobules that are separated and supported by fibrous tissue. Each lobule contains small sac-like alveoli surrounded by milk producing cells and small muscular cells. The muscular cells contract to express the milk during lactation. The lobules are drained by ducts that empty into a larger reservoir that lies just below the nipple. Reproductive hormones are important in the development

of the breast in puberty and in lactation. Oestrogen promotes the growth of the gland and ducts while progesterone stimulates the development of milk producing cells. Prolactin, released from the anterior pituitary, stimulates milk production. Oxytocin, released from the posterior pituitary in response to suckling, causes milk ejection from the lactating breast.

- **Puberty** - The first change to herald the coming of reproductive capability in females is the development of breasts. This is followed by the growth of axillary (underarm) and pubic (groin) hair and finally by the first menstrual period. Initial periods are usually anovulatory (i.e. no egg released) with regular ovulation occurring within a year. The age at the time of puberty is variable. In the US puberty occurs in girls around the age of 8 to age 13. Because of the individual variability in the onset of puberty, a delay cannot be considered pathological until menstruation has not begun sometime before the age of 17. Sometimes the delay is called primary menorrhoea and can be due to emotional stress, poor nutrition, weight loss or intensive athletic training.

Hormones and the Cycle

Females have four major hormones involved in the menstrual cycle — follicle-stimulating hormone (FSH), luteinizing hormone (LH), oestrogen (estradiol) and progesterone. FSH and LH are protein hormones produced by cells of the anterior pituitary within the brain, in response to small peptide hormones from the hypothalamus (hypothalamic releasing factors). These pituitary hormones travel in the blood to the ovary where they stimulate the development of one or more eggs, each within a follicle. A follicle consists of an ovum surrounded by cells responsible for the growth and nurturing of the ovum. As the cycle progresses, one follicle becomes dominant and all others regress. Oestrogen, and progesterone to a lesser degree, are steroid hormones produced by cells of the developing follicle. Oestrogen causes the endometrium to increase in thickness and vascularization (i.e., blood supply).

After ovulation (at the midpoint of the cycle), under the influence of LH, these same follicular cells shift to the production of progesterone. Progesterone causes the endometrial lining to become secretory and nutritive in anticipation of implantation of a fertilized egg. These four hormones are in a constant balance that shifts during progress through the menstrual cycle. The average menstrual cycle is 28 days, however only a very small percentage of cycles are exactly 28 days, most cycles range from 25–36 days.

The menstrual cycle can be divided into three phases — the follicular phase, the ovulatory phase, and the luteal phase. The follicular phase begins with the first day of menses (menstrual flow) and continues to approximately day 13 or 14 when ovulation takes place. During the follicular phase, FSH and

LH are slowly rising in preparation for the LH surge (very high level of LH) at the time of ovulation. FSH is stimulating the growth of follicles in the ovary. Oestrogen and progesterone are relatively low throughout this time but slowly begin to rise toward the end of this phase.

LH surges and peaks during the ovulatory phase (around day 14) and oestrogen peaks at the same time. These peaks trigger ovulation. The ovum lives about 72 hours after ovulation, but it is fertilizable for only about 36 hours. Just before ovulation, progesterone levels begin to rise rapidly. Changes in cervical mucus accompany ovulation. The amount of mucus increases and it becomes clear and thin. This facilitates conception by aiding the passage of sperm through the cervical canal. Sperm can live for up to 72 hours in the female reproductive system. Therefore, the fertile period during a 28-day cycle is only about 4–5 days.

After the egg is released, the remainder of the follicle stays intact in the ovary and produces both oestrogen and progesterone. This is called the corpus luteum (hence the luteal phase). The corpus luteum remains intact for the remainder of the cycle. The breast swelling, tenderness and pain experience by some is most likely due to the effects of progesterone on breast tissue.

Right after ovulation, the luteal phase begins and during this phase, progesterone levels are very high — progesterone is important during this phase because if the egg is fertilized, and implanted in the uterus, progesterone keeps the uterus intact so that the pregnancy is maintained. The continued health of the corpus luteum (progesterone secretion) is assured by the production of human chorionic gonadotropin (hCG) by the implanted embryo, until the placenta develops and can take over. The detection of hCG in urine is the basis of laboratory and home pregnancy tests.

If fertilization and implantation have occurred, than the corpus luteum will be stimulated by hCG to continue its production of oestrogen and progesterone to maintain the pregnancy. This is important because the corpus luteum dies 14–22 days after ovulation if fertilization and implantation do not occur. With no progesterone to keep it intact, the lining of the uterus (the endometrium) is then shed, resulting in the monthly menstrual flow that normally lasts about 5 days. A variety of feminine products are available to help women during menses, including absorptive pads and tampons, deodorants, and vaginal cleansers.

Chapter 6

Hormones

Estradiol Valerate

Estradiol Valerate is a naturally occurring oestrogen given in the form of Estradiol Valerate or one of its semisynthetic esters as oestrogen replacement therapy in menopausal women (TGC, 2015a).

Generally refers to the 17-beta-isomer of estradiol, an aromatized C18 steroid with hydroxyl group at 3-beta- and 17-beta-position. Estradiol-17-beta is the most potent form of mammalian oestrogenic steroids. In humans, it is produced primarily by the cyclic ovaries and the placenta. It is also produced by the adipose tissue of men and postmenopausal women. The 17-alpha-isomer of estradiol binds weakly to oestrogen receptors (receptors, oestrogen) and exhibits little oestrogenic activity in oestrogen-responsive tissues. Various isomers can be synthesised (drugbank, 2015c).

Also known as

Climaval, Estraderm MX, Estraderm TTS, Estradiol implant, Evorel, Progynova, Progynova TS, Zumenon, Estradiol in North America, Estradiol in Germany, Estradiol in France, Estradiol in Spain.

Manufacturer

Climaval = Novartis.

Description

Climaval = 1 mg grey-blue tablets marked E1; 2 mg blue tablets marked E2.

Contains

Climaval - Estradiol Valerate 1mg, 2 mgs.
Estraderm MX 25 - Estradiol 25 micrograms (mcgs)/24 hours.
Estraderm MX 50 - Estradiol 50 mcgs/24 hours.
Estraderm MX 75 - Estradiol 75 mcgs/24 hours.
Estraderm MX 100 - Estradiol 100 mcgs/24 hours.
Estraderm TTS 25 - Estradiol 25 mcgs/24 hours.
Estraderm TTS 50 - Estradiol 50 mcgs/24hours.
Estradiol implant - Estradiol 25mgs, 50 mgs, 100 mgs.
Evorel '25' patch - Estradiol 25 mcgs/24 hours.
Evorel '50' patch - Estradiol 50 mcgs/24 hours.
Evorel '75' patch - Estradiol 75 mcgs/24 hours.
Evorel '100' patch - Estradiol 100 mcgs/24 hours.
Progynova - Estradiol Valerate 1mg, 2 mgs.
Progynova TS - Estradiol 50 mcgs/24 hours, Estradiol 100 mcgs/24 hours.
Zumenon - Estradiol 1mg, 2mgs.

Typical dosage

Pre-op

Progynova - 6–12 mgs/day (unknown, 2005),
Progynova - 2–4 mgs/day (Asscheman and LJG Gooren, 1992),
Zumenon - 4–8 mgs/day,
Estraderm TTS - 0.1–0.2 mgs with the patch changed twice a week.

Post-op

Progynova - 2–6 mgs/day (unknown, 2005),
Zumenon - 1–4 mgs/day,
Estradiol implant - 25–100 mgs/4–8 months (according to oestrogen levels) (BNF, 2016a),
Evorel - 200mcg/twice a week.

Dosage of oral Estradiol

Dosage	Blood levels
2mg Estradiol	180–250 pmol/L
4mg Estradiol	360–500 pmol/L
6mg Estradiol	540–750 pmol/L

Table 6.1 – Normal range & dose of Estradiol, for oral tablets only

The above table gives the approximate normal range/dose for Estradiol

If you are significantly outside this then it would be worth seeing an endocrinologist.

Please note the following

1. This table is ONLY for tablets that are swallowed
2. Using Oestrogel will mess up the results. If you are using it, then do NOT use for at least 24 hours.
3. If taken sublingually, then add 10% to pmol/L and ensure that the blood test is at least 6 hours after taking. This is to allow the blood Estradiol to drop to base levels
4. Taking Estradiol tablets sublingually and Oestrogel leads to rapidly fluctuating Estradiol level, specifically a massive spike of approx 2000 pmol/L when applied. Followed by a very sharp drop in Estradiol. This peak and drop occurs within an hour of application which can and does lead to mood swings, and a down feeling.

Route

Tablets - Climaval, Progynova, Zumenon.
Skin patch - Progynova TS, Estraderm MX 25, Estraderm MX 50, Estraderm MX 100, Evorel.
Implant - Estradiol

Contraindications

- Known, past or suspected breast cancer,
- Known or suspected oestrogen-dependent malignant tumours e.g. endometrial cancer,
- Undiagnosed genital bleeding,
- Untreated endometrial hyperplasia,
- Previous idiopathic or current venous thromboembolism (deep venous thrombosis, pulmonary embolism),
- Known thrombophilic disorders (e.g. protein C, protein S, or antithrombin deficiency),
- Active or recent arterial thromboembolic disease e.g. angina, myocardial infarction,
- Acute liver disease, or a history of liver disease as long as liver function tests have failed to return to normal,
- Known hypersensitivity to the active substances or to any of the excipients,
- Porphyria (emc, 2012).

Interactions

Drug-drug

Abciximab - Estradiol may ↓ the anticoagulant activities of Abciximab.
Acenocoumarol - Estradiol may ↓ the anticoagulant activities of Acenocoumarol.
Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Estradiol.
Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Estradiol.
Amodiaquine - The serum concentration of Amodiaquine can be ↑ when it is combined with Estradiol.
Anastrozole - The therapeutic efficacy of Anastrozole can be ↓ when used in combination with Estradiol.
Anthrax immune globulin - Estradiol may ↑ the thrombogenic activities of Anthrax immune globulin.
Aripiprazole - The serum concentration of Aripiprazole can be ↓ when it is combined with Estradiol.
Bexarotene - The serum concentration of Estradiol can be ↓ when it is combined with Bexarotene.
Bosentan - The serum concentration of Estradiol can be ↓ when it is combined with Bosentan.
Butabarbital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Butabarbital.
Butethal - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Butethal.
C1 Esterase Inhibitor (Human) - Estradiol may ↑ the thrombogenic activities of C1 Esterase Inhibitor (Human).
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Estradiol.
Capromab - Estradiol may ↓ effectiveness of Capromab as a diagnostic agent.
Carbamazepine - The metabolism of Estradiol can be ↑ when combined with Carbamazepine.
Chenodeoxycholic acid - The therapeutic efficacy of Chenodeoxycholic acid can be ↓ when used in combination with Estradiol.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Estradiol.
Citric Acid - Estradiol may ↓ the anticoagulant activities of Citric Acid.
Colesevelam - The serum concentration of Estradiol can be ↓ when it is combined with Colesevelam.
Cyproterone acetate - The serum concentration of Estradiol can be ↓ when it is combined with Cyproterone acetate.
Dabrafenib - The serum concentration of Estradiol can be ↓ when it is combined with Dabrafenib.
Dalteparin - Estradiol may ↓ the anticoagulant activities of Dalteparin.

Deferasirox - The serum concentration of Estradiol can be ↓ when it is combined with Deferasirox.
Dehydroepiandrosterone - The risk or severity of adverse effects can be ↑ when Dehydroepiandrosterone is combined with Estradiol.
Dicoumarol - Estradiol may ↓ the anticoagulant activities of Dicoumarol.
Edetic Acid - Estradiol may ↓ the anticoagulant activities of Edetic Acid.
Enoxaparin - Estradiol may ↓ the anticoagulant activities of Enoxaparin.
Eslicarbazepine acetate - The serum concentration of Estradiol can be ↓ when it is combined with Eslicarbazepine acetate.
Ethyl biscoumacetate - Estradiol may ↓ the anticoagulant activities of Ethyl biscoumacetate.
Exemestane - The therapeutic efficacy of Exemestane can be ↓ when used in combination with Estradiol.
Fludrocortisone - The serum concentration of Fludrocortisone can be ↑ when it is combined with Estradiol.
Fondaparinux sodium - Estradiol may ↓ the anticoagulant activities of Fondaparinux sodium.
Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Estradiol.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Estradiol.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Estradiol.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Estradiol.
Heparin - Estradiol may ↓ the anticoagulant activities of Heparin.
Heptabarbital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Heptabarbital.
Hexobarbital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Hexobarbital.
Hyaluronidase - The therapeutic efficacy of Hyaluronidase can be ↓ when used in combination with Estradiol.
Hydrocodone - The serum concentration of Hydrocodone can be ↓ when it is combined with Estradiol.
Icosapent - Icosapent may ↑ the thrombogenic activities of Estradiol.
Infliximab - Infliximab may ↑ the hyperkalemic activities of Estradiol.
Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Estradiol.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Estradiol.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Estradiol.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Estradiol.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Estradiol.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Estradiol.

Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Estradiol.
Intravenous Immunoglobulin - Estradiol may ↑ the thrombogenic activities of Intravenous Immunoglobulin.
Lenalidomide - Estradiol may ↑ the thrombogenic activities of Lenalidomide.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Estradiol.
Liothyronine - The therapeutic efficacy of Liothyronine can be ↓ when used in combination with Estradiol.
Lumacaftor - The serum concentration of Estradiol can be ↓ when it is combined with Lumacaftor.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Estradiol.
Methohexital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Methohexital.
Mitotane - The serum concentration of Estradiol can be ↓ when it is combined with Mitotane.
Nelfinavir - The serum concentration of Estradiol can be ↑ when it is combined with Nelfinavir.
Nimodipine - The serum concentration of Nimodipine can be ↓ when it is combined with Estradiol.
Ospemifene - The risk or severity of adverse effects can be ↑ when Estradiol is combined with Ospemifene.
Pentobarbital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Pentobarbital.
Perindopril - Perindopril may ↑ the hyperkalemic activities of Estradiol.
Phenindione - Estradiol may ↓ the anticoagulant activities of Phenindione.
Phenprocoumon - Estradiol may ↓ the anticoagulant activities of Phenprocoumon.
Phenytoin - The metabolism of Estradiol can be ↑ when combined with Phenytoin.
Primidone - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Primidone.
Ranolazine - The serum concentration of Estradiol can be ↑ when it is combined with Ranolazine.
Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Estradiol.
Rifabutin - The serum concentration of Estradiol can be ↓ when it is combined with Rifabutin.
Ropinirole - The serum concentration of Ropinirole can be ↑ when it is combined with Estradiol.
Saquinavir - The serum concentration of Estradiol can be ↑ when it is combined with Saquinavir.
Saxagliptin - The serum concentration of Saxagliptin can be ↓ when it is combined with Estradiol.
Secobarbital - The therapeutic efficacy of Estradiol can be ↓ when used in combination with Secobarbital.

Siltuximab - The serum concentration of Estradiol can be ↓ when it is combined with Siltuximab.
Somatropin recombinant - The therapeutic efficacy of Somatropin recombinant can be ↓ when used in combination with Estradiol.
St. John's Wort - The serum concentration of Estradiol can be ↓ when it is combined with St. John's Wort.
Sulodexide - Estradiol may ↓ the anticoagulant activities of Sulodexide.
Teriflunomide - The serum concentration of Estradiol can be ↓ when it is combined with Teriflunomide.
Tesmilifene - The serum concentration of Estradiol can be ↓ when it is combined with Tesmilifene.
Thalidomide - Estradiol may ↑ the thrombogenic activities of Thalidomide.
Theophylline - The serum concentration of Theophylline can be ↑ when it is combined with Estradiol.
Tipranavir - Estradiol may ↑ the dermatologic adverse activities of Tipranavir.
Tizanidine - The serum concentration of Tizanidine can be ↑ when it is combined with Estradiol.
Tocilizumab - The serum concentration of Estradiol can be ↓ when it is combined with Tocilizumab.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Estradiol.
Treprostinil - Estradiol may ↓ the anticoagulant activities of Treprostinil.
Triamterene - Estradiol may ↑ the hyperkalemic activities of Triamterene.
Ursodeoxycholic acid - The therapeutic efficacy of Ursodeoxycholic acid can be ↓ when used in combination with Estradiol.
Valsartan - Valsartan may ↑ the hyperkalemic activities of Estradiol.
Verapamil - The serum concentration of Estradiol can be ↑ when it is combined with Verapamil.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Estradiol.
Vitamin C - The serum concentration of Estradiol can be ↑ when it is combined with Vitamin C.
Warfarin - Estradiol may ↓ the anticoagulant activities of Warfarin (drugbank, 2015c).

Drug-herb

- **Blue cohosh** - May ↑ drug's adverse effects. Discourage use together.
- **Saw palmetto** - May negate drug's effects. Discourage use together.
- **St. John's wort** - May ↓ effects of drug. Discourage use together (Abramovitz, 2016).

Drug-food

- **Caffeine** - May ↑ caffeine level. Advise patient to avoid or minimize use of caffeine.

- **Grapefruit juice** - May ↑ drug level. Tell patient to take drug with liquid other than grapefruit juice (Abramovitz, 2016).
- **General food interactions** - Take with food to ↓ nausea (drugbank, 2015c).

Drug-lifestyle

- **Smoking** - May ↑ risk of adverse cardiovascular effects. If smoking continues, may need another therapy.
- **Sunscreen use** - May ↑ absorption of Estrasorb. Tell patient to separate application times (Abramovitz, 2016).

Effects on Lab Test Results

- May ↑ clotting factor VII, VIII, IX, and X; total T4; thyroid-binding globulin; LFT results; and triglyceride levels.
- May ↑ norepinephrine-induced platelet aggregation and prothrombin time (PT).
- May ↓ metyrapone test results (Abramovitz, 2016).

Side-effects

Central Nervous System

- **Stroke**,
- **headache**,
- dizziness,
- chorea,
- depression,
- **seizures**, (Abramovitz, 2016).

Cardiovascular

- Thrombophlebitis,
- **thromboembolism**,
- hypertension,
- **oedema**,
- **pulmonary embolism**,
- **myocardial infarction**, (Abramovitz, 2016).

Eyes

- **Myopia/astigmatism worsens**,
- **contact lens intolerance** (Abramovitz, 2016).

Gastrointestinal

- **Nausea**,
- **vomiting**,
- **abdominal cramps**,
- **bloating**,
- increased appetite,
- **pancreatitis**,
- anorexia,
- gallbladder disease (Abramovitz, 2016).

Genito-urinary

- **Testicular atrophy**,
- **erectile dysfunction**,
- genital pruritus,
- haematuria (Abramovitz, 2016)

Hepatic

- Cholestatic jaundice,
- **hepatic adenoma** (Abramovitz, 2016).

Metabolic

- **Weight changes**,
- hypothyroidism (Abramovitz, 2016).

Respiratory

- Upper respiratory tract infection,
- allergy (Abramovitz, 2016).

Skin

- **Melasma**,
- urticaria,
- erythema nodosum,
- dermatitis,
- **hair loss**,
- pruritus (Abramovitz, 2016).

Other

- **Gynaecomastia**,
- **increased risk of breast cancer**,
- hot flashes,
- **breast tenderness**,
- **breast enlargement**,
- flu-like syndrome (Abramovitz, 2016).

What are the possible side effects of estradiol injection?

Get emergency medical help if you have any of these signs of an allergic reaction - **hives**, **difficulty breathing**, **swelling of your face, lips, tongue, or throat** (drugs.com, 2014c).

Pharmacology

Ester 17b of Estradiol with the same effect as endogenous oestrogen (unknown, 2005).

Pharmacodynamics

Estradiol, the principal intracellular human oestrogen, is substantially more active than its metabolites, estrone and estriol, at the cellular level (drugbank, 2013c).

Progynova contains estradiol valerate, the valeric-acid ester of the endogenous female oestrogen, estradiol.

The active ingredient, synthetic 17β-estradiol, is chemically and biologically identical to endogenous human estradiol. It substitutes for the loss of oestrogen production in menopausal women, and alleviates menopausal symptoms. Oestrogens prevent bone loss following menopause or ovariectomy (emc, 2012).

Pharmacokinetics

Absorbed from gastrointestinal tract and through skin and mucous membranes. Peak plasma concentrations achieved 1–2 hours after oral dose, and again about 8 hours due to enterohepatic recycling. Excreted in urine, with only a small amount excreted in the faeces (TGC, 2015a).

Absorption - After oral administration estradiol valerate is quickly and completely absorbed (emc, 2012).

Distribution - Already after 0.5–3 hours peak plasma levels of estradiol, the active drug substance, are measured. As a rule, after 6–8 hours a second maximum appears, possibly indicating an enterohepatic circulation of estradiol.
In plasma, estradiol is mainly found in its protein-bound form. About 37% are bound to SHBG and 61% to albumin. Cumulation of estradiol after daily repetitive intake of Progynova does not need to be expected.
The absolute bioavailability of estradiol amounts to 3–5% of the oral dose of estradiol valerate.

Metabolism - Esterases in plasma and the liver quickly decompose estradiol valerate into estradiol and valeric acid. Further decomposition of valeric acid through β-oxidation leads to C[2-]units and results in CO[2]and water as end products. Estradiol itself undergoes several hydroxylating steps. Its metabolites as well as the unchanged substance are finally conjugated. Intermediate products of metabolism are estrone and estriol, which exhibit a weak oestrogenic activity of their own, although this activity is not so pronounced as with estradiol. The plasma concentration of conjugated estrone is about 25 to 30 fold higher than the concentration of unconjugated estrone. In a study using radioactive labelled estradiol valerate about 20% of radioactive substances in the plasma could be characterised as unconjugated steroids, 17% as glucuronized steroids and 33% as steroid sulphates. About 30% of all substances could not be extracted from the aqueous phase and, therefore, probably represent metabolites of high polarity.

Excretion - Estradiol and its metabolites are mainly excreted by the kidneys (relation of urine:faeces = 9:1). Within 5 days about 78–96% of the administered dose are excreted with an excretion half-life of about 27 hours (emc, 2012).

Elimination - Estradiol, estrone and estriol are excreted in the urine along with glucuronide and sulfate conjugates.

Half life - 36 hours

How it works

Estradiol enters target cells freely (e.g., female organs, breasts, hypothalamus, pituitary) and interacts with a target cell receptor. When the oestrogen receptor has bound its ligand it can enter the nucleus of the target cell, and regulate gene transcription which leads to formation of messenger RNA. The mRNA interacts with ribosomes to produce specific proteins that express the effect of estradiol upon the target cell. Oestrogens increase the hepatic synthesis of SHBG, thyroxine-binding globulin (TBG), and other serum proteins and suppress FSH from the anterior pituitary (drugbank, 2015c).

Exogenous oestrogens are metabolised using the same mechanism as endogenous oestrogens. Oestrogens are partially metabolized by cytochrome P450 (drugbank, 2015c).

Notes

Take oral dose with food or milk to decrease/minimise gastrointestinal symptoms.

Apply transdermal patch to clean, dry, hairless, intact skin on abdomen or buttock. Don't apply to breasts, waistline, or other areas where clothing can loosen patch. When applying, ensure thorough contact between patch and skin, especially around edges, and hold in place for about 10 seconds. Apply patch immediately after opening and removing protective cover. Rotate application sites (Abramovitz, 2016).

This can be taken sublingually (i.e. just place it under your tongue and let it dissolve there).

Warn contact lens wearers that their vision may alter slightly; allow time for the eyes to settle before seeking your opticians advice.

Avoid sunlight or wear a sunscreen as burning may occur. See Sunshine protection for further information.

Also note that Estraderm patches are unavailable in the UK, supposedly because of "financial reasons" from the manufacturer.

Conditions which need supervision

If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment, in particular -

- Leiomyoma (uterine fibroids) or endometriosis,
- Risk factors for, thromboembolic disorders,
- Risk factors for oestrogen dependent tumours, e.g. 1st degree heredity for breast cancer,
- Hypertension,
- Liver disorders (e.g. liver adenoma),
- Diabetes mellitus with or without vascular involvement,
- Cholelithiasis,
- Migraine or (severe) headache,
- Systemic lupus erythematosus,
- A history of endometrial hyperplasia,
- Epilepsy,
- Asthma,
- Otosclerosis,
- Hereditary angioedema (emc, 2012).

Reasons for immediate withdrawal of therapy

Therapy should be discontinued in case a contraindication is discovered and in the following situations -

- Jaundice or deterioration in liver function,

- Significant increase in blood pressure,
- New onset of migraine-type headache,
- Pregnancy (emc, 2012).

Shelf life

5 years (emc, 2012).

Toxicology

Nausea and vomiting may occur with an overdose.

There are no specific antidotes, and treatment should be symptomatic (emc, 2012).

Blood results

See Oestrogen.

Oestrogel

Applied to the skin as an alternative route for administering oestrogen.

Also known as

Estrodose, divigel, elestrin, estrogel.

Manufacturer

Hoechst Marion Roussel, and Sanofi-aventis.

Indications

Menopausal symptoms and osteoporosis prophylaxis (BNF, 2016a).

Typical dosage

1.5mgs of Oestrogel in 2 measures of gel (BNF, 2016a).

Route

Gel applied to skin. Oestrogel.

Method of administration

The correct dose of gel should be dispensed and applied to clean, dry, intact areas of skin e.g. on the arms and shoulders, or inner thighs. The area of application should be at least 750 cm^2. One measure from the dispenser, or half the prescribed dose, should be applied to each arm/shoulder (or thigh). Oestrogel should NOT be applied on or near the breasts or on the vulval region.

Oestrogel should be allowed to dry for 5 minutes before covering the skin with clothing.

The gel should be applied by the patient themselves, not by anyone else, and skin contact, particularly with a male partner, should be avoided for one hour after application. Washing the skin or contact with other skin products should be avoided until at least one hour after application of Oestrogel (emc, 2013).

Contraindications

- Known, past or suspected breast cancer,
- Known or suspected oestrogen-dependent malignant tumours (e.g. endometrial cancer),
- Undiagnosed genital bleeding,
- Untreated endometrial hyperplasia,
- Previous or current venous thromboembolism (e.g. deep venous thrombosis, pulmonary embolism),
- Known thrombophilic disorders (e.g. protein C, protein S, or antithrombin deficiency),
- Active or recent arterial thromboembolic disease (e.g. angina, myocardial infarction),
- Acute liver disease, or a history of liver disease as long as liver function tests have failed to return to normal,
- Known hypersensitivity to the active substances or to any of the excipients,
- Porphyria (emc, 2013).

Warning

Should not be applied on or near the breasts. Avoid skin contact with another person or other skin products or washing the area for at least 1 hour after application (BNF, 2016a).

Interactions

Drug interactions are the same as in Estradiol Valerate (drugbank, 2015c).

Treatment with surface active agents (e.g. sodium lauryl sulphate), or other drugs which alter barrier structure or function, could remove drug bound to the skin, altering transdermal flux. Therefore patients should avoid the use of strong skin cleansers and detergents (e.g. benzalkonium or benzothonium chloride products), skin care products of high alcoholic content (astringents, sunscreens) and keratolytics (e.g. salicylic acid, lactic acid).

The use of any concomitant skin medication which alters skin production (e.g. cytotoxic drugs) should be avoided.

The metabolism of oestrogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants (e.g. phenobarbital, phenytoin, carbamezapin) and anti-infectives (e.g. rifampicin, rifabutin, nevirapine, efavirenz).

Ritonavir and nelfinavir, although known as strong inhibitors, by contrast exhibit inducing properties when used concomitantly with steroid hormones. Herbal preparations containing St John's wort (Hypericum perforatum) may induce the metabolism of oestrogens.

At transdermal administration, the first-pass effect in the liver is avoided and thus, transdermally applied oestrogens HRT might be less affected than oral hormones by enzyme inducers (emc, 2013).

Pregnancy and lactation

Pregnancy

Oestrogel is not indicated during pregnancy. If pregnancy occurs during medication with Oestrogel, treatments should be withdrawn immediately.

The results of most epidemiological studies to date relevant to inadvertent foetal exposure to oestrogens indicate no teratogenic of foetotoxic effects (emc, 2013).

Lactation

Oestrogel is not indicated during lactation (emc, 2013).

Side-effects

Skin

- **Irritation**,
- **reddening of the skin** or
- **mild and transient erythema** at the site of application (emc, 2016).
- **pruritis**,
- **acne** (emc, 2013).

Metabolic system

- **Glucose intolerance** (emc, 2013).

Psychiatric disorders

- **depression**,
- **mood swings**,
- **libido changes** (emc, 2013).

Nervous system

- **headache**,
- **vertigo**,
- **migraine**,
- **aggravation of epilepsy** (emc, 2013).

Vascular system

- **venous thromboembolic disease**,
- **arterial hypertension** (emc, 2013).

Gastrointestinal system

- **nausea**,
- **abdominal pain**,
- **flatulence**,
- **vomiting** (emc, 2013).

Hepato-biliary

- **liver function test abnormalities**

Reproductive system

- **breast swelling**,
- **breast pain**,
- **breast enlargement**,
- **dysmenorrhoea**,
- **menorrhagia**,
- **metrorraghia**.
- **leucorrohoea**,
- **vaginitis**,
- **vaginal candidiosis**,
- **galactorrhoea** (emc, 2013).

General disorders

- **weight change**,
- **water retention**,
- **peripheral oedema**,
- **asthenia**,
- **anaphylactic reaction** (emc, 2013).

Overdose

Pain in the breasts may be indicative of too high a dosage, but acute overdosage has not been reported and is unlikely to be a problem. Overdosages of oestrogen may cause **nausea**. There are no specific antidotes and treatment should be symptomatic (emc, 2013).

Pharmacokinetics

With the usual dose of 1.5mgs of Oestrogel in 2.5mgs of gel, only about 10% of this is absorbed into the vascular system, regardless of the age of the patient (emc, 2016).

Oestrogel contains 17β-estradiol as active ingredient, 0.06% w/w (emc, 2013).

The active ingredient, 17β-estradiol, is chemically and biologically identical to endogenous human estradiol. It substitutes for the loss of oestrogen production in menopausal women, and alleviates menopausal symptoms.

Oestrogel prevents bone loss following menopause or ovariectomy (emc, 2013).

Pharmacokinetic studies indicate that, when applied topically to a large area of skin in a volatile solvent, approximately 10% of the estradiol is percutaneously absorbed into the vascular system, regardless of the age of the patient. Daily application of 2.5 g or 5 g Oestrogel over a surface area of 400-750 cm^2 results in a gradual increase in oestrogen blood levels to steady state after approximately 3–5 days and provides circulating levels of both estradiol and estrone equivalent in absolute concentrations and in their respective ratio to those obtained during the early-mid follicular phase of the menstrual cycle.

Oestrogel was administered to 17 postmenopausal women once daily on the posterior surface of one arm from wrist to shoulder for 14 consecutive days.

Cmax of estradiol and estrone on Day 12 were 117 pg/ml and 128 pg/ml, respectively.

The time-averaged serum estradiol and estrone concentrations Cavg[36] over the 24 hour dose interval after administration of 2.5 g of Oestrogel on Day 12 were 76.8 pg/ml and 95.7 pg/ml, respectively.

Metabolism of estradiol takes place mainly in the liver under oestriol, estrone and their conjugated metabolites (glucuronides, sulphates). These metabolites also undergo enterohepatic recirculation.

When treatment is stopped, estradiol and urinary conjugated estradiol concentrations return to baseline in about 76 hours (emc, 2013).

Shelf Life

36 months (emc, 2013).

Notes

Apply gel to clean, dry, intact areas of skin such as arms, shoulders, or inner thighs and allow to dry for 5 minutes before covering skin with clothing. Not to be applied on or near breasts or on vulval region (BNF, 2016a). Anecdotally I've heard of it being applied to inner thighs and inner arms only, as it can only penetrate one layer of skin and in these regions the skin is thinnest.

Conditions which need supervision

If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with Oestrogel, in particular -

- Leiomyoma (uterine fibroids) or endometriosis,
- Risk factors for thromboembolic disorders,
- Risk factors for oestrogen dependent tumours, e.g. first degree heredity for breast cancer,
- Hypertension,
- Liver disorders (e.g. liver adenoma),
- Diabetes mellitus with or without vascular involvement,
- Cholelithiasis,
- Migraine or (severe) headache,
- Systemic lupus erythematosus (SLE),

[36] the average plasma concentration of a drug after administration

- A history of endometrial hyperplasia,
- Epilepsy,
- Asthma,
- Otosclerosis (emc, 2013).

Reasons for immediate withdrawal of therapy

Therapy should be discontinued in case a contraindication is discovered and in the following situations -

- Jaundice or deterioration in liver function,
- Significant increase in blood pressure,
- New onset of migraine-type headache,
- Pregnancy (emc, 2013).

Sandrena

Manufacturer

Organon.

Contains

Estradiol at 0.1% strength.

Typical dosage

Pre-op 2–3 sachets per day, at regular intervals.
Post-op not known.

Route

Sandrena is a gel for transdermal use.

If the patient has forgotten to apply one dose, the forgotten dose is to be applied as soon as possible if the dose is not more than 12 hours late. If the dose is more than 12 hours late, the dose should be forgotten and continue as normal (emc, 2010).

Method of administration

Apply on dry and clean skin.

The Sandrena dose is applied once daily on the skin of the lower trunk of the right or left thigh, on alternate days. The application surface should be 1-2 times the size of a hand. Sandrena should not be applied on the breasts, on the face or irritated skin. After application the gel should be allowed to dry for a few minutes and the application site should not be washed within 1 hour. Contact of the gel with eyes should be avoided. Hands should be washed after application (emc, 2010).

Contraindications

- Known, past or suspected breast cancer,
- Known or suspected oestrogen-dependent malignant tumours (e.g. endometrial cancer),
- Undiagnosed genital bleeding,
- Untreated endometrial hyperplasia,
- Previous or current venous thromboembolism (deep venous thrombosis, pulmonary embolism),
- Known thrombophilic disorders (e.g. protein C, protein S, or antithrombin deficiency),
- Active or recent arterial thromboembolic disease (e.g. angina, myocardial infarction),
- Acute liver disease, or a history of liver disease as long as liver functions have failed to return to normal,
- Known hypersensitivity to the active substance or to any of the excipients,
- Porphyria (emc, 2010).

Interactions/incompatibilities

Phenobarbital, phenytoin, carbamezapine - ↑ metabolism, Rifampicin, rifabutin, nevirapine, efavirenz - ↑ metabolism (emc, 2016).

Pregnancy and lactation

Pregnancy

Sandrena is not indicated during pregnancy. If pregnancy occurs during medication with Sandrena, treatment should be withdrawn immediately.

The results of most epidemiological studies to date relevant to inadvertent foetal exposure to oestrogens indicate no teratogenic or foetotoxic effects (emc, 2010).

Breastfeeding

Sandrena is not indicated during lactation (emc, 2010).

Side-effects

Central Nervous System

- **stroke**,
- **headache**,
- **dizziness**,
- chorea,
- depression,
- **seizures** (Abramovitz, 2016).
- **migraine**,
- **paraesthesia**,
- **tremor** (emc, 2010).

Cardiovascular

- Thrombophlebitis,
- **thromboembolism**,
- hypertension,
- **oedema**,
- **pulmonary embolism**,
- **myocardial infarction** (Abramovitz, 2016).
- **hot flushes** (rxisk, 2016e).
- **palpitations** (emc, 2010).

Eyes

- **Worsening myopia or astigmatism**,
- **intolerance of contact lenses** (Abramovitz, 2016).
- **dry eyes** (emc, 2010).

Gastrointestinal

- **nausea**,
- **vomiting**,
- **abdominal cramps**,
- **bloating**,
- increased appetite,
- **pancreatitis**,
- anorexia,
- gallbladder disease (Abramovitz, 2016).
- **flatulence**,
- **constipation**,
- **dyspepsia**,
- **diarrhoea**,
- **bloating**,
- **abdominal distension** (emc, 2010).

Genito-urinary

- **Testicular atrophy**,
- **erectile dysfunction**,
- genital pruritus,
- haematuria (Abramovitz, 2016).

Hepatic

- Cholestatic jaundice,
- **hepatic adenoma** (Abramovitz, 2016).

Metabolic

- **Weight changes**,
- hypothyroidism (Abramovitz, 2016).
- **increased appetite**,
- **hypercholesterolemia** (emc, 2010).

Respiratory

- Upper respiratory tract infection,
- allergy (Abramovitz, 2016).
- **dyspnoea**,
- **rhinitis** (emc, 2010).

Skin

- **Melasma**,
- urticaria,
- erythema nodosum,
- dermatitis,
- **hair loss** (Abramovitz, 2016).
- **pruritus**,
- **rash**,
- **acne**,
- **alopecia**,
- **dry skin**,
- **hirsutism** (emc, 2010).

Other

- **Gynaecomastia**,
- **increased risk of breast cancer**,
- hot flushes,
- **breast tenderness**,
- **breast enlargement**,
- flu-like syndrome (Abramovitz, 2016).

Immune system

- **hypersensitivity reaction** (emc, 2010).

Psychiatric disorders

- **depression**,
- **nervousness**,
- **lethargy**,
- **anxiety**,
- **insomnia**,
- **apathy**,
- **emotional lability**,
- **impaired concentration**,
- **libido changes**,
- **agitation** (emc, 2010).

Vascular disorders

- **hot flushes**,
- **hypertension**,
- **superficial phlebitis**
- **purpura**
- **venous thromboembolism** (emc, 2010).

Musculoskeletal disorders

- **joint disorders**,
- **muscle cramps** (emc, 2010).

Renal & urinary disorders

- **increased urinary frequency**,
- **increased urinary urgency**,
- **urinary incontinence**,
- **cystitis**,
- **urine discolouration**,
- **haematuria** (emc, 2010).

Pharmacology

Sandrena is a synthetic 17β-estradiol, which is chemically and biologically identical to endogenous human estradiol (emc, 2016).

Pharmacokinetics

Sandrena is an alcohol-based estradiol gel. When applied to the skin the alcohol evaporates rapidly and estradiol is absorbed through the skin into the circulation. To some extent, however, the estradiol is stored in the subcutaneous tissue from where it is released gradually into circulation (emc, 2016).

Shelf life

3 years (emc, 2016).

Note

Apply the gel to intact areas of skin such as the lower trunk or thighs, using the right and left sides on alternate days. Wash your hands after each application. Should not be applied on the breasts or the face, and avoid any contact with your eyes. Allow the area of application to dry for 5 minutes and do not wash the area for at least 1 hour (BNF, 2016a). However, it can be applied on the breasts and below the neckline, and not in any area exposed to sunlight, quite safely for us.

Conditions which need supervision

If any of the following conditions are present, have occurred previously and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with Sandrena, in particular -

- Leiomyoma (uterine fibroids) or endometriosis,
- Risk factors for thromboembolic disorders,
- Risk factors for oestrogen dependent tumours e.g. 1st degree heredity for breast cancer,
- Hypertension,
- Liver disorders (e.g. liver adenoma),
- Diabetes mellitus with or without vascular involvement,
- Cholelithiasis,
- Migraine or (severe) headache,
- Systemic lupus erythematosus,
- A history of endometrial hyperplasia,
- Epilepsy,
- Asthma,
- Otosclerosis,
- Hereditary angioedema (emc, 2010).

Reasons for immediate withdrawal of therapy

Therapy should be discontinued in case a contraindication is discovered and in the following situations -

- Jaundice or deterioration in liver function,
- Significant increase in blood pressure,
- New onset of migraine-type headache,
- Pregnancy (emc, 2010).

Testosterone

Administration is by deep muscular injection, in the form of a gel, or as a patch.

Testosterone is a steroid sex hormone found in both men and women. In men, testosterone is produced primarily by the Leydig (interstitial) cells of the testes when stimulated by LH. It functions to stimulate spermatogenesis, promote physical and functional maturation of spermatozoa, maintain accessory organs of the male reproductive tract, support development of secondary sexual characteristics, stimulate growth and metabolism throughout the body and influence brain development by stimulating sexual behaviors and sexual drive (drugbank, 2015d).

In women, testosterone is produced by the ovaries (25%), adrenals (25%) and via peripheral conversion from androstenedione (50%). Testerone in women functions to maintain libido and general wellbeing. Testosterone exerts a negative feedback mechanism on pituitary release of LH and FSH. Testosterone may be further converted to dihydrotestosterone or estradiol depending on the tissue (drugbank, 2015d).

Also known as

Sustanon 100, Sustanon 250, Testogel, Andropatch, Restandol, Testosteron in Germany, Testostérone in France, Testosterona in Spain.

Manufacturer

Restandol = Organon
Sustanon 100 & 250 = Organon
Andropatch = GlaxoSmithKline
Testogel = Schering Health (BNF, 2016a).

Pharmacology

During exogenous administration of androgens, endogenous testosterone release is inhibited through feedback inhibition of pituitary luteinizing hormone (LH). At large doses of exogenous androgens, spermatogenesis may also be suppressed through feedback inhibition of pituitary follicle stimulating hormone (FSH) (Abramovitz, 2016).

Indications

Hypogonadism (males), androgen deficiency (BNF, 2016a).

Pharmacokinetics

Absorbed from the gastrointestinal tract, skin and oral mucosa. When absorbed via the gastrointestinal tract it is almost completely metabolised in the liver before it reaches the systemic circulation. Alkylation in the 17-position reduces its hepatic metabolism and produces derivatives such as methyltestosterone with increased oral activity. Testosterone is extensively bound to the sex hormone binding globulin, a plasma globulin that also binds Estradiol to other plasma proteins. Only about 2% of testosterone is unbound, and the plasma half-life ranges from about 10 - 100 minutes. It is largely metabolised in the liver via oxidation at the 17-OH group with the formation of Androstenedione, which is further metabolised to the weakly androgenic Androsterone and inactive Etiocholaolone which are excreted in the urine mainly as Glucoronides and sulphates. About 6% is excreted unchanged in the faeces after undergoing enterohepatic recirculation. Testosterone is believed to be converted to the more active Dihydrotestosterone in some target organs. Small amounts of testosterone are aromatised to form oestrogenic derivatives in the body. Esters of testosterone are less polar than the free compound, and are absorbed slowly following intramuscular injection, and are hydrolysed to testosterone following injection (TGC, 2015a).

Testosterone is the primary androgen produced by the Leydig cells of the testes and is responsible for sexual differentiation and male secondary sex characteristics. Young men exhibit a diurnal pattern of testosterone secretion, with a peak at about 08:00 and a nadir at about 20:00. Levels increase after exercise. In women, levels are 5 to 10% of male levels.

Testosterone circulates in the blood 98% bound to protein. In men, approximately 40% is bound with high affinity to sex hormone binding globulin (SHBG) and approximately 60% is bound weakly to albumin. The testosterone fraction that is bound to albumin dissociates freely in the capillary bed, becoming available for tissue uptake. Only 2 to 3% of testosterone exists in the free state. All non-SHBG bound testosterone is considered to be bioavailable.

Measurement of serum testosterone concentration is useful in the evaluation of hypogonadism, infertility, impotence and replacement therapy monitoring in males and hirsutism and virilization in females (exeter, 2014).

Pharmacodynamics

Testosterone is a steroid hormone from the androgen group. Testosterone is primarily secreted from the testes of males. In females, it is produced in the ovaries, adrenal glands and by conversion of adrostenedione in the periphery. It is the principal male sex hormone and an anabolic steroid. In both males and females, it plays key roles in health and well-

being. Examples include enhanced libido, energy, immune function, and protection against osteoporosis. On average, the adult male body produces about twenty times the amount of testosterone than an adult female's body does (drugbank, 2015d).

40% of testosterone in plasma is bound to sex hormone-binding globulin and 2% remains unbound and the rest is bound to albumin and other proteins. Testosterone is metabolized to 17-keto steroids through two different pathways. The major active metabolites are estradiol and DHT (drugbank, 2015d).

Elimination - About 90% of a dose of testosterone given intramuscularly is excreted in the urine as glucuronic and sulfuric acid conjugates of testosterone and its metabolites; about 6% of a dose is excreted in the faeces, mostly in the unconjugated form.
Half life - 10-100 minutes (drugbank, 2015d).

How it works

The effects of testosterone in humans and other vertebrates occur by way of two main mechanisms: by activation of the androgen receptor (directly or as DHT), and by conversion to estradiol and activation of certain oestrogen receptors. Free testosterone (T) is transported into the cytoplasm of target tissue cells, where it can bind to the androgen receptor, or can be reduced to 5-dihydrotestosterone (DHT) by the cytoplasmic enzyme 5-reductase. DHT binds to the same androgen receptor even more strongly than T, so that its androgenic potency is about 2.5 times that of T. The T-receptor or DHT-receptor complex undergoes a structural change that allows it to move into the cell nucleus and bind directly to specific nucleotide sequences of the chromosomal DNA. The areas of binding are called hormone response elements (HREs), and influence transcriptional activity of certain genes, producing the androgen effects (drugbank, 2015d).

Typical dosage

Pre-op - Not known at present
Post-op - Not known at present

Route

Injection - Sustanon 100, Sustanon 250, Restandol
Topical - Testogel.

Contraindications

Contraindicated in patients hypersensitive to drug and in those with hypercalcemia or cardiac, hepatic, or renal decompensation.

Contraindicated in men with breast or prostate cancer and in pregnant or breast-feeding women.

Use cautiously in elderly patients (Abramovitz, 2016). Nephrotic syndrome, pregnancy, lactation, hypercalcaemia (BNF, 2016a).

Side-effects

Side effects include -

- amnesia,
- anxiety,
- discoloured hair,
- dizziness,
- dry skin,
- hirsutism,
- hostility,
- impaired urination,
- paresthesia,
- penis disorder,
- peripheral oedema,
- sweating, and
- vasodilation (drugbank, 2015d).

Central nervous system

- Headache,
- anxiety,
- depression,
- paresthesia,
- sleep apnoea (Abramovitz, 2016).

Cardiovascular

- Oedema (Abramovitz, 2016).

Gastrointestinal

- Nausea,
- **gum or mouth irritation**,
- bitter taste,
- **gum pain**,
- **gum tenderness**, or
- **gum oedema**,
- taste perversion (with buccal application) (Abramovitz, 2016)

Genitourinary

- Amenorrhoea,
- oligospermia,
- decreased ejaculatory volume,
- priapism (Abramovitz, 2016).
- **decreased libido**
- **PSA increased** (rxisk, 2016f).

Haematologic

- **haematocrit increased**
- **polycythaemia** (Abramovitz, 2016).

Hepatic

- Reversible jaundice,
- **cholestatic hepatitis** (Abramovitz, 2016).

Metabolic

- Hypernatremia,
- **hyperkalemia**,
- hypercalcemia,
- hyperphosphatemia,
- hypercholesterolemia (Abramovitz, 2016).

Skin

- Pain,
- induration[37] at injection site,
- local oedema,
- acne (Abramovitz, 2016).

Other

- Androgenic effects in women,
- **gynaecomastia**,
- hypersensitivity reactions,
- hypoestrogenic effects in women,
- excessive hormonal effects in men,
- male pattern baldness (Abramovitz, 2016).

[37] localised swelling

Interactions

Drug-drug

- **Corticosteroids** - May ↑ risk of oedema. Use together cautiously, especially in patients with cardiac or hepatic disease (Abramovitz, 2016),
- **Hepatotoxic drugs** - May ↑ risk of hepatotoxicity. Monitor liver function closely (Abramovitz, 2016),
- **Insulin, oral antidiabetics** - May ↓ glucose level; may alter dosage requirements. Monitor glucose level in diabetic patients (Abramovitz, 2016).
- **Oral anticoagulants** - May ↑ sensitivity; may alter dosage requirements. Monitor PT and international normalized ratio (INR); decrease anticoagulant dose if necessary (Abramovitz, 2016),
- **Oxyphenbutazone** - May ↑ oxyphenbutazone level. Monitor patient (Abramovitz, 2016).

Acarbose - Testosterone may ↑ the hypoglycaemic activities of Acarbose.

Acenocoumarol - Testosterone may ↑ the anticoagulant activities of Acenocoumarol.

Albiglutide - Testosterone may ↑ the hypoglycaemic activities of Albiglutide.

Alogliptin - Testosterone may ↑ the hypoglycaemic activities of Alogliptin.

Betamethasone - Betamethasone may ↑ the fluid retaining activities of Testosterone.

Bromocriptine - Testosterone may ↑ the hypoglycaemic activities of Bromocriptine.

C1 Esterase Inhibitor (Human) - Testosterone may ↑ the thrombogenic activities of C1 Esterase Inhibitor (Human).

Canagliflozin - Testosterone may ↑ the hypoglycaemic activities of Canagliflozin.

Chlorpropamide - Testosterone may ↑ the hypoglycaemic activities of Chlorpropamide.

Corticotropin - Corticotropin may ↑ the fluid retaining activities of Testosterone.

Cortisone acetate - Cortisone acetate may ↑ the fluid retaining activities of Testosterone.

Cyclosporine - Testosterone may ↑ the hepatotoxic activities of Cyclosporine.

Dapagliflozin - Testosterone may ↑ the hypoglycaemic activities of Dapagliflozin.

Dehydroepiandrosterone - The risk or severity of adverse effects can be ↑d when Dehydroepiandrosterone is combined with Testosterone.

Dexamethasone - Dexamethasone may ↑ the fluid retaining activities of Testosterone.

Dicoumarol - Testosterone may ↑ the anticoagulant activities of Dicoumarol.

Disopyramide - Testosterone may ↑ the hypoglycaemic activities of Disopyramide.
Dulaglutide - Testosterone may ↑ the hypoglycaemic activities of Dulaglutide.
Empagliflozin - Testosterone may ↑ the hypoglycaemic activities of Empagliflozin.
Erythromycin - Testosterone may ↑ the hypoglycaemic activities of Erythromycin.
Exenatide - Testosterone may ↑ the hypoglycaemic activities of Exenatide.
Fludrocortisone - Fludrocortisone may ↑ the fluid retaining activities of Testosterone.
Gliclazide - Testosterone may ↑ the hypoglycaemic activities of Gliclazide.
Glimepiride - Testosterone may ↑ the hypoglycaemic activities of Glimepiride.
Glipizide - Testosterone may ↑ the hypoglycaemic activities of Glipizide.
Glyburide - Testosterone may ↑ the hypoglycaemic activities of Glyburide.
Hydrocortisone - Hydrocortisone may ↑ the fluid retaining activities of Testosterone.
Inhaled Insulin - Testosterone may ↑ the hypoglycaemic activities of inhaled insulin.
Insulin Aspart - Testosterone may ↑ the hypoglycaemic activities of Insulin Aspart.
Insulin degludec - Testosterone may ↑ the hypoglycaemic activities of Insulin degludec.
Insulin Detemir - Testosterone may ↑ the hypoglycaemic activities of Insulin Detemir.
Insulin Glargine - Testosterone may ↑ the hypoglycaemic activities of Insulin Glargine.
Insulin Glulisine - Testosterone may ↑ the hypoglycaemic activities of Insulin Glulisine.
Insulin Lispro - Testosterone may ↑ the hypoglycaemic activities of Insulin Lispro.
Insulin Regular - Testosterone may ↑ the hypoglycaemic activities of Insulin Regular.
Lanreotide - Testosterone may ↑ the hypoglycaemic activities of Lanreotide.
Liraglutide - Testosterone may ↑ the hypoglycaemic activities of Liraglutide.
Mecasermin - Testosterone may ↑ the hypoglycaemic activities of Mecasermin.
Metformin - Testosterone may ↑ the hypoglycaemic activities of Metformin.
Methylprednisolone - Methylprednisolone may ↑ the fluid retaining activities of Testosterone.
Mifepristone - Testosterone may ↑ the hypoglycaemic activities of Mifepristone.
Miglitol - Testosterone may ↑ the hypoglycaemic activities of Miglitol.

Nateglinide - Testosterone may ↑ the hypoglycaemic activities of Nateglinide.
Octreotide - Testosterone may ↑ the hypoglycaemic activities of Octreotide.
Pasireotide - Testosterone may ↑ the hypoglycaemic activities of Pasireotide.
Pentamidine - Testosterone may ↑ the hypoglycaemic activities of Pentamidine.
Pioglitazone - Testosterone may ↑ the hypoglycaemic activities of Pioglitazone.
Pramlintide - Testosterone may ↑ the hypoglycaemic activities of Pramlintide.
Prednisolone - Prednisolone may ↑ the fluid retaining activities of Testosterone.
Prednisone - Prednisone may ↑ the fluid retaining activities of Testosterone.
Quinine - Testosterone may ↑ the hypoglycaemic activities of Quinine.
Repaglinide - Testosterone may ↑ the hypoglycaemic activities of Repaglinide.
Repository corticotropin - Repository corticotropin may ↑ the fluid retaining activities of Testosterone.
Rosiglitazone - Testosterone may ↑ the hypoglycaemic activities of Rosiglitazone.
Saxagliptin - Testosterone may ↑ the hypoglycaemic activities of Saxagliptin.
Sitagliptin - Testosterone may ↑ the hypoglycaemic activities of Sitagliptin.
Sulfadiazine - Testosterone may ↑ the hypoglycaemic activities of Sulfadiazine.
Sulfamethoxazole - Testosterone may ↑ the hypoglycaemic activities of Sulfamethoxazole.
Sulfisoxazole - Testosterone may ↑ the hypoglycaemic activities of Sulfisoxazole.
Sunitinib - Testosterone may ↑ the hypoglycaemic activities of Sunitinib.
Tolazamide - Testosterone may ↑ the hypoglycaemic activities of Tolazamide.
Tolbutamide - Testosterone may ↑ the hypoglycaemic activities of Tolbutamide.
Triamcinolone - Triamcinolone may ↑ the fluid retaining activities of Testosterone.
Trimethoprim - Testosterone may ↑ the hypoglycaemic activities of Trimethoprim.
Warfarin - Testosterone may ↑ the anticoagulant activities of Warfarin (drugbank, 2015d).

Drug-food

Licorice - May ↓ testosterone level. Avoid use (Abramovitz, 2016).

Effects on Lab Test Results

- May ↑ sodium, potassium, phosphate, cholesterol, liver enzyme, calcium, creatinine, and serum prostate-specific antigen (PSA) levels.
- May ↓ thyroxine-binding globulin, total T4 levels, serum creatinine, and 17-ketosteroid levels.
- May ↑ RBC count and resin uptake of T3 and T4.
- May cause abnormal glucose tolerance test results (Abramovitz, 2016).

Long term monitoring

Before initiating Sustanon 250 for female-to-male transsexuals, specialist assessment should be undertaken, including psychiatric assessment. A complete personal and medical history should be taken. During treatment, periodic check-ups are recommended of a frequency and nature adapted to the individual. The following should be monitored -

- signs of osteoporosis,
- changes in lipid profile.

In patients with a personal or family history of breast cancer and with a personal history of endometrial cancer, careful monitoring should be undertaken.

Subject to specialist advice, hysterectomy and bilateral oophorectomy should be considered after 18-24 months of testosterone treatment, to reduce the possible increased risk of endometrial and ovarian cancer.

Continued surveillance is required to detect osteoporosis in patients who have undergone oophorectomy, as testosterone may not fully reverse the decline in bone density in these patients.

Continued surveillance is required to detect endometrial and ovarian cancer in patients on long term treatment who have not proceeded to hysterectomy and bilateral oophorectomy (emc, 2015).

In elderly people

There is limited experience on the safety and efficacy of the use of Sustanon 250 in patients over 65 years of age. Currently, there is no consensus about age specific testosterone reference values. However, it should be taken into account that physiologically testosterone serum levels are lower with increasing age (emc, 2015).

Overdose

The acute intramuscular toxicity of Sustanon 100 or 250 is very low. Priapism in men is a symptom of chronic overdose. If this occurs, Sustanon treatment should be interrupted and, after disappearance of the symptom, be resumed at a lower dose.

Andropatch = This is not likely due to the mode of administration.

Serum testosterone has a half-life of 70 minutes and therefore falls rapidly once the Andropatch 2.5mg or 5mg Systems are removed. Only one case of acute testosterone overdose following an injection has been reported in the literature. This was a case of a cerebrovascular accident in a patient with a high plasma testosterone concentration of 114 ng/ml (395 nmol/l). It would be most unlikely that such plasma testosterone concentrations be achieved using the transdermal route (emc, 2016).

Note

In the United States, the possession and distribution of anabolic steroids, such as testosterone, is a felony offense unless prescribed by a physician for medical use. The **Steroid Control Act of 1990** made the use of anabolic steroids for the purpose of performance enhancement illegal. This legislation would be enhanced and strengthened by the **Steroid Control Act of 2004** and again in 2014 under the **Designer Steroid Control Act of 2014**. Failure to abide by the guidelines enacted by the aforementioned legislation can lead to severe punishments including fines and prison sentences. Such punishments can range from charges of simple possession, to distribution and the intent to distribute.

As the federal government's war on steroids has increasingly gained fire, the enforcement of the legislation has followed suit with many otherwise law-abiding citizens finding themselves in the presence of the courts in disastrous ways. U.S. federal law classifies anabolic androgenic steroids, and testosterone, as Schedule III controlled substances. Schedule III classification puts anabolic steroids in the same category as barbiturates and LSD precursors.

In the U.S. there are five classes of scheduled drugs and they are as follows:

Schedule I - Drugs with no viable medical purpose and that have a high rate of both dependency and abuse that can in turn lead to severe physical damage.

Schedule II - Drugs that while possessing a viable medical purpose have a high potential for abuse and dependency and can in turn lead to severe physical damage.

Schedule III - Drugs that possess a viable medical purpose but do carry with them the risk of dependency and physical damage but to a lesser extent than compared to Schedule II drugs.

Schedule IV - Drugs that carry with them a viable medical purpose but only a slight potential for abuse and very limited physical damage or dependency.

Schedule V - Drugs that carry with them a viable medical purpose but only a slight potential for abuse and very limited to physical damage or dependency to an even lesser degree than Schedule IV drugs (unknown, 2014i).

What this means is that in the USA you are unable to get testosterone unless it is prescribed by a Doctor. You may be lucky and be able to buy it from an offshore internet pharmacy, but if it is intercepted by US Customs, then it will be confiscated and you will never receive it! You may also have a visit from the local police asking questions about it too!

Shelf Life

Sustanon is 5 years, Andropatch is 24 months, Testogel is 3 years (emc, 2016).

Warning

Both of these injections contain arachis oil, so if you have a nut allergy then do NOT take (BNF, 2016a).

Blood results

See Testosterone.

Chapter 7

DHT-blockers

Dutasteride

What is it?

Dutasteride is a 5 α-reductase enzyme inhibitor. It works by lowering levels of a hormone called dihydrotestosterone (DHT), which is a major cause of prostate growth. Lowering DHT leads to shrinkage of the enlarged prostate gland (drugs.com, 2014a).

Dutasteride belongs to a class of drugs called 5-alpha-reductase inhibitors, which block the action of the 5-alpha-reductase enzymes that convert testosterone into dihydrotestosterone (DHT). Finasteride also belongs to this group, but while dutasteride inhibits both isoforms of 5-alpha reductase, finasteride inhibits only one. Even so, a clinical study done by GlaxoSmithKline, the EPICS trial, did not find dutasteride to be more effective than finasteride in treating Benign Prostatic Hyperplasia (BPH).

Also known as

Avodart, Dutasterid in Germany, Dutasterida in Spain.

Manufacturer

Avodart = GlaxoSmithKline (BNF, 2016a).

Contains

Dutasteride 500 mcgs [38], a yellow capsule (BNF, 2016a). The capsules are opaque, yellow, oblong soft gelatin capsules imprinted with GX CE2 on one side in red ink (Abramovitz, 2016). They also contain mono- and diglycerides of caprylic/capric acid, butylhydroxytoluene (E321), with the capsule shell containing gelatin, glycerol, titanium dioxide (E171), iron oxide yellow (E172), triglycerides, medium chain, and lecithin. The red printing ink containing iron oxide red (E172) as the colourant, polyvinyl acetate phthalate, propylene glycol and polyethylene glycol (emc, 2016).

Pharmacology

Inhibits the conversion of testosterone to 5-α-dihydrotestosterone, a potent androgen (drugs.com, 2014a).

Indications

Used for treatment of benign prostatic hyperplasia (BNF, 2016a), and (anecdotally) for treatment of male pattern baldness.

Pharmacodynamics

Dutasteride is a synthetic 4-azasteroid compound that is a selective inhibitor of both the type 1 and type 2 isoforms of steroid 5 alpha-reductase (5AR), intracellular enzymes that convert testosterone to 5 alpha-dihydrotestosterone DHT. Type I 5a-reductase is predominant in the sebaceous glands of most regions of skin, including scalp, and liver. Type I 5a-reductase is responsible for approximately one-third of circulating DHT. The Type II 5a-reductase isozyme is primarily found in prostate, seminal vesicles, epididymides, and hair follicles as well as liver, and is responsible for two-thirds of circulating DHT (drugbank, 2013b).

How it works

Dutasteride inhibits the conversion of testosterone to 5 alpha-dihydrotestosterone (DHT), which is the androgen primarily responsible for the initial development and subsequent enlargement of the prostate gland. Testosterone is converted to DHT by the enzyme 5 alpha-reductase, which exists as 2 isoforms, type 1 and type 2. Dutasteride is a competitive and specific inhibitor of both type 1 and type 2 5 alpha-reductase isoenzymes,

[38] micrograms

with which it forms a stable enzyme complex. Dissociation from this complex has been evaluated under in-vitro[39] and in-vivo[40] conditions and is extremely slow. Dutasteride does not bind to the human androgen receptor (drugbank, 2013b).

Pharmacokinetics

Following oral administration of a single 0.5 mg dutasteride dose, the time to peak serum concen- trations of dutasteride is 1 to 3 hours. The absolute bioavailability is approximately 60%. The bioavailability of dutasteride is not affected by food (emc, 2016).

Dutasteride is highly bound to plasma proteins greater than 99.5%. Following daily dosing, dutasteride serum concentrations achieve 65% of steady state concentration after 1 month and approximately 90% after 3 months.

Steady state serum concentrations (steady state serum concentrations (CSS) [41]) of approximately 40 ng/mL are achieved after 6 months of dosing 0.5mg once a day. Dutasteride partitioning from serum into semen averaged 11.5% (emc, 2016). Following oral dosing of dutasteride 0.5 mg/day to steady state, 1.0% to 15.4% (mean of 5.4%) of the administered dose is excreted as unchanged dutasteride in the faeces. The remainder is excreted in the faeces as 4 major metabolites comprising 39%, 21%, 7%, and 7% each of drug- related material and 6 minor metabolites (less than 5% each). Only trace amounts of unchanged dutasteride (less than 0.1% of the dose) are detected in human urine.

The elimination of dutasteride is dose dependent and the process appears to be described by two elimination pathways in parallel, one that is saturable at clinically relevant concentrations and one that is non-saturable.

At low serum concentrations (less than 3ng/mL), dutasteride is cleared rapidly by both the concentration dependent and concentration independent elimination pathways. Single doses of 5 mg or less showed evidence of rapid clearance and a short half-life of 3 to 9 days.

At therapeutic concentrations, following repeat dosing of 0.5 mg/day, the slower, linear elimination pathway is dominating and the half-life is approximately 3–5 weeks (emc, 2016).

Elimination - Dutasteride is extensively metabolized in humans. Dutasteride and its metabolites were excreted mainly in faeces.
Half life - 5 weeks (drugbank, 2013b).

[39] outside the body

[40] within the living organism

[41] steady state serum concentrations

Pharmacodynamics

The onset is rapid, with a peak within 2–3 hours. Its mechanism of action inhibits types I and II 5-alpha-reductase, interfering with the conversion of testosterone to 5-α-dihydrotestosterone. It is excreted in the faeces 45% (5% unchanged), urine $< 1\%$, and with a half-life of about 5 weeks (Abramovitz, 2016).

Typical dosage

Pre-op - 0.5mg/day.
Post-op - Not needed.

Route

Orally.

Contraindications

Should not be taken by women, children or adolescents (BNF, 2016a). Avodart is contraindicated in patients with hypersensitivity to dutasteride, other 5-alpha reductase inhibitors, or any of the excipients. Avodart is also contraindicated in patients with severe hepatic impairment (emc, 2016).

Side-effects

Genito-Urinary

- Erectile dysfunction,
- decreased libido,
- ejaculation disorder (Abramovitz, 2016).
- **Semen volume decreased**,
- **Penile size decreased**,
- **urine flow decreased** (rxisk, 2016b).

Other

- **Gynaecomastia** (Abramovitz, 2016).
- **Nipple pain** (rxisk, 2016b).

The most frequently observed adverse effects with Avodart were **impotence** (6.0%), **decreased libido** (3.7%), **ejaculation disorders** (e.g., decrease in volume) (1.8%), **breast tenderness**, and **breast enlargement** (1.3%). Most of these effects tended to decrease over time (unknown, 2015b).

Interactions

Drug-drug

- **CYP3A4 inhibitors (such as cimetidine, ciprofloxacin, diltiazem, ketoconazole, ritonavir, verapamil)** - May increase dutasteride level. Use together cautiously (Abramovitz, 2016).

Atazanavir - The serum concentration of Dutasteride can be ↑ when it is combined with Atazanavir.
Boceprevir - The serum concentration of Dutasteride can be ↑ when it is combined with Boceprevir.
Ceritinib - The serum concentration of Dutasteride can be ↑ when it is combined with Ceritinib.
Clarithromycin - The serum concentration of Dutasteride can be ↑ when it is combined with Clarithromycin.
Cobicistat - The serum concentration of Dutasteride can be ↑ when it is combined with Cobicistat.
Darunavir - The serum concentration of Dutasteride can be ↑ when it is combined with Darunavir.
Idelalisib - The serum concentration of Dutasteride can be ↑ when it is combined with Idelalisib.
Indinavir - The serum concentration of Dutasteride can be ↑ when it is combined with Indinavir.
Itraconazole - The serum concentration of Dutasteride can be ↑ when it is combined with Itraconazole.
Ketoconazole - The serum concentration of Dutasteride can be ↑ when it is combined with Ketoconazole.
Nefazodone - The serum concentration of Dutasteride can be ↑ when it is combined with Nefazodone.
Nelfinavir - The serum concentration of Dutasteride can be ↑ when it is combined with Nelfinavir.
Posaconazole - The serum concentration of Dutasteride can be ↑ when it is combined with Posaconazole.
Ritonavir - The serum concentration of Dutasteride can be ↑ when it is combined with Ritonavir.
Saquinavir - The serum concentration of Dutasteride can be ↑ when it is combined with Saquinavir.
Telaprevir - The serum concentration of Dutasteride can be ↑ when it is combined with Telaprevir.
Telithromycin - The serum concentration of Dutasteride can be ↑ when it is combined with Telithromycin.
Voriconazole - The serum concentration of Dutasteride can be ↑ when it is combined with Voriconazole (drugbank, 2013b).

Effects on Lab Test Results

May lower prostate-specific antigen PSA [42] level (Abramovitz, 2016).

Overdose

In volunteer studies of Avodart, single daily doses of dutasteride up to 40 mg/day (80 times the therapeutic dose) have been administered for 7 days without significant safety concerns. In clinical studies, doses of 5mg daily have been administered to subjects for 6 months with no additional adverse effects to those seen at therapeutic doses of 0.5 mg. There is no specific antidote for Avodart, therefore, in suspected overdosage symptomatic and supportive treatment should be given as appropriate (emc, 2016).

Note

Women of childbearing potential should avoid handling crushed, broken or leaking capsules of dutasteride, as it can be absorbed through the skin (BNF, 2016a), dutasteride may inhibit development of the exterior genitalia of a male foetus; therefore, pregnant women should not come into contact with the drug as it can be absorbed through the skin (unknown, 2015b). If contact is made then the affected area should be washed immediately with soap and water (emc, 2016).

Alert

This drug is considered a teratogen[43]. Follow safe-handling procedures when preparing, administering, or dispensing drug (Abramovitz, 2016).

Finasteride

An orally active testosterone 5-alpha-reductase inhibitor. It is used as a surgical alternative for treatment of benign prostatic hyperplasia (drugbank, 2013d).

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[42] prostate specific antigen which is a marker for prostate cancer. The higher the PSA level the greater the chance you have prostate cancer

[43] Any substance that causes birth defects

Also known as

Proscar, Propecia, Finasterid in Germany, Finastéride in France, Finasterida in Spain.

Manufacturer

Merck Sharp & Dohme Ltd [MSD]

Contains

Proscar - Finasteride 5mgs in blue-coloured, apple-shaped, film coated tablets marked 'Proscar' on one side and 'MSD 72' on the other (emc, 2016).

Propecia - Finasteride 1mg. in a film-coated tablet. Tan octagonal, film-coated, convex tablets, marked with a 'P' logo on one side and 'PROPECIA' on the other (emc, 2016).

Pharmacology

A specific inhibitor of the enzyme 5a-reductase that metabolises testosterone into the more potent androgen, dihydrotestosterone (BNF, 2016a).

Indications

Benign prostatic enlargement (BNF, 2016a), male-pattern baldness in men (BNF, 2016a).

How it works

The mechanism of action of Finasteride is based on its preferential inhibition of Type II 5a-reductase through the formation of a stable complex with the enzyme. Inhibition of Type II 5a-reductase blocks the peripheral conversion of testosterone to DHT, resulting in significant decreases in serum and tissue DHT concentrations, minimal to moderate increase in serum testosterone concentrations, and substantial increases in prostatic testosterone concetrations. As DHT appears to be the principal androgen responsible for stimulation of prostatic growth, a decrease in DHT concentrations will result in a decrease in prostatic volume (approximately 20-30% after 6-24 months of continued therapy). In men with androgenic alopecia, the mechanism of action has not been fully determined, but finasteride has shown to decrease scalp DHT concentration to the levels found in hairy scalp, reduce serum DHT, increase hair regrowth, and slow hair loss (drugbank, 2013d).

Pharmacodynamics

Finasteride is a synthetic 4-azasteroid compound. This drug is a competitive and specific inhibitor of Type II 5a-reductase, an intracellular enzyme that converts the androgen testosterone into 5-dihydrotestosterone (DHT). Two distinct isozymes are found in mice, rats, monkeys, and humans: Type I and II. Each of these isozymes is differentially expressed in tissues and developmental stages. In humans, Type I 5a-reductase is predominant in the sebaceous glands of most regions of skin, including scalp, and liver. Type I 5a-reductase is responsible for approximately one-third of circulating DHT. The Type II 5a-reductase isozyme is primarily found in prostate, seminal vesicles, epididymides, and hair follicles as well as liver, and is responsible for two-thirds of circulating DHT. Although finasteride is 100-fold more selective for type II 5a-reductase than for the type I isoenzyme, chronic treatment with this drug may have some effect on type I 5a-reductase (drugbank, 2013d).

Pharmacokinetics

Finasteride is variably absorbed following oral administration, with a mean bioavailability of about 63% (RxList, 2014), peak plasma concentrations are achieved 1-2 hours after taking an oral dose. It is metabolised in the liver, and excreted in the urine and faeces as its metabolites. The mean half- life is 6 hours in patients less than 60 years, but may be prolonged to about 8 hours in patients older than 70 years (TGC, 2015a), and in some patients up to about 15 hours (RxList, 2014). 39% excreted in the urine, and 57% excreted in the faeces (RxList, 2014), and it is also excreted in the semen (BNF, 2016a).

Elimination - Following an oral dose of 14C-finasteride in man (n = 6), a mean of 39% (range, 32 to 46%) of the dose was excreted in the urine in the form of metabolites; 57% (range, 51 to 64%) was excreted in the faeces. Urinary excretion of metabolites was decreased in patients with renal impairment. This decrease was associated with an increase in faecal excretion of metabolites.

Half life - 4.5 hours (range 3.3-13.4 hours)

Clearance - 165 mL/min [healthy young subjects] (drugbank, 2013d).

Typical dosage

Pre-op - 0.05–1 mg/day

Post-op - 0.05–1 mg/day (unknown, 2005).

Route

Oral - Tablets - Proscar, Propecia.

Contraindications

Hypersensitivity to any component of this product; women who are or may potentially be pregnant; children (emc, 2016).

Side-effects

Central Nervous System

- **Dizziness**,
- asthenia,
- headache (Abramovitz, 2016).

Cardiovascular

- Hypotension,
- **orthostatic hypotension** (Abramovitz, 2016).

Genitourinary

- Erectile dysfunction,
- decreased volume of ejaculate,
- decreased libido (Abramovitz, 2016).
- **Semen volume decreased**,
- **Hypogonadism**,
- **Sexual dysfunction**,
- **Ejaculation disorder**,
- **Ejaculation failure**,
- **Testicular pain**,
- **Loss of libido** (rxisk, 2016c).

Other

- **Gynaecomastia** (Abramovitz, 2016).

Interactions

Drug-herb

- **St. John's wort** - May ↓ finasteride level. Avoid use together (Abramovitz, 2016).

Effects on Lab Test Results

May ↓ prostate-specific antigen (PSA) level (Abramovitz, 2016).

Patient Teaching

Tell patient that drug may be taken with or without meals.

Warn woman who is or may become pregnant not to handle crushed tablets because of risk of adverse effects on male foetus.

Inform patient that signs of improvement may require at least 3 months of daily use when drug is used to treat hair loss.

Reassure patient that drug may decrease volume of ejaculate without impairing normal sexual function.

Instruct patient to report breast changes, such as lumps, pain, or nipple discharge (Abramovitz, 2016).

Note

Propecia results may not occur for 3 months.
Proscar results may not occur for 6–12 months (Abramovitz, 2016).

Warning

Finasteride may produce genital abnormalities in the male foetus, and therefore crushed or broken tablets should not be handled by females who are or may become pregnant (Abramovitz, 2016). Women of childbearing potential should avoid handling crushed or broken tablets of finasteride (BNF, 2016a).

Chapter 8

Anti-androgens

Bicalutamide

What is it?

Bicalutamide is an oral non-steroidal anti-androgen[44]. It binds to the androgen receptor and works by blocking the action of testosterone.

Administration

Oral, as tablets

Also known as

Casodex, Bicalutamid in Germany, and Bicalutamida in Spain.

Manufacturer

Zentiva, and Winthrop Pharmaceuticals.

Contains

Contents of one 50mg bicalutamide tablet -

- Tablet core - Lactose monohydrate, Povidone K-29/32, Crospovidone (type A), Sodium lauryl sulphate, Magnesium stearate
- Film-coating - Lactose monohydrate, Hypromellose, Titanium dioxide (E171), Macrogol 4000 (emc, 2016).

[44] counteracts the effects of androgens on various body organs and tissues

Pharmacology

Bicalutamide acts as a pure anti-androgen by binding to the androgen receptor (AR) and preventing the activation of the AR[45] and subsequent upregulation of androgen responsive genes by androgenic hormones (wikipedia, 2014a).

Pharmacodynamics

Bicalutamide is an antineoplastic hormonal agent primarily used in the treatment of prostate cancer. Bicalutamide is a pure, nonsteroidal anti-androgen with affinity for androgen receptors (but not for progestogen, oestrogen, or glucocorticoid receptors). Consequently, Bicalutamide blocks the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue. Prostate cancer is mostly androgen-dependent and can be treated with surgical or chemical castration. To date, antiandrogen monotherapy has not consistently been shown to be equivalent to castration (drugbank, 2013a).

How it works

Bicalutamide competes with androgen for the binding of androgen receptors, consequently blocking the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue (drugbank, 2013a).

Indications

Used for treating prostate cancer, used in combination with a luteinizing-hormone releasing hormone LHRH[46] analog (eg, goserelin, leuprolide). Also used to treat hirsutism (unknown, 2014a).

Pharmacokinetics

Half-Life - 5–8 days
Peak plasma time - 31 hours
Peak plasma concentration - 0.77 mcg/mL
Protein Bound - 96%
Excretion - Urine (36%), faeces (42%)(Medscape, 2014).

[45] androgen receptor

[46] luteinizing-hormone releasing hormone

Metabolism - Bicalutamide undergoes stereo specific metabolism. The S (inactive) isomer is metabolised primarily by glucuronidation. The R (active) isomer also undergoes glucuronidation but is predominantly oxidised to an inactive metabolite followed by glucuronidation.
Clearance - Apparent oral cl=0.32 L/h [Normal Males] (drugbank, 2013a).

Typical Dosage

Pre-op - 25mgs every other day
Post-op - not needed.

Route

Oral.

Contraindications

Not to be taken if 'lomitapide' is currently prescribed. Do not take if you are hypersensitive to any of its contents, nor if you are female and with the possibility of getting pregnant, as it is teratogenic.

Side-effects

- **Back pain - 15%**,
- **pelvic pain - 13%**,
- **stomach pain**, or
- **general body pain - 27%**,
- **headache**,
- **weakness**,
- **asthenia - 15%**[47], and
- infection - 10%.
- **abdominal pain**, and
- **flu syndrome** have also been reported (Abramovitz, 2016).
- **extreme tiredness**,
- **lack of energy**, and
- **loss of appetite** (medlineplus, 2015b).

Gastrointestinal

- **constipation - 17%**,
- **diarrhoea - 10%**,
- **flatulence**,
- **nausea - 11%**,
- **stomach upset** (Abramovitz, 2016).

Cardiovascular

- **hot flashes - 49%**

[47] Weakness, lack of energy and strength

Hepatic

Hepatic side effects including severe liver injury leading to hospitalisation and death have been reported rarely. Hepatitis or marked increases in liver enzymes leading to drug discontinuation have been reported in approximately 1% of bicalutamide patients. One case of fulminant hepatic failure associated with bicalutamide use has also been reported.

Increased values in liver enzyme tests include increased AST, ALT, or both. This effect has occurred in approximately 6% of treated patients (Abramovitz, 2016).

Genitourinary

- **nocturia**,
- **impotence** (Abramovitz, 2016)
- haematuria,
- urinary tract infection, and
- urinary incontinence,
- **PSA increased** (rxisk, 2016a)

Metabolic

- **Peripheral oedema**,
- **hyperglycaemia**, and
- **weight loss** (Abramovitz, 2016)
- **jaundice** (medlineplus, 2015b)

Haematologic

- Anaemia (7%) and
- decreased white blood cell counts (Abramovitz, 2016).

Renal

New or worsened renal insufficiency (as measured by elevated BUN[48] and creatinine) have been reported (Abramovitz, 2016).

Nervous system

- **insomnia**,
- **dizziness** (Abramovitz, 2016)

[48]This stands for blood urea nitrogen. Urea nitrogen is what is formed when protein breaks down. This test is often done to check kidney function

Respiratory

Dyspnoea. Uncommon cases of interstitial lung disease, including interstitial pneumonitis and pulmonary fibrosis have been reported with the use of bicalutamide. One case of pneumonitis has also been reported (Abramovitz, 2016)

Dermatological

- **sweating** (Abramovitz, 2016)
- **unusual bleeding or bruising** (medlineplus, 2015b)

Other

In one phase II clinical trial with bicalutamide used as a single agent -

- **breast tenderness - 63.4%**,
- **breast swelling - 52.5%**, and
- **hot flashes - 23.6%** were reported respectively (unknown, 2014a),

Another phase II clinical trial with bicalutamide used as a single agent reported -

- **breast pain - 76%**, and
- **gynaecomastia - 60%** of treated patients, respectively. This study also showed
- **generalized pain - 30%** of treated patients,
- **hot flashes - 28%**,
- **pelvic pain - 26%**, and
- **libido decrease - 25%** and
- **impotence - 25%** (unknown, 2014a).

Interactions

Although the usage of warfarin is not contra-indicated, you should be monitored closely.

Acenocoumarol - The serum concentration of Acenocoumarol can be ↑ when it is combined with Bicalutamide.

Aripiprazole - The serum concentration of Aripiprazole can be ↑ when it is combined with Bicalutamide.

Astemizole - The serum concentration of Astemizole can be ↑ when it is combined with Bicalutamide.

Capromab - Bicalutamide may ↓ effectiveness of Capromab as a diagnostic agent.

Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Bicalutamide.

Cisapride - The serum concentration of Cisapride can be ↑ when it is combined with Bicalutamide.
Dicoumarol - The serum concentration of Dicoumarol can be ↑ when it is combined with Bicalutamide.
Dofetilide - The serum concentration of Dofetilide can be ↑ when it is combined with Bicalutamide.
Flibanserin - The serum concentration of Flibanserin can be ↑ when it is combined with Bicalutamide.
Hydrocodone - The serum concentration of Hydrocodone can be ↑ when it is combined with Bicalutamide.
Lomitapide - The serum concentration of Lomitapide can be ↑ when it is combined with Bicalutamide.
Nimodipine - The serum concentration of Nimodipine can be ↑ when it is combined with Bicalutamide.
Pimozide - The serum concentration of Pimozide can be ↑ when it is combined with Bicalutamide.
Porfimer - Bicalutamide may ↑ the photosensitizing activities of Porfimer.
Terfenadine - The serum concentration of Terfenadine can be ↑ when it is combined with Bicalutamide.
Verteporfin - Bicalutamide may ↑ the photosensitizing activities of Verteporfin.
Warfarin - The serum concentration of Warfarin can be ↑ when it is combined with Bicalutamide (drugbank, 2013a).

Clinical assessment

LFT[49] at baseline, regular intervals for 4 months, then periodically (Medscape, 2014).

Overdose

No case of overdose has been reported. There is no specific antidote, and any treatment should be symptomatic. Dialysis is unlikely to be helpful, since bicalutamide is highly protein bound and is not recovered unchanged in the urine. General supportive care, including frequent monitoring of vital signs, is indicated (emc, 2016).

Shelf Life

Five years (emc, 2016).

[49] liver function test

Note

Bicalutamide is extensively metabolised in the liver. Data suggests that its elimination may be slower in people with severe hepatic impairment and this could lead to increased accumulation of bicalutamide. Therefore, bicalutamide should be used with caution in patients with moderate to severe hepatic impairment.

Periodic liver function testing should be considered due to possibility of hepatic changes. The majority of changes are expected to occur within the first 6 months of bicalutamide therapy.

Severe hepatic changes and hepatic failure have been observed rarely with bicalutamide, and fatal outcomes have been reported. Bicalutamide therapy should be discontinued if changes are severe.

Warning

Bicalutamide is a teratogen and must not be handled by females who are or may become pregnant. It is known to cause foetal harm.

Cyproterone Acetate

What is it?

Cyproterone acetate, sometimes abbreviated as CPA, and sold under brand names such as Androcur and Cyprostat, is a synthetic steroidal antiandrogen drug with additional progestogen and antigonadotropic properties (Neumann and Topert, 1986). Its primary action is to suppress the activity of the androgen hormones such as testosterone and its more potent metabolite dihydrotestosterone (DHT) in the body, effects which it mediates via competitive antagonism of the androgen receptor and inhibition of enzymes in the androgen biosynthesis pathway. The main therapeutic indications of cyproterone acetate are prostate cancer, benign prostatic hyperplasia, priapism, hypersexuality (e.g., as a form of chemical castration), and other conditions in which androgen action maintains the disease process. In addition, it can also be used to treat acne and hirsutism in females, and is a common component in hormone therapy for transsexual women.

An anti-androgen that, in the form of its acetate (cyproterone acetate), also has progestational properties. It is used in the treatment of hypersexuality in males, as a palliative in prostatic carcinoma, and, in combination with oestrogen, for the therapy of severe acne and hirsutism in females (drugbank, 2014a).

Administration

Administration is oral in the form of tablets, or by intramuscular injection.

Also known as

Androcur, Cyprostat, Dianette, Siterone in USA, Diane-35 in Canada, and Dixi-35 in Chile.

Manufacturer

- Androcur = Schering Health.
- Cyprostat = Schering Health.
- Dianette = Schering Health.

Contains

Cyproterone Acetate 50 mgs, 100mgs
Androcur also contains lactose, maize starch, povidone 25 000, silicon dioxide (aerosil) (E551), magnesium stearate (E572) (emc, 2016).

Cyprostat also contains maize starch, povidone 25 000, magnesium stearate (E572), lactose, aerosil (Cyprostat 50mg only) (emc, 2016).

Dianette contains 2mgs of cyproterone acetate and 35 mcgs of ethinylestradiol. It also contains lactose, maize starch, povidone, talc, magnesium stearate (E 572), sucrose, polyethylene glycol 6,000, calcium carbonate (E 170), titanium dioxide (E 171), glycerol 85%, montan glycol wax, yellow ferric oxide pigment (E 172) (emc, 2016).

Pharmacology

Cyproterone acetate competes with testosterone at receptor sites, inhibits the synthesis of testosterone both in testes and the adrenals thus causing a decrease in plasma testosterone levels and suppresses the secretion of gonadotrophins thus preventing a re-elevation of testosterone by a bio-feedback mechanism (emc, 2016). Antigonadotropic, and androgenreceptor blocker (James, 2014). It competes with testosterone at prostatic receptors (Mackenzie, Downie, and A. Williams, 2004). It also has progestogenic activity, which exerts a negative feedback effect on hypothalamic receptors, so leading to a reduction in gonadotrophin release, and hence to diminished production of testicular androgens. Sexual drive and potency are reduced and gonadal function is inhibited. An occasional tendency for the prolactin levels to increase slightly has been observed under higher doses of cyproterone acetate (emc, 2016).

Pharmacodynamics

Cyproterone is an antiandrogen. It suppresses the actions of testosterone (and its metabolite dihydrotestosterone) on tissues. It acts by blocking androgen receptors which prevents androgens from binding to them and suppresses luteinizing hormone (which in turn reduces testosterone levels) (drugbank, 2014a).

Pharmacokinetics

Absorption - Completely absorbed following oral administration (drugbank, 2014a).
Bioavailability - 100%,
Protein binding - 96%,
Metabolism - hepatic (unknown-wikipedia, 2014).
Half-life - following oral administration - plasma half-life is 38 hours, following intramuscular injection - plasma half-life is 96 hours (**0327**),
Excretion - 60% bile, 33% renal (unknown-wikipedia, 2014).

Cyproterone Acetate is absorbed from the gastrointestinal tract. Peak plasma concentrations are achieved in 3–4 hours and decrease rapidly during the first 24 hours because of tissue distribution and excretion. The plasma half-life is about 38 hours. Excreted in the faeces and urine as the unchanged drug and its metabolites (TGC, 2015a). Following oral administration, cyproterone acetate is completely absorbed over a wide dose range. The ingestion of two cyproterone acetate 50 mg tablets gives maximum serum levels of about 285 ng/ml at about 3 hours. Thereafter, drug serum levels declined during a time interval of typically 24 to 120 h, with a terminal half-life of 43.9 +/- 12.8 h.. The total clearance of cyproterone acetate from serum is 3.5+/-1.5 ml/min/kg. Cyproterone acetate is metabolised by various pathways, including hydroxylations and conjugations.

The main metabolite in human plasma is the 15b-hydroxy derivative.

Some drug is excreted unchanged with bile fluid. Most of the dose is excreted in the form of metabolites at a urinary to biliary ratio of 3:7. The renal and biliary excretion proceeds with a half-life of 1.9 days. Metabolites from plasma are eliminated at a similar rate (half-life of 1.7 days).

Cyproterone acetate is almost exclusively bound to plasma albumin. About 3.5–4% of total drug levels are present unbound. Because protein binding is non-specific, changes in SHBG (sex hormone binding globulin) levels do not affect the pharmacokinetics of cyproterone acetate. The absolute bioavailability of cyproterone acetate is almost complete (88% of dose) (emc, 2016).

How it works

The direct anti-androgenic effect of cyproterone is blockage of the binding of dihydrotestosterone to the specific receptors in the body cells. In addition, cyproterone exerts a negative feed-back on the hypothalamo-pituitary axis, by inhibiting the secretion of luteinizing hormone resulting in diminished production of testicular testosterone (drugbank, 2014a).

Typical Dosage

Pre-op - 50–100mgs/day (private emails)
Post-op - Not recommended post-SRS (unknown, 2005).

Route

Tablets = Androcur, Cyprostat, Cyproterone acetate, Dianette.

Contraindications

Hepatic disease, severe diabetes (with vascular changes), sickle-cell anaemia, malignant or wasting disease, severe depression, history of thromboembolic disorders, youths under 18 years (may arrest bone maturation and testicular development) (BNF, 2016a).

Interactions

Abciximab - The therapeutic efficacy of Abciximab can be ↓ when used in combination with Cyproterone acetate.
Acenocoumarol - The therapeutic efficacy of Acenocoumarol can be ↓ when used in combination with Cyproterone acetate.
Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Cyproterone acetate.
Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Cyproterone acetate.
Aminophylline - The serum concentration of Aminophylline can be ↓ when it is combined with Cyproterone acetate.
Amodiaquine - The serum concentration of Amodiaquine can be ↑ when it is combined with Cyproterone acetate.
Aprepitant - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Aprepitant.
Aripiprazole - The serum concentration of Aripiprazole can be ↑ when it is combined with Cyproterone acetate.
Asenapine - The serum concentration of Asenapine can be ↓ when it is combined with Cyproterone acetate.

Atorvastatin - The serum concentration of Atorvastatin can be ↑ when it is combined with Cyproterone acetate.
Betaxolol - The serum concentration of Betaxolol can be ↓ when it is combined with Cyproterone acetate.
Bexarotene - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Bexarotene.
Bortezomib - The serum concentration of Bortezomib can be ↓ when it is combined with Cyproterone acetate.
Bosentan - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Bosentan.
C1 Esterase Inhibitor (Human) - Cyproterone acetate may ↑ the thrombogenic activities of C1 Esterase Inhibitor (Human).
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Cyproterone acetate.
Capromab - Cyproterone acetate may ↓ effectiveness of Capromab as a diagnostic agent.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Cyproterone acetate.
Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Cyproterone acetate.
Citric Acid - The therapeutic efficacy of Citric Acid can be ↓ when used in combination with Cyproterone acetate.
Clomipramine - The serum concentration of Clomipramine can be ↓ when it is combined with Cyproterone acetate.
Clozapine - The serum concentration of Clozapine can be ↓ when it is combined with Cyproterone acetate.
Conivaptan - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Conivaptan.
Dabrafenib - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Dabrafenib.
Dacarbazine - The serum concentration of Dacarbazine can be ↓ when it is combined with Cyproterone acetate.
Dalteparin - The therapeutic efficacy of Dalteparin can be ↓ when used in combination with Cyproterone acetate.
Dasatinib - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Dasatinib.
Deferasirox - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Deferasirox.
Dicoumarol - The therapeutic efficacy of Dicoumarol can be ↓ when used in combination with Cyproterone acetate.
Drospirenone - The serum concentration of Drospirenone can be ↓ when it is combined with Cyproterone acetate.
Duloxetine - The serum concentration of Duloxetine can be ↓ when it is combined with Cyproterone acetate.
Edetic Acid - The therapeutic efficacy of Edetic Acid can be ↓ when used in combination with Cyproterone acetate.
Enoxaparin - The therapeutic efficacy of Enoxaparin can be ↓ when used in combination with Cyproterone acetate.

Estradiol - The serum concentration of Estradiol can be ↓ when it is combined with Cyproterone acetate.
Estropipate - The serum concentration of Estropipate can be ↓ when it is combined with Cyproterone acetate.
Ethanol - The therapeutic efficacy of Cyproterone acetate can be ↓ when used in combination with Ethanol.
Ethyl biscoumacetate - The therapeutic efficacy of Ethyl biscoumacetate can be ↓ when used in combination with Cyproterone acetate.
Fluconazole - The metabolism of Cyproterone acetate can be ↓ when combined with Fluconazole.
Flutamide - The serum concentration of Flutamide can be ↓ when it is combined with Cyproterone acetate.
Fluvastatin - The serum concentration of Fluvastatin can be ↑ when it is combined with Cyproterone acetate.
Fluvoxamine - The serum concentration of Fluvoxamine can be ↓ when it is combined with Cyproterone acetate.
Fondaparinux sodium - The therapeutic efficacy of Fondaparinux sodium can be ↓ when used in combination with Cyproterone acetate.
Fosaprepitant - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Fosaprepitant.
Fusidic Acid - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Fusidic Acid.
Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Cyproterone acetate.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Cyproterone acetate.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Cyproterone acetate.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Cyproterone acetate.
Heparin - The therapeutic efficacy of Heparin can be ↓ when used in combination with Cyproterone acetate.
Idelalisib - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Idelalisib.
Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Cyproterone acetate.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Cyproterone acetate.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Cyproterone acetate.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Cyproterone acetate.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Cyproterone acetate.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Cyproterone acetate.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Cyproterone acetate.

Isoniazid - The serum concentration of Isoniazid can be ↓ when it is combined with Cyproterone acetate.
Ivacaftor - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Ivacaftor.
Lidocaine - The serum concentration of Lidocaine can be ↓ when it is combined with Cyproterone acetate.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Cyproterone acetate.
Lovastatin - The serum concentration of Lovastatin can be ↑ when it is combined with Cyproterone acetate.
Luliconazole - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Luliconazole.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Cyproterone acetate.
Mexiletine - The serum concentration of Mexiletine can be ↓ when it is combined with Cyproterone acetate.
Mifepristone - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Mifepristone.
Mirtazapine - The serum concentration of Mirtazapine can be ↓ when it is combined with Cyproterone acetate.
Mitotane - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Mitotane.
Nelfinavir - The metabolism of Cyproterone acetate can be ↓ when combined with Nelfinavir.
Netupitant - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Netupitant.
Nicotine - The serum concentration of Nicotine can be ↓ when it is combined with Cyproterone acetate.
Norgestimate - The serum concentration of Norgestimate can be ↓ when it is combined with Cyproterone acetate.
Olanzapine - The serum concentration of Olanzapine can be ↓ when it is combined with Cyproterone acetate.
Palbociclib - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Palbociclib.
Phenindione - The therapeutic efficacy of Phenindione can be ↓ when used in combination with Cyproterone acetate.
Phenprocoumon - The therapeutic efficacy of Phenprocoumon can be ↓ when used in combination with Cyproterone acetate.
Phenytoin - The metabolism of Cyproterone acetate can be ↑ when combined with Phenytoin.
Pimozide - The serum concentration of Pimozide can be ↓ when it is combined with Cyproterone acetate.
Pomalidomide - The serum concentration of Pomalidomide can be ↓ when it is combined with Cyproterone acetate.
Propranolol - The serum concentration of Propranolol can be ↓ when it is combined with Cyproterone acetate.
Rasagiline - The serum concentration of Rasagiline can be ↓ when it is combined with Cyproterone acetate.

Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Cyproterone acetate.
Riluzole - The serum concentration of Riluzole can be ↓ when it is combined with Cyproterone acetate.
Ropinirole - The serum concentration of Ropinirole can be ↓ when it is combined with Cyproterone acetate.
Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with Cyproterone acetate.
Siltuximab - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Siltuximab.
Simeprevir - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Simeprevir.
Simvastatin - The serum concentration of Simvastatin can be ↑ when it is combined with Cyproterone acetate.
Stiripentol - The serum concentration of Cyproterone acetate can be ↑ when it is combined with Stiripentol.
Sulodexide - The therapeutic efficacy of Sulodexide can be ↓ when used in combination with Cyproterone acetate.
Tasimelteon - The serum concentration of Tasimelteon can be ↓ when it is combined with Cyproterone acetate.
Theophylline - The serum concentration of Theophylline can be ↓ when it is combined with Cyproterone acetate.
Thiothixene - The serum concentration of Thiothixene can be ↓ when it is combined with Cyproterone acetate.
Tocilizumab - The serum concentration of Cyproterone acetate can be ↓ when it is combined with Tocilizumab.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Cyproterone acetate.
Treprostinil - The therapeutic efficacy of Treprostinil can be ↓ when used in combination with Cyproterone acetate.
Trifluoperazine - The serum concentration of Trifluoperazine can be ↓ when it is combined with Cyproterone acetate.
Ulipristal - The therapeutic efficacy of Cyproterone acetate can be ↓ when used in combination with Ulipristal.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Cyproterone acetate.
Warfarin - The therapeutic efficacy of Warfarin can be ↓ when used in combination with Cyproterone acetate (drugbank, 2014a).

Herbal interactions

St. John's Wort - The serum concentration of Cyproterone acetate can be ↓ when it is combined with St. John's Wort (drugbank, 2014a).

Side-effects

Respiratory

- **Breathlessness**, (BNF, 2016a),
- **shortness of breath**, (emc, 2016).

Gastrointestinal

- **Weight changes** (BNF, 2016a) which could be decreased or increased, and which can be associated with fluid retention (emc, 2016).

Skin

- Reduced sebum production (but it may clear acne),
- changes in hair pattern, rarely
- **hypersensitivity reactions**,
- **rash** (BNF, 2016a).

Genitourinary

- **Breast swelling** sometimes with tenderness,
- **decreased sex drive**,
- **impotence**,
- **reduced sperm count**,
- **reduced volume of ejaculate**,
- **tender lumps in breasts** and
- **oozing of milky fluid from nipples** (emc, 2016).

Other

- **tiredness** and
- **lassitude** are common in the first few weeks but become much less from the third month.
- **hot flushes**,
- **sweating**,
- **depressed mood**,
- **restlessness** (emc, 2016).

Overdose

Overdose of Dianette may cause **nausea** and/or **vomiting**, There are no specific antidotes and further treatment should be just to treat the symptoms of overdose (emc, 2016) There are no reports of overdosage of Androcur or Cyprostat.

Note

Should be taken after the morning and evening meals (emc, 2016)

Warning

The lassitude and loss of strength that may be experienced, particularly during the first few weeks of treatment, necessitate care whilst driving, (BNF, 2016a) or operating machinery (TGC, 2015a).

Flutamide

Description

An anti-androgen with about the same potency as cyproterone in rodent and canine species (drugbank, 2014c).

Also known as

Flutamid in Germany, Flutamida in Spain.

Manufacturer

Schering-Plough Ltd.

Contains

Flutamide = Flutamide 250 mgs.
Drogenil = Flutamide 250 mgs plus lactose, sodium lauryl sulphate, microcrystalline cellulose, starch, silica gel, magnesium stearate (emc, 2016).

Action

Flutamide is a nonsteroidal anti-androgen that blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor. In addition Flutamide is a potent inhibitor of testosterone-stimulated prostatic DNA synthesis. Moreover, it is capable of inhibiting prostatic nuclear uptake of androgen (drugbank, 2014b)

Indications

Advanced prostatic cancer.

Pharmacodynamics

Flutamide is a nonsteroidal anti-androgen. In animal studies, flutamide demonstrates potent anti-androgenic effects. It exerts its anti-androgenic action by inhibiting androgen uptake and/or by inhibiting nuclear binding of androgen in target tissues or both. Prostatic carcinoma is known to be androgen-sensitive and responds to treatment that counteracts the effect of androgen and/or removes the source of androgen, e.g. castration. Elevations of plasma testosterone and estradiol levels have been noted following flutamide administration (drugbank, 2014c).

How it works

Flutamide is a nonsteroidal anti-androgen that blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor. In addition Flutamide is a potent inhibitor of testosterone-stimulated prostatic DNA synthesis. Moreover, it is capable of inhibiting prostatic nuclear uptake of androgen (drugbank, 2014c).

Pharmacokinetics

Absorption - Rapidly and completely absorbed,
Metabolism - Flutamide is rapidly and extensively metabolized, with flutamide comprising only 2.5% of plasma radioactivity 1 hour after administration,
Elimination - Flutamide and its metabolites are excreted mainly in the urine with only 4.2% of a single dose excreted in the faeces over 72 hours,
Half-life - The plasma half-life for the alpha-hydroxylated metabolite of flutamide (an active metabolite) is approximately 6 hours (drugbank, 2014b).

Typical dosage

Pre-op - 750 mgs/day (Asscheman and LJG Gooren, 1992).
Post-op - Not known at present.

Route

Tablets - Flutamide, Drogenil.

Interactions

Drug-drug

Warfarin - May ↑ PT and INR (Abramovitz, 2016)

Abiraterone - The serum concentration of Flutamide can be ↑ when it is combined with Abiraterone.
Aprepitant - The serum concentration of Flutamide can be ↑ when it is combined with Aprepitant.
Bexarotene - The serum concentration of Flutamide can be ↓ when it is combined with Bexarotene.
Bortezomib - The metabolism of Flutamide can be ↓ when combined with Bortezomib.
Bosentan - The serum concentration of Flutamide can be ↓ when it is combined with Bosentan.
Capromab - Flutamide may decrease effectiveness of Capromab as a diagnostic agent.
Carbamazepine - The metabolism of Flutamide can be ↑ when combined with Carbamazepine.
Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Flutamide.
Conivaptan - The serum concentration of Flutamide can be ↑ when it is combined with Conivaptan.
Cyproterone acetate - The serum concentration of Flutamide can be ↓ when it is combined with Cyproterone acetate.
Dabrafenib - The serum concentration of Flutamide can be ↓ when it is combined with Dabrafenib.
Dapsone - The risk or severity of adverse effects can be ↑ when Dapsone is combined with Flutamide.
Dasatinib - The serum concentration of Flutamide can be ↑ when it is combined with Dasatinib.
Deferasirox - The serum concentration of Flutamide can be ↓ when it is combined with Deferasirox.
Fluconazole - The metabolism of Flutamide can be ↓ when combined with Fluconazole.
Fluvoxamine - The metabolism of Flutamide can be ↓ when combined with Fluvoxamine.
Fosaprepitant - The serum concentration of Flutamide can be ↑ when it is combined with Fosaprepitant.
Fusidic Acid - The serum concentration of Flutamide can be ↑ when it is combined with Fusidic Acid.
Idelalisib - The serum concentration of Flutamide can be ↑ when it is combined with Idelalisib.
Ivacaftor - The serum concentration of Flutamide can be ↑ when it is combined with Ivacaftor.
Luliconazole - The serum concentration of Flutamide can be ↑ when it is combined with Luliconazole.

Mexiletine - The metabolism of Flutamide can be ↓ when combined with Mexiletine.
Mifepristone - The serum concentration of Flutamide can be ↑ when it is combined with Mifepristone.
Mitotane - The serum concentration of Flutamide can be ↓ when it is combined with Mitotane.
Nelfinavir - The metabolism of Flutamide can be ↓ when combined with Nelfinavir.
Netupitant - The serum concentration of Flutamide can be ↑ when it is combined with Netupitant.
Nitric Oxide - The risk or severity of adverse effects can be ↑ when Nitric Oxide is combined with Flutamide.
Palbociclib - The serum concentration of Flutamide can be ↑ when it is combined with Palbociclib.
Peginterferon alfa-2b - The serum concentration of Flutamide can be ↑ when it is combined with Peginterferon alfa-2b.
Phenytoin - The metabolism of Flutamide can be ↑ when combined with Phenytoin.
Prilocaine - The risk or severity of adverse effects can be ↑ when Flutamide is combined with Prilocaine.
Siltuximab - The serum concentration of Flutamide can be ↓ when it is combined with Siltuximab.
Simeprevir - The serum concentration of Flutamide can be ↑ when it is combined with Simeprevir.
Sodium Nitrite - The risk or severity of adverse effects can be ↑ when Flutamide is combined with Sodium Nitrite.
Stiripentol - The serum concentration of Flutamide can be ↑ when it is combined with Stiripentol.
Teriflunomide - The serum concentration of Flutamide can be ↓ when it is combined with Teriflunomide.
Tizanidine - The serum concentration of Tizanidine can be ↑ when it is combined with Flutamide.
Tocilizumab - The serum concentration of Flutamide can be ↓ when it is combined with Tocilizumab.
Vemurafenib - The serum concentration of Flutamide can be ↑ when it is combined with Vemurafenib (drugbank, 2014c).

Herbal interactions

St. John's Wort - The serum concentration of Flutamide can be ↓ when it is combined with St. John's Wort.

Drug-lifestyle

Sun exposure - May cause photosensitivity reactions. Advise patient to avoid excessive sunlight exposure (Abramovitz, 2016)

Contraindications

Sensitivity to Flutamide.

Side-effects

Central Nervous System

- Drowsiness,
- confusion,
- depression,
- anxiety,
- nervousness,
- paresthesia (Abramovitz, 2016).

Cardiovascular

- Peripheral oedema,
- hypertension,
- hot flashes (Abramovitz, 2016).

Gastrointestinal

- **diarrhoea**,
- **nausea**,
- **vomiting**,
- anorexia (Abramovitz, 2016).

Genitourinary

- **Erectile dysfunction**,
- urine discolouration (Abramovitz, 2016).

Haematologic

- Anaemia,
- **leucopenia**[50],
- **thrombocytopenia**,
- haemolytic anaemia (Abramovitz, 2016).

Hepatic

[50] Any condition in which the number of leukocytes in the circulating blood is lower than normal, the lower limit of which is generally regarded as 4000-5000/mm^3

- **hepatic encephalopathy**,
- **liver failure** (Abramovitz, 2016).

Skin

- Rash,
- photosensitivity[51] (Abramovitz, 2016).

Other

- loss of libido,
- gynaecomastia (Abramovitz, 2016).

Effects on Lab Test Results

- May ↑ BUN, creatinine, haemoglobin, and liver enzyme levels.
- May ↓ platelet and WBC counts.
- May alter pituitary-gonadal system tests during therapy and for 12 weeks after (Abramovitz, 2016).

Overdose

In animal studies with flutamide alone, signs of overdose included -

- **hypoactivity**,
- **piloerection**[52],
- **slow respiration**,
- **ataxia** and/or
- **lacrimation**,
- **anorexia**,
- **tranquilization**,
- **emesis** and
- **methemoglobinaemia**, (drugbank, 2014c).

The single dose of flutamide ordinarily associated with symptoms of overdose or considered to be life-threatening has not been established. One patient survived after taking more than 5g as a single dose - no adverse effects were observed.

Since flutamide is highly protein bound, dialysis may not be of any use as treatment for overdose (emc, 2016).

[51] an abnormal degree of sensitivity of the skin to sunlight

[52] hair standing erect and on end

Shelf life

Drogenil = 60 months (emc, 2016).

Discontinued

Drogenil was discontinued from the UK pharmacy in 2009.

Goserelin

Also known as

Zoladex, Zoladex LA, Goséréline (French), Goserelina (Spanish).

Goserelin is a synthetic hormone. In men, it stops the production of the hormone testosterone, which may stimulate the growth of cancer cells. In women, goserelin decreases the production of the hormone estradiol (which may stimulate the growth of cancer cells) to levels similar to a postmenopausal state. When the medication is stopped, hormone levels return to normal (drugbank, 2013e).

Manufacturer

Zoladex = AstraZeneca UK Limited.
Zoladex LA = AstraZeneca UK Limited.

Contains

Zoladex = Goserelin 3.6mgs plus lactide/glycolide co-polymer.
Zoladex LA = Goserelin 10.8 mgs plus a blend of high and low molecular weight lactide/glycolide copolymers (emc, 2016).

Action

A luteinizing hormonereleasing hormone (LH-RH) analogue that acts on the pituitary gland to decrease the release of follicle-stimulating hormone and LH, dramatically lowering sex hormone levels (oestrogen in women and testosterone in men) (Abramovitz, 2016).

Indications

Used for the treatment of advanced prostate cancer, endometriosis, advanced breast cancer, endometrial thinning (Abramovitz, 2016).

Pharmacodynamics

The pharmacokinetics of goserelin have been determined in both male and female healthy volunteers and patients. In these studies, goserelin was administered as a single 250µg (aqueous solution) dose and as a single or multiple 3.6 mg depot dose by subcutaneous route (drugbank, 2013e).

Pharmacokinetics

Zoladex is poorly protein bound and has a serum elimination half-life of two to four hours in subjects with normal renal function. The half-life is increased in patients with impaired renal function. For the compound given in a 10.8 mg depot formulation every 12 weeks this change will not lead to any accumulation. Hence, no change in dosing is necessary in these patients (emc, 2016).

Elimination route - Clearance of goserelin following subcutaneous administration of a radiolabeled solution of goserelin was very rapid and occurred via a combination of hepatic and urinary excretion. More than 90% of a subcutaneous radiolabeled solution formulation dose of goserelin was excreted in urine (drugbank, 2013e).

Half life - 4–5 hours (drugbank, 2013e).

How it works

Goserelin is a synthetic decapeptide analogue of LHRH. Goserelin acts as a potent inhibitor of pituitary gonadotropin secretion when administered in the biodegradable formulation. The result is sustained suppression of LH and serum testosterone levels (drugbank, 2013e).

Inactive orally, rapidly absorbed following subcutaneous administration.

Goserelin is classified as a leutinizing hormone releasing hormone (LHRH) agonist.

LHRH agonists work by telling the pituitary gland located in the brain to stop producing leutinizing hormone, which (in men) stimulates the testicles to release testosterone and (in women) stimulates the ovaries to release oestrogen (chemocare, 2016).

Typical dosage

Pre-op 3.6mgs for 28 days cover, 10.8 mgs for 3 months cover,
Post-op Not required.

Route

This is a biodegradable subcutaneous implant = Zoladex, Zoladex LA (Abramovitz, 2016).

Contraindications

Hypersensitivity to LHRH, LHRH-agonist analogues, lactation, breast cancer (Abramovitz, 2016). Not recommended for use longer than 6 months (BNF, 2016a).

Side-effects

Important things to remember about the side effects of goserelin -

- Most people do not experience all of the side effects listed.
- Side effects are often predictable in terms of their onset and duration.
- Side effects are almost always reversible and will go away after treatment is complete.
- There are many options to help minimize or prevent side effects.
- There is no relationship between the presence or severity of side effects and the effectiveness of the medication (chemocare, 2016).

The following side effects are common (occurring in greater than 30%) for people taking goserelin -

- Hot flashes (see sexuality),
- Loss of interest in sex (decreased libido) (see sexuality),
- Inability to obtain or sustain an erection (impotence) (see sexuality) (chemocare, 2016).

These side effects are less common side effects (occurring in about 10-29%) of people receiving goserelin -

- Headache,
- Vaginal dryness (see sexuality),
- Swelling of the breasts (gynaecomastia) (see sexuality),
- Depression,
- Sleepiness,
- Skin rash (chemocare, 2016).

Rare but significant side effects may include heart problems such as arrhythmias, congestive heart failure or heart attack (<5%) (chemocare, 2016).

Contact your health care provider immediately, day or night, if you should experience any of the following symptoms: -

- Urinary retention or inability to urinate,
- Weakness, numbness or tingling in arms or legs (**0318**).

The following symptoms require medical attention, but are not an emergency. Contact your health care provider within 24 hours of noticing any of the following -

- Extreme fatigue (unable to carry on self-care activities),
- Swelling of the feet or ankles. Sudden weight gain,
- Swelling, redness and/or pain in one leg or arm and not the other,
- Changes in mood or memory (chemocare, 2016).

Central Nervous System

- Lethargy,
- pain,
- dizziness,
- insomnia,
- anxiety,
- depression,
- **headache**,
- chills,
- emotional lability,
- **stroke**,
- asthenia (Abramovitz, 2016).
- **Hot flushes** (drugs.com, 2014c).

Cardiovascular

- Oedema,
- **heart failure**,
- **arrhythmias**,
- peripheral oedema,
- hypertension,
- **myocardial infarction**,
- peripheral vascular disorder,
- chest pain,
- **hot flashes** (Abramovitz, 2016).

Gastrointestinal

- Nausea,
- vomiting,
- diarrhoea,
- constipation,
- ulcer,
- anorexia,
- abdominal pain (Abramovitz, 2016).

Genitourinary

- **Sexual dysfunction**,
- impotence,
- renal insufficiency,
- urinary obstruction,
- **vaginitis**,
- urinary tract infection, (Abramovitz, 2016),
- **amenorrhoea**
- **PSA increased**
- **decreased libido** (rxisk, 2016d).

Haematologic

- Anaemia (Abramovitz, 2016).

Metabolic

- Hypercalcaemia,
- hyperglycaemia,
- weight increase,
- gout (Abramovitz, 2016).

Musculoskeletal

- Back pain,
- osteoporosis,
- decreased bone mineral density (Abramovitz, 2016).

Respiratory

- Chronic obstructive pulmonary disease,
- upper respiratory tract infection (Abramovitz, 2016).

Skin

- Rash,
- diaphoresis[53],
- acne,
- seborrhea,
- hirsutism (Abramovitz, 2016).

Other

- **Changes in breast size**,
- **changes in libido**,
- infection,
- **breast swelling**,
- pain,
- tenderness (Abramovitz, 2016).

[53] perspiration or sweating

Interactions

Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Goserelin.
Alfuzosin - Alfuzosin may ↑ the QTc-prolonging activities of Goserelin.
Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ decreased when used in combination with Goserelin.
Amantadine - Amantadine may ↑ increase the QTc-prolonging activities of Goserelin.
Amiodarone - Goserelin may ↑ the QTc-prolonging activities of Amiodarone.
Amitriptyline - Amitriptyline may ↑ the QTc-prolonging activities of Goserelin.
Amoxapine - Amoxapine may ↑ the QTc-prolonging activities of Goserelin.
Anagrelide - Goserelin may ↑ the QTc-prolonging activities of Anagrelide.
Apomorphine - Apomorphine may ↑ the QTc-prolonging activities of Goserelin.
Arformoterol - Arformoterol may ↑ the QTc-prolonging activities of Goserelin.
Aripiprazole - Aripiprazole may ↑ the QTc-prolonging activities of Goserelin.
Arsenic trioxide - Goserelin may ↑ the QTc-prolonging activities of Arsenic trioxide.
Artemether - Goserelin may ↑ the QTc-prolonging activities of Artemether.
Asenapine - Goserelin may ↑ the QTc-prolonging activities of Asenapine.
Atazanavir - Atazanavir may ↑ the QTc-prolonging activities of Goserelin.
Atomoxetine - Atomoxetine may ↑ the QTc-prolonging activities of Goserelin.
Azithromycin - Goserelin may ↑ the QTc-prolonging activities of Azithromycin.
Bedaquiline - Goserelin may ↑ the QTc-prolonging activities of Bedaquiline.
Bortezomib - Bortezomib may ↑ the QTc-prolonging activities of Goserelin.
Bosutinib - Bosutinib may ↑ the QTc-prolonging activities of Goserelin.
Buserelin - Buserelin may ↑ the QTc-prolonging activities of Goserelin.
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Goserelin.
Capromab - Goserelin may ↓ effectiveness of Capromab as a diagnostic agent.
Ceritinib - Goserelin may ↑ the QTc-prolonging activities of Ceritinib.
Chloroquine - Goserelin may ↑ the QTc-prolonging activities of Chloroquine.
Chlorpromazine - Goserelin may ↑ the QTc-prolonging activities of Chlorpromazine.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Goserelin.
Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Goserelin.

Ciprofloxacin - Goserelin may ↑ the QTc-prolonging activities of Ciprofloxacin.
Cisapride - Goserelin may ↑ the QTc-prolonging activities of Cisapride.
Citalopram - Goserelin may ↑ the QTc-prolonging activities of Citalopram.
Clarithromycin - Goserelin may ↑ the QTc-prolonging activities of Clarithromycin.
Clomipramine - Clomipramine may ↑ the QTc-prolonging activities of Goserelin.
Clozapine - Goserelin may ↑ the QTc-prolonging activities of Clozapine.
Corifollitropin Alfa - The therapeutic efficacy of Corifollitropin Alfa can be ↑ when used in combination with Goserelin.
Crizotinib - Goserelin may ↑ the QTc-prolonging activities of Crizotinib.
Dabrafenib - Dabrafenib may ↑ the QTc-prolonging activities of Goserelin.
Dasatinib - Dasatinib may ↑ the QTc-prolonging activities of Goserelin.
Degarelix - Degarelix may ↑ the QTc-prolonging activities of Goserelin.
Desflurane - Desflurane may ↑ the QTc-prolonging activities of Goserelin.
Desipramine - Desipramine may ↑ the QTc-prolonging activities of Goserelin.
Diphenhydramine - Diphenhydramine may ↑ the QTc-prolonging activities of Goserelin.
Disopyramide - Goserelin may ↑ the QTc-prolonging activities of Disopyramide.
Dofetilide - Goserelin may ↑ the QTc-prolonging activities of Dofetilide.
Dolasetron - Goserelin may ↑ the QTc-prolonging activities of Dolasetron.
Domperidone - Goserelin may ↑ the QTc-prolonging activities of Domperidone.
Doxepin - Doxepin may ↑ the QTc-prolonging activities of Goserelin.
Dronedarone - Goserelin may ↑ the QTc-prolonging activities of Dronedarone.
Droperidol - Goserelin may ↑ the QTc-prolonging activities of Droperidol.
Eliglustat - Goserelin may ↑ the QTc-prolonging activities of Eliglustat.
Eribulin - Eribulin may ↑ the QTc-prolonging activities of Goserelin.
Erythromycin - Goserelin may ↑ the QTc-prolonging activities of Erythromycin.
Escitalopram - Goserelin may ↑ the QTc-prolonging activities of Escitalopram.
Ezogabine - Ezogabine may ↑ the QTc-prolonging activities of Goserelin.
Famotidine - Famotidine may ↑ the QTc-prolonging activities of Goserelin.
Felbamate - Felbamate may ↑ the QTc-prolonging activities of Goserelin.
Fingolimod - Fingolimod may ↑ the QTc-prolonging activities of Goserelin.
Flecainide - Goserelin may ↑ the QTc-prolonging activities of Flecainide.
Fluconazole - Fluconazole may ↑ the QTc-prolonging activities of Goserelin.
Fluoxetine - Goserelin may ↑ the QTc-prolonging activities of Fluoxetine.
Flupentixol - Goserelin may ↑ the QTc-prolonging activities of Flupentixol.
Fluticasone Propionate - Fluticasone Propionate may ↑ the QTc-prolonging activities of Goserelin.
Formoterol - Formoterol may ↑ the QTc-prolonging activities of Goserelin.

Foscarnet - Foscarnet may ↑ the QTc-prolonging activities of Goserelin.
Fosphenytoin - Fosphenytoin may ↑ the QTc-prolonging activities of Goserelin.
Gadobenate Dimeglumine - Goserelin may ↑ the QTc-prolonging activities of Gadobenate Dimeglumine.
Galantamine - Galantamine may ↑ the QTc-prolonging activities of Goserelin.
Gemifloxacin - Goserelin may ↑ the QTc-prolonging activities of Gemifloxacin.
Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Goserelin.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Goserelin.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Goserelin.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Goserelin.
Granisetron - Goserelin may ↑ the QTc-prolonging activities of Granisetron.
Haloperidol - Goserelin may ↑ the QTc-prolonging activities of Haloperidol.
Histrelin - Histrelin may ↑ the QTc-prolonging activities of Goserelin.
Hydroxyzine - Hydroxyzine may ↑ the QTc-prolonging activities of Goserelin.
Ibandronate - Ibandronate may ↑ the QTc-prolonging activities of Goserelin.
Ibutilide - Goserelin may ↑ the QTc-prolonging activities of Ibutilide.
Iloperidone - Goserelin may ↑ the QTc-prolonging activities of Iloperidone.
Imipramine - Imipramine may ↑ the QTc-prolonging activities of Goserelin.
Indacaterol - Indacaterol may ↑ the QTc-prolonging activities of Goserelin.
Indapamide - Indapamide may ↑ the QTc-prolonging activities of Goserelin.
Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Goserelin.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Goserelin.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Goserelin.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Goserelin.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Goserelin.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Goserelin.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Goserelin.
Isoflurane - Isoflurane may ↑ the QTc-prolonging activities of Goserelin.
Isradipine - Isradipine may ↑ the QTc-prolonging activities of Goserelin.

Itraconazole - Itraconazole may ↑ the QTc-prolonging activities of Goserelin.
Ivabradine - Ivabradine may ↑ the QTc-prolonging activities of Goserelin.
Ketoconazole - Ketoconazole may ↑ the QTc-prolonging activities of Goserelin.
Lapatinib - Lapatinib may ↑ the QTc-prolonging activities of Goserelin.
Lenvatinib - Goserelin may ↑ the QTc-prolonging activities of Lenvatinib.
Leuprolide - Goserelin may ↑ the QTc-prolonging activities of Leuprolide.
Levofloxacin - Goserelin may ↑ the QTc-prolonging activities of Levofloxacin.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Goserelin.
Lithium - Lithium may ↑ the QTc-prolonging activities of Goserelin.
Lopinavir - Goserelin may ↑ the QTc-prolonging activities of Lopinavir.
Lumefantrine - Goserelin may ↑ the QTc-prolonging activities of Lumefantrine.
Maprotiline - Maprotiline may ↑ the QTc-prolonging activities of Goserelin.
Mefloquine - Mefloquine may ↑ the QTc-prolonging activities of Goserelin.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Goserelin.
Methadone - Goserelin may ↑ the QTc-prolonging activities of Methadone.
Methotrimeprazine - Methotrimeprazine may ↑ the QTc-prolonging activities of Goserelin.
Metoclopramide - Metoclopramide may ↑ the QTc-prolonging activities of Goserelin.
Metronidazole - Metronidazole may ↑ the QTc-prolonging activities of Goserelin.
Mifepristone - Mifepristone may ↑ the QTc-prolonging activities of Goserelin.
Mirabegron - Mirabegron may ↑ the QTc-prolonging activities of Goserelin.
Mirtazapine - Mirtazapine may ↑ the QTc-prolonging activities of Goserelin.
Moexipril - Moexipril may ↑ the QTc-prolonging activities of Goserelin.
Moxifloxacin - Goserelin may ↑ the QTc-prolonging activities of Moxifloxacin.
Nelfinavir - Nelfinavir may ↑ the QTc-prolonging activities of Goserelin.
Nicardipine - Nicardipine may ↑ the QTc-prolonging activities of Goserelin.
Nilotinib - Goserelin may ↑ the QTc-prolonging activities of Nilotinib.
Norfloxacin - Norfloxacin may ↑ the QTc-prolonging activities of Goserelin.
Nortriptyline - Nortriptyline may ↑ the QTc-prolonging activities of Goserelin.
Octreotide - Octreotide may ↑ the QTc-prolonging activities of Goserelin.
Ofloxacin - Goserelin may ↑ the QTc-prolonging activities of Ofloxacin.
Olanzapine - Olanzapine may ↑ the QTc-prolonging activities of Goserelin.
Olodaterol - Olodaterol may ↑ the QTc-prolonging activities of Goserelin.

Ondansetron - Goserelin may ↑ the QTc-prolonging activities of Ondansetron.
Osimertinib - Goserelin may ↑ the QTc-prolonging activities of Osimertinib.
Oxytocin - Oxytocin may ↑ the QTc-prolonging activities of Goserelin.
Paliperidone - Goserelin may ↑ the QTc-prolonging activities of Paliperidone.
Panobinostat - Goserelin may ↑ the QTc-prolonging activities of Panobinostat.
Paroxetine - Paroxetine may ↑ the QTc-prolonging activities of Goserelin.
Pasireotide - Pasireotide may ↑ the QTc-prolonging activities of Goserelin.
Pazopanib - Goserelin may ↑ the QTc-prolonging activities of Pazopanib.
Pentamidine - Goserelin may ↑ the QTc-prolonging activities of Pentamidine.
Perflutren - Goserelin may ↑ the QTc-prolonging activities of Perflutren.
Pimozide - Goserelin may ↑ the QTc-prolonging activities of Pimozide.
Posaconazole - Posaconazole may ↑ the QTc-prolonging activities of Goserelin.
Primaquine - Goserelin may ↑ the QTc-prolonging activities of Primaquine.
Procainamide - Goserelin may ↑ the QTc-prolonging activities of Procainamide.
Promazine - Goserelin may ↑ the QTc-prolonging activities of Promazine.
Promethazine - Promethazine may ↑ the QTc-prolonging activities of Goserelin.
Propafenone - Goserelin may ↑ the QTc-prolonging activities of Propafenone.
Propofol - Propofol may ↑ the QTc-prolonging activities of Goserelin.
Protriptyline - Protriptyline may ↑ the QTc-prolonging activities of Goserelin.
Quetiapine - Goserelin may ↑ the QTc-prolonging activities of Quetiapine.
Quinidine - Goserelin may ↑ the QTc-prolonging activities of Quinidine.
Quinine - Goserelin may ↑ the QTc-prolonging activities of Quinine.
Ranolazine - Ranolazine may ↑ the QTc-prolonging activities of Goserelin.
Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Goserelin.
Rilpivirine - Rilpivirine may ↑ the QTc-prolonging activities of Goserelin.
Risperidone - Risperidone may ↑ the QTc-prolonging activities of Goserelin.
Ritonavir - Ritonavir may ↑ the QTc-prolonging activities of Goserelin.
Salbutamol - Salbutamol may ↑ the QTc-prolonging activities of Goserelin.
Salmeterol - Salmeterol may ↑ the QTc-prolonging activities of Goserelin.
Saquinavir - Goserelin may ↑ the QTc-prolonging activities of Saquinavir.
Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with Goserelin.
Sertraline - Sertraline may ↑ the QTc-prolonging activities of Goserelin.
Sevoflurane - Sevoflurane may ↑ the QTc-prolonging activities of Goserelin.
Solifenacin - Solifenacin may ↑ the QTc-prolonging activities of Goserelin.

Sorafenib - Sorafenib may ↑ the QTc-prolonging activities of Goserelin.
Sotalol - Goserelin may ↑ the QTc-prolonging activities of Sotalol.
Sulfamethoxazole - Sulfamethoxazole may ↑ the QTc-prolonging activities of Goserelin.
Sulfisoxazole - Goserelin may ↑ the QTc-prolonging activities of Sulfisoxazole.
Sunitinib - Sunitinib may ↑ the QTc-prolonging activities of Goserelin.
Tacrolimus - Tacrolimus may ↑ the QTc-prolonging activities of Goserelin.
Tamoxifen - Tamoxifen may ↑ the QTc-prolonging activities of Goserelin.
Telavancin - Goserelin may ↑ the QTc-prolonging activities of Telavancin.
Telithromycin - Goserelin may ↑ the QTc-prolonging activities of Telithromycin.
Terbutaline - Terbutaline may ↑ the QTc-prolonging activities of Goserelin.
Tetrabenazine - Goserelin may ↑ the QTc-prolonging activities of Tetrabenazine.
Thioridazine - Goserelin may ↑ the QTc-prolonging activities of Thioridazine.
Thiothixene - Thiothixene may ↑ the QTc-prolonging activities of Goserelin.
Tizanidine - Tizanidine may ↑ the QTc-prolonging activities of Goserelin.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Goserelin.
Tolterodine - Tolterodine may ↑ the QTc-prolonging activities of Goserelin.
Toremifene - Goserelin may ↑ the QTc-prolonging activities of Toremifene.
Trazodone - Trazodone may ↑ the QTc-prolonging activities of Goserelin.
Treprostinil - Treprostinil may ↑ the QTc-prolonging activities of Goserelin.
Trimethoprim - Trimethoprim may ↑ the QTc-prolonging activities of Goserelin.
Trimipramine - Trimipramine may ↑ the QTc-prolonging activities of Goserelin.
Triptorelin - Triptorelin may ↑ the QTc-prolonging activities of Goserelin.
Vandetanib - Goserelin may ↑ the QTc-prolonging activities of Vandetanib.
Vardenafil - Vardenafil may ↑ the QTc-prolonging activities of Goserelin.
Vemurafenib - Goserelin may ↑ the QTc-prolonging activities of Vemurafenib.
Venlafaxine - Venlafaxine may ↑ the QTc-prolonging activities of Goserelin.
Vilanterol - Vilanterol may ↑ the QTc-prolonging activities of Goserelin.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Goserelin.
Voriconazole - Voriconazole may ↑ the QTc-prolonging activities of Goserelin.
Vorinostat - Vorinostat may ↑ the QTc-prolonging activities of Goserelin.
Ziprasidone - Goserelin may ↑ the QTc-prolonging activities of Ziprasidone.
Zuclopenthixol - Goserelin may ↑ the QTc-prolonging activities of Zuclopenthixol (drugbank, 2013e).

Effects on Lab Test Results

- May ↑ calcium and glucose levels.
- May ↓ haemoglobin level.
- May cause inaccurate diagnostic tests of pituitary-gonadotropic and gonadal functions conducted during treatment (Abramovitz, 2016).

Precautions

Before starting goserelin treatment, make sure you tell your doctor about any other medications you are taking (including prescription, over-the-counter, vitamins, herbal remedies, etc.). Do not take aspirin, products containing aspirin unless your doctor specifically permits this.

- Inform your health care professional if you are pregnant or may be pregnant prior to starting this treatment. Pregnancy category X (goserelin may cause fetal harm when given to a pregnant woman. This drug must not be given to a pregnant woman or a woman who intends to become pregnant. If a woman becomes pregnant while taking goserelin, the medication must be stopped immediately and the woman given appropriate counselling).
- For both men and women: Do not conceive a child (get pregnant) while taking goserelin. Barrier methods of contraception, such as condoms, are recommended. Discuss with your doctor when you may safely become pregnant or conceive a child after therapy.
- Do not breast feed while taking this medication (chemocare, 2016).

Clinical/Nursing assessment

Before giving to transmen, rule out pregnancy (Abramovitz, 2016)

Patient Teaching

Advise patient to return every 28 days for a new implant. A delay of a couple of days is permissible.

Tell patient that pain may worsen for first 30 days of treatment.

Tell women to use a nonhormonal form of contraception during treatment. Caution patient about significant risks to foetus.

Urge women to call prescriber if menstruation persists or if breakthrough bleeding occurs. Menstruation should stop during treatment.

Inform women that a delayed return of menstruation may occur after therapy ends. Persistent lack of menstruation is rare (Abramovitz, 2016).

Self-care tips

- If you are experiencing hot flushes/flashes, wearing light clothing, staying in a cool environment, and putting cool cloths on your head may reduce symptoms. Consult your GP if these worsen, or become intolerable.
- Avoid sun exposure. Wear sun protection factor (SPF) 15 (or higher) sunblock and protective clothing.
- Get plenty of rest.
- Maintain good nutrition.
- If you experience severe or troublesome side effects, be sure to discuss them with your GP (chemocare, 2016).

Shelf Life

Both drugs have a shelf life of 36 months (emc, 2016).

Toxicology

No experience of overdosage from clinical trials (drugbank, 2013e).

Leuprorelin Acetate

Leuprolide belongs to the general class of drugs known as hormones or hormone antagonists. It is a synthetic 9 residue peptide analog of gonadotropin releasing hormone. Leuprolide is used to treat advanced prostate cancer. It is also used to treat uterine fibroids and endometriosis. Leuprolide is also under investigation for possible use in the treatment of mild to moderate Alzheimers disease (drugbank, 2013f).

Also known as

Prostap SR, and Prostap 3.

Manufacturer

Wyeth.

Contains

Prostap SR = Leuprorelin Acetate 3.75mgs
Prostap 3 = Leuprorelin Acetate 11.25mgs

Action

Leuprolide is a gonadotropin-releasing hormone (GnRH) agonist. It works by decreasing levels of certain hormones produced by the testes and ovaries (drugs.com, 2014c).

Indications

Metastatic prostate cancer

Pharmacokinetics

Leuprorelin acetate is well absorbed after subcutaneous and intramuscular injections. It binds to the luteinising hormone releasing hormone (LHRH) receptors and is rapidly degraded. An initially high plasma level of leuprorelin peaks at around 3 hours after a PROSTAP 3 subcutaneous injection, followed by a decrease to maintenance levels in 7 to 14 days. PROSTAP 3 provides continuous plasma levels for up to 117 days resulting in suppression of testosterone to below castration level within 4 weeks of the first injection in the majority of patients. The metabolism, distribution and excretion of leuprorelin acetate in humans have not been fully determined (emc, 2016).

Absorption - Bioavailability by subcutaneous administration is comparable to that by intravenous administration.
Metabolism - Primarily degraded by peptidase and not by cytochrome P450 enzymes.
Elimination - Excreted in the urine.
Half life - 3 hours (drugbank, 2013f).

Pharmacodynamics

These drugs contain leuprorelin acetate, a synthetic nonapeptide analogue of naturally occurring gonadotrophin releasing hormone (GnRH), which possesses greater potency than the natural hormone. Leuprorelin acetate is a peptide and therefore unrelated to the steroids. Chronic administration results in an inhibition of gonadotrophin production and subsequent suppression of ovarian and testicular steroid secretion. This effect is reversible on discontinuation of therapy. Administration of leuprorelin acetate results in an initial increase in circulating levels of gonadotrophins,

which leads to a transient increase in gonadal steroid levels in both men and women. Continued administration of leuprorelin acetate results in a decrease of gonadotrophin and sex steroid levels. In men serum testosterone levels, initially raised in response to early luteinising hormone (LH) release, fall to castrate levels in about 2–4 weeks (emc, 2016).

Used in the palliative treatment of advanced prostate cancer. Leuprolide is a luteinizing hormone agonist that results in suppression of testicular or follicular steroidogenesis (drugbank, 2013f).

How it works

Leuprolide binds to the gonadotropin releasing hormone receptor and acts as a potent inhibitor of gonadotropin secretion (drugbank, 2013f).

Typical dosage

Pre-op - 3.75–7.5mg/month.
Post-op - Should not be needed.

Route

Subcutaneous or intramuscular injection Prostap SR, Prostap 3

Contraindications

Hypersensitivity to GnRH or analogues, thromboembolic disorders (drugs.com, 2014c).

Side-effects

Central Nervous system

- **Headache**,
- rarely migraine (Macmillan, 2014).

Cardiovascular

- Heart disease (Macmillan, 2014).

Gastrointestinal

- Nausea,
- vomiting,
- diarrhoea (Macmillan, 2014).

Genitourinary

- **Hot flushes**,
- **impotence**,
- ↓ **libido**,
- **gynaecomastia** (Macmillan, 2014).

Skeletal

- **Osteoporosis**

NB - You may be at a higher risk of osteoporosis if you're taking Prostap for long periods of time (Macmillan, 2014)

Skin

- **Hypersensitivity reactions** including
- **urticaria**,
- **pruritus**,
- **skin rashes** (BNF, 2016a).

Interactions

Individual drugs = Megesterol ↑ antineoplastic action
Flutamide ↑ antineoplastic action (Rove and Crawford, 2013)

Acarbose - The therapeutic efficacy of Acarbose can be ↓ when used in combination with Leuprolide.
Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Leuprolide.
Albiglutide - The therapeutic efficacy of Albiglutide can be ↓ when used in combination with Leuprolide.
Alfuzosin - Alfuzosin may ↑ the QTc-prolonging activities of Leuprolide.
Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Leuprolide.
Amantadine - Amantadine may ↑ the QTc-prolonging activities of Leuprolide.
Amiodarone - Leuprolide may ↑ the QTc-prolonging activities of Amiodarone.
Amitriptyline - Amitriptyline may ↑ the QTc-prolonging activities of Leuprolide.
Amoxapine - Amoxapine may ↑ the QTc-prolonging activities of Leuprolide.

Anagrelide - Leuprolide may ↑ the QTc-prolonging activities of Anagrelide.
Apomorphine - Apomorphine may ↑ the QTc-prolonging activities of Leuprolide.
Arformoterol - Arformoterol may ↑ the QTc-prolonging activities of Leuprolide.
Aripiprazole - Aripiprazole may ↑ the QTc-prolonging activities of Leuprolide.
Arsenic trioxide - Leuprolide may ↑ the QTc-prolonging activities of Arsenic trioxide.
Artemether - Leuprolide may ↑ the QTc-prolonging activities of Artemether.
Asenapine - Leuprolide may ↑ the QTc-prolonging activities of Asenapine.
Atazanavir - Atazanavir may ↑ the QTc-prolonging activities of Leuprolide.
Atomoxetine - Atomoxetine may ↑ the QTc-prolonging activities of Leuprolide.
Azithromycin - Leuprolide may ↑ the QTc-prolonging activities of Azithromycin.
Bedaquiline - Leuprolide may ↑ the QTc-prolonging activities of Bedaquiline.
Bortezomib - Bortezomib may ↑ the QTc-prolonging activities of Leuprolide.
Bosutinib - Bosutinib may ↑ the QTc-prolonging activities of Leuprolide.
Bromocriptine - The therapeutic efficacy of Bromocriptine can be ↓ when used in combination with Leuprolide.
Buserelin - Buserelin may ↑ the QTc-prolonging activities of Leuprolide.
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Leuprolide.
Capromab - Leuprolide may decrease effectiveness of Capromab as a diagnostic agent.
Ceritinib - Leuprolide may ↑ the QTc-prolonging activities of Ceritinib.
Chloroquine - Leuprolide may ↑ the QTc-prolonging activities of Chloroquine.
Chlorpromazine - Leuprolide may ↑ the QTc-prolonging activities of Chlorpromazine.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Leuprolide.
Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Leuprolide.
Ciprofloxacin - Leuprolide may ↑ the QTc-prolonging activities of Ciprofloxacin.
Cisapride - Leuprolide may ↑ the QTc-prolonging activities of Cisapride.
Citalopram - Leuprolide may ↑ the QTc-prolonging activities of Citalopram.
Clarithromycin - Leuprolide may ↑ the QTc-prolonging activities of Clarithromycin.
Clomipramine - Clomipramine may ↑ the QTc-prolonging activities of Leuprolide.

Clozapine - Leuprolide may ↑ the QTc-prolonging activities of Clozapine.
Corifollitropin Alfa - The therapeutic efficacy of Corifollitropin Alfa can be ↑d when used in combination with Leuprolide.
Crizotinib - Leuprolide may ↑ the QTc-prolonging activities of Crizotinib.
Dabrafenib - Dabrafenib may ↑ the QTc-prolonging activities of Leuprolide.
Dapagliflozin - The therapeutic efficacy of Dapagliflozin can be ↓ when used in combination with Leuprolide.
Dasatinib - Dasatinib may ↑ the QTc-prolonging activities of Leuprolide.
Degarelix - Degarelix may ↑ the QTc-prolonging activities of Leuprolide.
Desflurane - Desflurane may ↑ the QTc-prolonging activities of Leuprolide.
Desipramine - Desipramine may ↑ the QTc-prolonging activities of Leuprolide.
Diphenhydramine - Diphenhydramine may ↑ the QTc-prolonging activities of Leuprolide.
Disopyramide - Leuprolide may ↑ the QTc-prolonging activities of Disopyramide.
Dofetilide - Leuprolide may ↑ the QTc-prolonging activities of Dofetilide.
Dolasetron - Leuprolide may ↑ the QTc-prolonging activities of Dolasetron.
Domperidone - Leuprolide may ↑ the QTc-prolonging activities of Domperidone.
Doxepin - Doxepin may ↑ the QTc-prolonging activities of Leuprolide.
Dronedarone - Leuprolide may ↑ the QTc-prolonging activities of Dronedarone.
Droperidol - Leuprolide may ↑ the QTc-prolonging activities of Droperidol.
Dulaglutide - The therapeutic efficacy of Dulaglutide can be ↓ when used in combination with Leuprolide.
Eliglustat - Leuprolide may ↑ the QTc-prolonging activities of Eliglustat.
Empagliflozin - The therapeutic efficacy of Empagliflozin can be ↓ when used in combination with Leuprolide.
Eribulin - Eribulin may ↑ the QTc-prolonging activities of Leuprolide.
Erythromycin - Leuprolide may ↑ the QTc-prolonging activities of Erythromycin.
Escitalopram - Leuprolide may ↑ the QTc-prolonging activities of Escitalopram.
Exenatide - The therapeutic efficacy of Exenatide can be ↓ when used in combination with Leuprolide.
Ezogabine - Ezogabine may ↑ the QTc-prolonging activities of Leuprolide.
Famotidine - Famotidine may ↑ the QTc-prolonging activities of Leuprolide.
Felbamate - Felbamate may ↑ the QTc-prolonging activities of Leuprolide.
Fingolimod - Fingolimod may ↑ the QTc-prolonging activities of Leuprolide.
Flecainide - Leuprolide may ↑ the QTc-prolonging activities of Flecainide.
Fluconazole - Fluconazole may ↑ the QTc-prolonging activities of Leuprolide.
Fluoxetine - Leuprolide may ↑ the QTc-prolonging activities of Fluoxetine.

Flupentixol - Leuprolide may ↑ the QTc-prolonging activities of Flupentixol.

Fluticasone Propionate - Fluticasone Propionate may ↑ the QTc-prolonging activities of Leuprolide.

Formoterol - Formoterol may ↑ the QTc-prolonging activities of Leuprolide.

Foscarnet - Foscarnet may ↑ the QTc-prolonging activities of Leuprolide.

Fosphenytoin - Fosphenytoin may ↑ the QTc-prolonging activities of Leuprolide.

Gadobenate Dimeglumine - Leuprolide may ↑ the QTc-prolonging activities of Gadobenate Dimeglumine.

Galantamine - Galantamine may ↑ the QTc-prolonging activities of Leuprolide.

Gemifloxacin - Leuprolide may ↑ the QTc-prolonging activities of Gemifloxacin.

Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Leuprolide.

Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Leuprolide.

Glipizide - The therapeutic efficacy of Glipizide can be ↓ when used in combination with Leuprolide.

Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Leuprolide.

Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Leuprolide.

Goserelin - Goserelin may ↑ the QTc-prolonging activities of Leuprolide.

Granisetron - Leuprolide may ↑ the QTc-prolonging activities of Granisetron.

Haloperidol - Leuprolide may ↑ the QTc-prolonging activities of Haloperidol.

Histrelin - Histrelin may ↑ the QTc-prolonging activities of Leuprolide.

Hydroxyzine - Hydroxyzine may ↑ the QTc-prolonging activities of Leuprolide.

Ibandronate - Ibandronate may ↑ the QTc-prolonging activities of Leuprolide.

Ibutilide - Leuprolide may ↑ the QTc-prolonging activities of Ibutilide.

Iloperidone - Leuprolide may ↑ the QTc-prolonging activities of Iloperidone.

Imipramine - Imipramine may ↑ the QTc-prolonging activities of Leuprolide.

Indacaterol - Indacaterol may ↑ the QTc-prolonging activities of Leuprolide.

Indapamide - Indapamide may ↑ the QTc-prolonging activities of Leuprolide.

inhaled insulin - The therapeutic efficacy of inhaled insulin can be ↓ when used in combination with Leuprolide.

Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Leuprolide.

Insulin degludec - The therapeutic efficacy of Insulin degludec can be ↓ when used in combination with Leuprolide.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Leuprolide.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Leuprolide.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Leuprolide.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Leuprolide.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Leuprolide.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Leuprolide.
Isoflurane - Isoflurane may ↑ the QTc-prolonging activities of Leuprolide.
Isradipine - Isradipine may ↑ the QTc-prolonging activities of Leuprolide.
Itraconazole - Itraconazole may ↑ the QTc-prolonging activities of Leuprolide.
Ivabradine - Ivabradine may ↑ the QTc-prolonging activities of Leuprolide.
Ketoconazole - Ketoconazole may ↑ the QTc-prolonging activities of Leuprolide.
Lapatinib - Lapatinib may ↑ the QTc-prolonging activities of Leuprolide.
Lenvatinib - Leuprolide may ↑ the QTc-prolonging activities of Lenvatinib.
Levofloxacin - Leuprolide may ↑ the QTc-prolonging activities of Levofloxacin.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Leuprolide.
Liraglutide - The therapeutic efficacy of Liraglutide can be ↓ when used in combination with Leuprolide.
Lithium - Lithium may ↑ the QTc-prolonging activities of Leuprolide.
Lopinavir - Leuprolide may ↑ the QTc-prolonging activities of Lopinavir.
Lumefantrine - Leuprolide may ↑ the QTc-prolonging activities of Lumefantrine.
Maprotiline - Maprotiline may ↑ the QTc-prolonging activities of Leuprolide.
Mefloquine - Mefloquine may ↑ the QTc-prolonging activities of Leuprolide.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Leuprolide.
Methadone - Leuprolide may ↑ the QTc-prolonging activities of Methadone.
Methotrimeprazine - Methotrimeprazine may ↑ the QTc-prolonging activities of Leuprolide.
Metoclopramide - Metoclopramide may ↑ the QTc-prolonging activities of Leuprolide.
Metronidazole - Metronidazole may ↑ the QTc-prolonging activities of Leuprolide.

Mifepristone - Mifepristone may ↑ the QTc-prolonging activities of Leuprolide.
Miglitol - The therapeutic efficacy of Miglitol can be ↓ when used in combination with Leuprolide.
Mirabegron - Mirabegron may ↑ the QTc-prolonging activities of Leuprolide.
Mirtazapine - Mirtazapine may ↑ the QTc-prolonging activities of Leuprolide.
Moexipril - Moexipril may ↑ the QTc-prolonging activities of Leuprolide.
Moxifloxacin - Leuprolide may ↑ the QTc-prolonging activities of Moxifloxacin.
Nateglinide - The therapeutic efficacy of Nateglinide can be ↓ when used in combination with Leuprolide.
Nelfinavir - Nelfinavir may ↑ the QTc-prolonging activities of Leuprolide.
Nicardipine - Nicardipine may ↑ the QTc-prolonging activities of Leuprolide.
Nilotinib - Leuprolide may ↑ the QTc-prolonging activities of Nilotinib.
Norfloxacin - Norfloxacin may ↑ the QTc-prolonging activities of Leuprolide.
Nortriptyline - Nortriptyline may ↑ the QTc-prolonging activities of Leuprolide.
Octreotide - Octreotide may ↑ the QTc-prolonging activities of Leuprolide.
Ofloxacin - Leuprolide may ↑ the QTc-prolonging activities of Ofloxacin.
Olanzapine - Olanzapine may ↑ the QTc-prolonging activities of Leuprolide.
Olodaterol - Olodaterol may ↑ the QTc-prolonging activities of Leuprolide.
Ondansetron - Leuprolide may ↑ the QTc-prolonging activities of Ondansetron.
Osimertinib - Leuprolide may ↑ the QTc-prolonging activities of Osimertinib.
Oxytocin - Oxytocin may ↑ the QTc-prolonging activities of Leuprolide.
Paliperidone - Leuprolide may ↑ the QTc-prolonging activities of Paliperidone.
Panobinostat - Leuprolide may ↑ the QTc-prolonging activities of Panobinostat.
Paroxetine - Paroxetine may ↑ the QTc-prolonging activities of Leuprolide.
Pasireotide - Pasireotide may ↑ the QTc-prolonging activities of Leuprolide.
Pazopanib - Leuprolide may ↑ the QTc-prolonging activities of Pazopanib.
Pentamidine - Leuprolide may ↑ the QTc-prolonging activities of Pentamidine.
Perflutren - Leuprolide may ↑ the QTc-prolonging activities of Perflutren.
Pimozide - Leuprolide may ↑ the QTc-prolonging activities of Pimozide.
Pioglitazone - The therapeutic efficacy of Pioglitazone can be ↓ when used in combination with Leuprolide.
Posaconazole - Posaconazole may ↑ the QTc-prolonging activities of Leuprolide.

Pramlintide - The therapeutic efficacy of Pramlintide can be ↓ when used in combination with Leuprolide.
Primaquine - Leuprolide may ↑ the QTc-prolonging activities of Primaquine.
Procainamide - Leuprolide may ↑ the QTc-prolonging activities of Procainamide.
Promazine - Leuprolide may ↑ the QTc-prolonging activities of Promazine.
Promethazine - Promethazine may ↑ the QTc-prolonging activities of Leuprolide.
Propafenone - Leuprolide may ↑ the QTc-prolonging activities of Propafenone.
Propofol - Propofol may ↑ the QTc-prolonging activities of Leuprolide.
Protriptyline - Protriptyline may ↑ the QTc-prolonging activities of Leuprolide.
Quetiapine - Leuprolide may ↑ the QTc-prolonging activities of Quetiapine.
Quinidine - Leuprolide may ↑ the QTc-prolonging activities of Quinidine.
Quinine - Leuprolide may ↑ the QTc-prolonging activities of Quinine.
Ranolazine - Ranolazine may ↑ the QTc-prolonging activities of Leuprolide.
Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Leuprolide.
Rilpivirine - Rilpivirine may ↑ the QTc-prolonging activities of Leuprolide.
Risperidone - Risperidone may ↑ the QTc-prolonging activities of Leuprolide.
Ritonavir - Ritonavir may ↑ the QTc-prolonging activities of Leuprolide.
Rosiglitazone - The therapeutic efficacy of Rosiglitazone can be ↓ when used in combination with Leuprolide.
Salbutamol - Salbutamol may ↑ the QTc-prolonging activities of Leuprolide.
Salmeterol - Salmeterol may ↑ the QTc-prolonging activities of Leuprolide.
Saquinavir - Leuprolide may ↑ the QTc-prolonging activities of Saquinavir.
Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with Leuprolide.
Sertraline - Sertraline may ↑ the QTc-prolonging activities of Leuprolide.
Sevoflurane - Sevoflurane may ↑ the QTc-prolonging activities of Leuprolide.
Sitagliptin - The therapeutic efficacy of Sitagliptin can be ↓ when used in combination with Leuprolide.
Solifenacin - Solifenacin may ↑ the QTc-prolonging activities of Leuprolide.
Sorafenib - Sorafenib may ↑ the QTc-prolonging activities of Leuprolide.
Sotalol - Leuprolide may ↑ the QTc-prolonging activities of Sotalol.
Sulfamethoxazole - Sulfamethoxazole may ↑ the QTc-prolonging activities of Leuprolide.
Sulfisoxazole - Leuprolide may ↑ the QTc-prolonging activities of Sulfisoxazole.
Sunitinib - Sunitinib may ↑ the QTc-prolonging activities of Leuprolide.

Tacrolimus - Tacrolimus may ↑ the QTc-prolonging activities of Leuprolide.
Tamoxifen - Tamoxifen may ↑ the QTc-prolonging activities of Leuprolide.
Telavancin - Leuprolide may ↑ the QTc-prolonging activities of Telavancin.
Telithromycin - Leuprolide may ↑ the QTc-prolonging activities of Telithromycin.
Terbutaline - Terbutaline may ↑ the QTc-prolonging activities of Leuprolide.
Tetrabenazine - Leuprolide may ↑ the QTc-prolonging activities of Tetrabenazine.
Thioridazine - Leuprolide may ↑ the QTc-prolonging activities of Thioridazine.
Thiothixene - Thiothixene may ↑ the QTc-prolonging activities of Leuprolide.
Tizanidine - Tizanidine may ↑ the QTc-prolonging activities of Leuprolide.
Tolazamide - The therapeutic efficacy of Tolazamide can be ↓ when used in combination with Leuprolide.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Leuprolide.
Tolterodine - Tolterodine may ↑ the QTc-prolonging activities of Leuprolide.
Toremifene - Leuprolide may ↑ the QTc-prolonging activities of Toremifene.
Trazodone - Trazodone may ↑ the QTc-prolonging activities of Leuprolide.
Treprostinil - Treprostinil may ↑ the QTc-prolonging activities of Leuprolide.
Trimethoprim - Trimethoprim may ↑ the QTc-prolonging activities of Leuprolide.
Trimipramine - Trimipramine may ↑ the QTc-prolonging activities of Leuprolide.
Triptorelin - Triptorelin may ↑ the QTc-prolonging activities of Leuprolide.
Vandetanib - Leuprolide may ↑ the QTc-prolonging activities of Vandetanib.
Vardenafil - Vardenafil may ↑ the QTc-prolonging activities of Leuprolide.
Vemurafenib - Leuprolide may ↑ the QTc-prolonging activities of Vemurafenib.
Venlafaxine - Venlafaxine may ↑ the QTc-prolonging activities of Leuprolide.
Vilanterol - Vilanterol may ↑ the QTc-prolonging activities of Leuprolide.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Leuprolide.
Voriconazole - Voriconazole may ↑ the QTc-prolonging activities of Leuprolide.
Vorinostat - Vorinostat may ↑ the QTc-prolonging activities of Leuprolide.
Ziprasidone - Leuprolide may ↑ the QTc-prolonging activities of Ziprasidone.
Zuclopenthixol - Leuprolide may ↑ the QTc-prolonging activities of Zuclopenthixol (drugbank, 2013f).

Laboratory test interferences

- ↑ LFT's, BUN, serum calcium, uric acid, glucose, lipids, WBC, PT,
- ↓ serum potassium, platelets (Institute, 2014).

Overdose

There is no clinical experience with the effects of an acute overdose of leuprorelin acetate. In animal studies, doses of up to 500 times the recommended human dose resulted in **dyspnoea**, decreased activity and local irritation at the injection site. In cases of overdosage, the patients should be monitored closely and management should be symptomatic and supportive (emc, 2016).

Shelf life

36 months unopened.

Once reconstituted with sterile vehicle, the suspension should be administered immediately (emc, 2016).

Warning

Development or aggravation of diabetes may occur, therefore diabetic patients may require more frequent monitoring of blood glucose during treatment with Prostap.

Hepatic dysfunction and jaundice with elevated liver enzyme levels have been reported. Therefore, close observation should be made and appropriate measures taken if necessary.

Hypotension and worsening of depression have been reported.

The ability to drive and use machinery may be impaired due to visual disturbances and dizziness.

Toxicity

In rats subcutaneous administration of 250 to 500 times the recommended human dose, expressed on a per body weight basis, resulted in dyspnoea, decreased activity, and local irritation at the injection site. There is no evidence at present that there is a clinical counterpart of this phenomenon. In early clinical trials with leuprolide acetate doses as high as 20 mg/day for up to two years caused no adverse effects differing from those observed with the 1 mg/day dose (drugbank, 2013f).

Triptorelin

Alternative names

Decapeptyl SR, Gonapeptyl Depot, Salvacyl, triptorelina, triptoreline.

Manufacturer

Decapeptyl SR - Ipsen.
Gonapeptyl Depot - Ferring.
Salvacyl - Ipsen (BNF, 2016b).

Description

Triptorelin is a synthetic decapeptide agonist analog of luteinizing hormone releasing hormone LHRH. Possessing greater potency than endogenous LHRH, triptorelin reversibly represses gonadotropin secretion. After chronic, continuous administration, this agent effects sustained decreases in LH and FSH production and testicular and ovarian steroidogenesis. Serum testosterone concentrations may fall to levels typically observed in surgically castrated men (drugbank, 2016).

Typical dosage

Dosage	3.75mg	11.25mg	22.5mg
Recommended dose	1 injection every 4 weeks	1 injection every 12 weeks	I injection every 24 weeks (rxisk, 2014)

Table 8.1 – Dosages of Triptorelin

Pre-op - 11.25 mg every 3 months,
Post-op - Not required (NHS, 2015f).

Route

Intramuscular injection (NHS, 2015f).

Contraindications

Progressive brain tumours, Salvacyl: Severe osteoporosis (MIMS, 2016a).

Warnings and precautions

Anti-androgen treatment may be required at initiation and before withdrawal. Risk of bone loss with long-term use; exercise particular caution in patients with additional risk factors for osteoporosis. Maintain adequate dietary intake of calcium and vit D. Risk of depression; warn patient and monitor existing depression. Monitor patients at high risk of metabolic or cardiovascular diseases (MIMS, 2016a).

Interactions

Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Triptorelin.
Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Triptorelin.
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Triptorelin.
Capromab - Triptorelin may ↓ effectiveness of Capromab as a diagnostic agent.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Triptorelin.
Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Triptorelin.
Citalopram - Triptorelin may ↑ the QTc-prolonging activities of Citalopram.
Corifollitropin Alfa - The therapeutic efficacy of Corifollitropin Alfa can be ↑ when used in combination with Triptorelin.
Dofetilide - Triptorelin may ↑ the QTc-prolonging activities of Dofetilide.
Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Triptorelin.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Triptorelin.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Triptorelin.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Triptorelin.
Goserelin - Triptorelin may ↑ the QTc-prolonging activities of Goserelin.
Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Triptorelin.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Triptorelin.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Triptorelin.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Triptorelin.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Triptorelin.

Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Triptorelin.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Triptorelin.
Leuprolide - Triptorelin may ↑ the QTc-prolonging activities of Leuprolide.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Triptorelin.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Triptorelin.
Mifepristone - Mifepristone may ↑ the QTc-prolonging activities of Triptorelin.
Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Triptorelin.
Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with Triptorelin.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Triptorelin.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Triptorelin (drugbank, 2016).

Pregnancy

The use of gonadorelin analogues in pregnancy is contra-indicated. Pregnancy should be excluded before treatment; the first injection should be given during menstruation or shortly afterwards or use barrier contraception for 1 month beforehand (BNF, 2016b).

Breast-feeding

Gonadorelin analogues are contra-indicated in breast-feeding (BNF, 2016b).

Side-effects

Some of the most commonly reported adverse effects of triptorelin are hot flushes reported in 58.6% of patients, skeletal pain in 12.1%, impotence in 7.1%, and headache in 5.0% (drugbank, 2016).

Blood and lymphatic system disorders

- **purpura** (emc, 2009).

Ear disorders

- **tinnitus**,
- **vertigo** (emc, 2009).

Endocrine disorders

- **diabetes mellitus** (emc, 2009).

Eye disorders

- **visual disturbance** (emc, 2009).

Gastrointestinal disorders

- **Nausea**,
- **abdominal pain**,
- **constipation**,
- **diarrhoea**,
- **vomiting**,
- **abdominal distension**,
- **dry mouth**,
- **flatulence** (emc, 2009).

General disorders

- **asthenia**,
- **hyperhidrosis**,
- **fatigue**,
- **injection site erythema**,
- **injection site inflammation**,
- **injection site pain**,
- **injection site reaction**,
- **oedema**,
- **lethargy**,
- **pain**,
- **rigors**,
- **somnolence**,
- **chest pain**,
- **influenza-like illness**,
- **pyrexia** (emc, 2009).

Immune system disorders

- **anaphylactic reaction**,
- **hypersensitivity** (emc, 2009).

Infections and infestations

- **nasopharyngitis** (emc, 2009).

Metabolic disorders

- **anorexia**,
- **gout**,
- **increased appetite** (emc, 2009).

Musculoskeletal disorders

- **back pain**,
- **musculoskeletal pain**,
- **pain in extremity**,
- **arthralgia**,
- **muscle cramps**,
- **muscular weakness**,
- **myalgia**,
- **joint stiffness**,
- **joint swelling**,
- **musculoskeletal stiffness**,
- **osteoarthritis** (emc, 2009).

Nervous system

- **paraesthesia in lower limbs**,
- **dizziness**,
- **headache**,
- **paraesthesia**,
- **memory impairment** (emc, 2009).

Psychiatric disorders

- **depression**,
- **mood changes**,
- **insomnia**,
- **irritability**,
- **confusional state**,
- **decreased activity**,
- **euphoric mood** (emc, 2009).

Reproductive system

- **erectile dysfunction**,
- **loss of libido**,
- **gynaecomastia**,
- **breast pain**,
- **testicular atrophy**,
- **testicular pain**,
- **ejaculation failure** (emc, 2009).

Respiratory system

- **dyspnoea**,
- **orthopnoea** (emc, 2009).

Skin disorders

- **hyperhidrosis**,
- **acne**,
- **alopecia**,
- **pruritus**,
- **rash**,
- **blister**,
- **urticaria** (emc, 2009).

Vascular disorders

- **hot flush**,
- **hypertension**,
- **epistaxis**,
- **hypotension** (emc, 2009).

Overdose

There is no experience of overdosage in clinical trials. In single dose toxicity studies in mice and rats, the subcutaneous LD-50 of triptorelin was 400 mg/kg in mice and 250 mg/kg in rats, approximately 500 and 600 times, respectively, the estimated monthly human dose based on body surface area. If overdosage occurs, therapy should be discontinued immediately and the appropriate supportive and symptomatic treatment administered (rxisk, 2014).

Pharmakinetics

Metabolism

The metabolism of triptorelin in humans is not well understood; however, metabolism likely does not involve hepatic enzymes such as cytochrome P450. Whether or not triptorelin affects, or how it affects other metabolizing enzymes is also poorly understood. Triptorelin has no identified metabolites (drugbank, 2016).

Absorption

Following a single intramuscular injection of Triptorelin to patients with prostate cancer, mean peak serum concentrations of 28.4 ng/mL, 38.5 ng/mL, and 44.1 ng/mL occurred in 1 to 3 hours after the 3.75 mg, 11.25 mg, and 22.5 mg formulations, respectively.

Triptorelin did not accumulate over 9 months (3.75 mg and 11.25 mg) or 12 months (22.5 mg) of treatment (rxisk, 2014).

Distribution

The volume of distribution following a single intravenous bolus dose of 0.5 mg of triptorelin peptide was 30–33 L in healthy male volunteers. There is no evidence that triptorelin, at clinically relevant concentrations, binds to plasma proteins (rxisk, 2014).

Metabolism

The metabolism of triptorelin in humans is unknown, but is unlikely to involve hepatic microsomal enzymes (cytochrome P-450). The effect of triptorelin on the activity of other drug metabolising enzymes is also unknown. Thus far, no metabolites of triptorelin have been identified. Pharmacokinetic data suggest that C-terminal fragments produced by tissue degradation are either completely degraded in the tissues, or rapidly degraded in plasma, or cleared by the kidneys (rxisk, 2014).

Half-life

The pharmacokinetics of triptorelin follows a 3 compartment model. The half lives are estimated to be 6 minutes, 45 minutes, and 3 hours respectively (drugbank, 2016).

Clearance

In healthy male volunteers, total clearance of triptorelin was 211.9 mL/min (drugbank, 2016).

Excretion

Triptorelin is eliminated by both the liver and the kidneys. Following intravenous administration of 0.5 mg triptorelin peptide to six healthy male volunteers with a creatinine clearance of 149.9 mL/min, 41.7% of the dose was excreted in urine as intact peptide with a total triptorelin clearance of 211.9 mL/min. This percentage increased to 62.3% in patients with liver disease who have a lower creatinine clearance (89.9 mL/min). It has also been observed that the nonrenal clearance of triptorelin (patient anuric, CIcreat = 0) was 76.2 mL/min, thus indicating that the nonrenal elimination of triptorelin is mainly dependent on the liver (rxisk, 2014).

Pharmacodynamics

Following the first administration, there is a transient surge in circulating levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol. After chronic and continuous administration, usually 2 to 4 weeks after initiation of therapy, a sustained decrease in LH and FSH secretion and marked reduction of testicular steroidogenesis are observed. A reduction of serum testosterone concentration to a level typically seen in surgically castrated men is obtained. Consequently, the result is that tissues and functions that depend on these hormones for maintenance become quiescent. These effects are usually reversible after cessation of therapy (rxisk, 2014).

Following a single intramuscular injection of Triptorelin -

3.75 mg - serum testosterone levels first increased, peaking on Day 4, and declined thereafter to low levels by Week 4 in healthy male volunteers.

11.25 mg - serum testosterone levels first increased, peaking on Days 2–3, and declined thereafter to low levels by Weeks 3–4 in men with advanced prostate cancer.

22.5 mg - serum testosterone levels first increased, peaking on Day 3, and declined thereafter to low levels by Weeks 3–4 in men with advanced prostate cancer (rxisk, 2014).

How it works

Triptorelin is a synthetic agonist analog of gonadotropin releasing hormone (GnRH). Animal studies comparing triptorelin to native GnRH found that triptorelin had 13 fold higher releasing activity for luteinizing hormone, and 21-fold higher releasing activity for follicle-stimulating hormone (drugbank, 2016).

Triptorelin is a synthetic decapeptide agonist analog of gonadotropin releasing hormone (GnRH). Comparative in-vitro studies showed that triptorelin was 100-fold more active than native GnRH in stimulating luteinizing hormone release from monolayers of dispersed rat pituitary cells in culture and 20-fold more active than native GnRH in displacing 125I-GnRH from pituitary receptor sites. In animal studies, triptorelin pamoate was found to have 13fold higher luteinizing hormone-releasing activity and 21-fold higher follicle-stimulating hormone-releasing activity compared to the native GnRH (rxisk, 2014).

Special precautions for disposal and other handling

The suspension for injection must be reconstituted using an aseptic technique and only using the ampoule of mannitol solution 0.8% for injection that is provided as the suspension vehicle for Decapeptyl SR 11.25 mg.

The suspension vehicle should be drawn into the syringe provided using one of the injection needles and transferred to the vial containing the powder for injection. The vial should be shaken from side to side until a homogenous suspension is formed, and the mixture then drawn back into the syringe without inverting the vial. The injection needle should then be changed and the second needle used to administer the injection. As the product is a suspension, the injection should be administered immediately after reconstitution to prevent sedimentation. The suspension should be discarded if it is not administered immediately after reconstitution.

To ensure patients receive the correct dose, each vial of Decapeptyl contains a small overage to allow for predictable losses on reconstitution and injection.

The vial is intended for single use only and any remaining product should be discarded (emc, 2009).

Excipients

D,L lactide-glycolide copolymer, mannitol, carmellose sodium, polysorbate 80 (emc, 2009).

Shelf life

2 years (emc, 2009).

Toxicology

In rats, doses of 120, 600, and 3000 mcg/kg given every 28 days (approximately 0.3, 2, and 8 times the human monthly dose based on body surface area) resulted in increased mortality with a drug treatment period of 13–19 months. The incidences of benign and malignant pituitary tumours and histiosarcomas were increased in a dose-related manner. No oncogenic effect was observed in mice administered triptorelin for 18 months at doses up to 6000 mcg/kg every 28 days (approximately 8 times the human monthly dose based on body surface area).

Mutagenicity studies performed with triptorelin using bacterial and mammalian systems (in-vitro Ames test and chromosomal aberration test in CHO cells and an in-vivo mouse micronucleus test) provided no evidence of mutagenic potential.

After 60 days of subcutaneous treatment followed by a minimum of four estrus cycles prior to mating, triptorelin, at doses of 2, 20, and 200 mcg/kg/day in saline (approximately 0.2, 2, and 16 times the estimated human daily dose based on body surface area) or 2 monthly injections as slow release microspheres (20 mcg/kg/day), had no effect on the fertility or general reproductive function of female rats.

No studies were conducted to assess the effect of triptorelin on male fertility (rxisk, 2014).

Warnings

Important safety information -

- Triptorelin may cause dizziness or vision changes. These effects may be worse if you take it with alcohol or certain medicines. Use triptorelin with caution. Do not drive or perform other possibly unsafe tasks until you know how you react to it.
- Certain hormone levels may increase during the first few weeks of treatment with triptorelin. This may cause you to experience worsening symptoms or onset of new symptoms (eg, bone pain; blood in the urine; difficulty urinating; burning, numbness, or tingling) during the first few weeks of treatment.
- Triptorelin lowers the amount of certain hormones in your body. This may cause certain expected side effects to occur, such as -
  - ⋆ breast enlargement, soreness, or tenderness;
  - ⋆ testicular changes, pain, or soreness;
  - ⋆ decreased sexual ability;
  - ⋆ hot flashes;
  - ⋆ night sweats. Contact your doctor if you have questions or concerns or if you experience any of these side effects.
- Lowering the amount of male hormones in the body may increase the risk of a certain type of irregular heartbeat (prolonged QT interval). Discuss any questions or concerns with your doctor.
- A slight increase in the risk of stroke or serious and sometimes fatal heart problems has been reported with the use of GnRH agonists in men. Although the risk appears to be low, seek **immediate medical attention** if you experience -
  - ⋆ **chest, jaw, or left arm pain**;
  - ⋆ **confusion**;
  - ⋆ **fainting**;
  - ⋆ **numbness of an arm or leg**;
  - ⋆ **one-sided weakness**;
  - ⋆ **slurred speech**;
  - ⋆ **sudden, severe headache or vomiting**; or
  - ⋆ **vision changes**. Discuss any questions or concerns with your doctor (drugbank, 2016).

- Triptorelin may raise your blood sugar. High blood sugar may make you feel confused, drowsy, or thirsty. It can also make you flush, breathe faster, or have a fruit-like breath odour. If these symptoms occur, tell your doctor right away.
- Diabetes patients - Check blood sugar levels closely. Ask your doctor before you change the dose of your diabetes medicine.
- Rarely, a serious pituitary gland problem (pituitary apoplexy) may occur after you use triptorelin. This serious problem usually occurs shortly after you begin to use triptorelin. Contact your doctor **immediately** if you experience a -
  - ⋆ **sudden headache**,
  - ⋆ **vomiting**,
  - ⋆ **fainting**,
  - ⋆ **eye weakness**,
  - ⋆ **inability to move your eyes**,
  - ⋆ **mental status changes**, or
  - ⋆ **vision changes** (drugbank, 2016).
- Triptorelin may interfere with certain lab tests, including certain hormone and pituitary gland function tests. Be sure your doctor and lab personnel know you are using triptorelin.
- Lab tests, including testosterone, prostate specific antigen (PSA) levels, haemoglobin A1c, or blood glucose, may be performed while you use triptorelin. These tests may be used to monitor your condition or check for side-effects. Be sure to keep all doctor and lab appointments (drugbank, 2016).

Hypersensitivity reactions

Anaphylactic shock, hypersensitivity, and angioedema related to triptorelin administration have been reported. In the event of a hypersensitivity reaction, therapy with triptorelin should be discontinued immediately and the appropriate supportive and symptomatic care should be administered (rxisk, 2014).

Transient Increase in Serum Testosterone

Initially, triptorelin, like other GnRH agonists, causes a transient increase in serum testosterone levels (rxisk, 2014).

Effect on QT/QTc Interval

Androgen deprivation therapy may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes (rxisk, 2014).

Hyperglycemia and Diabetes

Hyperglycemia and an increased risk of developing diabetes have been reported in men receiving GnRH agonists. Hyperglycemia may represent development of diabetes mellitus or worsening of glycemic control in patients with diabetes. Monitor blood glucose and/or glycosylated haemoglobin (HbA1c) periodically in patients receiving a GnRH agonist and manage with current practice for treatment of hyperglycemia or diabetes (rxisk, 2014).

Cardiovascular Diseases

Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice (rxisk, 2014).

Chapter 9

Progestogens

Dydrogesterone

A synthetic progestational hormone with no androgenic or oestrogenic properties. Unlike many side progestational compounds, dydrogesterone produces no increase in temperature and does not inhibit ovulation (drugbank, 2014b).

Administration

Administration is oral in the form of tablets (BNF, 2016a).

Also known as

Duphaston, Duphaston HRT.

Manufacturer

Duphaston = Solvay.
Duphaston HRT = Solvay.

Contains

Duphaston = Dydrogesterone 10 mgs. The tablets are round and white, with an 'u' on one side.

The side side is marked '155' on each half of the tablet. The tablets also contain lactose, maize starch, methylhydroxypropylcellulose, silica, magnesium stearate and E171 (emc, 2016).

Duphaston HRT = Dydrogesterone 10 mgs. The tablets are round and white, with an 'u' on one side.

The side side is marked '155' on each half of the tablet. The tablets also contain lactose, maize starch, methylhydroxypropylcellulose, silica, magnesium stearate and E171 (emc, 2016).

Indications

To counteract the effects of unopposed oestrogen in hormone replacement therapy (emc, 2016).

Pharmacokinetics

50% of dose excreted in urine within 24 hours (emc, 2016). Within 72 hours the excretion is complete (emc, 2016). After oral administration of dydrogesterone, on average 63% of the dose is excreted into the urine. Within 72 hours, excretion is complete. Dydrogesterone is completely metabolised. The main metabolite of dydrogesterone is 20alpha-dihydrodydrogesterone (DHD) and is present in the urine predominantly as the glucuronic acid conjugate. A common feature of all metabolites characterised is the retention of the 4,6 diene-3-one configuration of the parent compound and the absence of 17alpha-hydroxylation. This explains the lack of oestrogenic and androgenic effects of dydrogesterone.

After oral administration of dydrogesterone, plasma concentrations of DHD are substantially higher as compared to the parent drug. The AUC[54] and Cmax[55] ratios of DHD to dydrogesterone are in the order of 40 and 25, respectively.

Dydrogesterone is rapidly absorbed. The Tmax[56] values of dydrogesterone and DHD vary between 0.5 and 2.5 hours.

Mean terminal half lives of dydrogesterone and DHD vary between 5 to 7 and 14 to 17 hours, respectively.

Unlike progesterone, dydrogesterone is not excreted in the urine as pregnanediol. It is therefore possible to analyse production of endogenous progesterone even in the presence of dydrogesterone (emc, 2016).

[54] a method of measurement of the bioavailability of a drug based on a plot of blood concentrations sampled at frequent intervals. It is directly proportional to the total amount of unaltered drug in the patients blood

[55] The maximum or "peak" concentration of a drug observed after its administration

[56] the time after administration of a drug when the maximum plasma concentration is reached; when the rate of absorption equals the rate of elimination

Pharmacodynamics

Dydrogesterone is an orally active progestogen which acts directly on the uterus, producing a complete secretory endometrium in an oestrogen-primed uterus. At therapeutic levels, dydrogesterone has no contraceptive effect as it does not inhibit or interfere with ovulation or the corpus luteum. Furthermore, dydrogesterone is non-androgenic, non-oestrogenic, non-corticoid, non-anabolic and is not excreted as pregnanediol. Dydrogesterone helps to regulate the healthy growth and normal shedding of the uterus lining. Therefore, it may be useful in the treatment of menstrual disorders such as absent, irregular or painful menstrual periods, infertility, premenstrual syndrome and endometriosis (drugbank, 2014b).

Absorption - Rapidly absorbed in the gastrointestinal tract with a bioavailability of 28%.

Metabolism - Metabolism is complete to a 20-dihydrodydrogesterone (DHD) metabolite.

Half-life - Dydrogesterone: 5–7 hours, 20-dihydrodydrogesterone (DHD) metabolite: 14–17 hours (drugbank, 2014b).

How it works

Dydrogesterone is a progestogen that works by regulating the healthy growth and normal shedding of the womb lining by acting on progesterone receptors in the uterus (drugbank, 2014b).

Typical dosage

Pre-op - 5–20 mgs/day
Post-op - 2.5–10 mgs/day (unknown, 2005)

Route

Tablets - Duphaston, Duphaston HRT.

Contraindications

Liver impairment or liver tumours, severe arterial disease, breast or genital tract carcinoma (BNF, 2016a).

Side-effects

Central Nervous System

- **headache**,
- **dizziness**,
- **insomnia**,
- **drowsiness**,
- **depression**, (BNF, 2016a).

Gastrointestinal

- **weight gain**,
- **nausea** (BNF, 2016a).

Skin

- **skin reactions** (including urticaria, pruritis, rash, and acne),
- melasma or chloasma,
- **urticaria**,
- **hirsutism** and
- **alopecia**, (BNF, 2016a).

Metabolism

- **bloating**,
- **fluid retention**,
- **weight gain**,
- **nausea**, (BNF, 2016a).

Genitourinary

- **breast tenderness** (BNF, 2016a).

Interactions/incompatibilities

Progestogens antagonise hypoglycaemic effect of anti-diabetics drugs, progestogens antagonise anti-coagulant effect of coumarins (i.e. warfarin) (BNF, 2016a).

Acenocoumarol - The therapeutic efficacy of Acenocoumarol can be ↓ when used in combination with Dydrogesterone.

Apixaban - The therapeutic efficacy of Apixaban can be ↓ when used in combination with Dydrogesterone.

Argatroban - The therapeutic efficacy of Argatroban can be ↓ when used in combination with Dydrogesterone.

Bivalirudin - The therapeutic efficacy of Bivalirudin can be ↓ when used in combination with Dydrogesterone.

Dabigatran etexilate - The therapeutic efficacy of Dabigatran etexilate can be ↓ when used in combination with Dydrogesterone.

Dalteparin - The therapeutic efficacy of Dalteparin can be ↓ when used in combination with Dydrogesterone.

Danaparoid - The therapeutic efficacy of Danaparoid can be ↓ when used in combination with Dydrogesterone.
Desirudin - The therapeutic efficacy of Desirudin can be ↓ when used in combination with Dydrogesterone.
Edoxaban - The therapeutic efficacy of Edoxaban can be ↓ when used in combination with Dydrogesterone.
Enoxaparin - The therapeutic efficacy of Enoxaparin can be ↓ when used in combination with Dydrogesterone.
Fondaparinux sodium - The therapeutic efficacy of Fondaparinux sodium can be ↓ when used in combination with Dydrogesterone.
Heparin - The therapeutic efficacy of Heparin can be ↓ when used in combination with Dydrogesterone.
Nadroparin - The therapeutic efficacy of Nadroparin can be ↓ when used in combination with Dydrogesterone.
Rivaroxaban - The therapeutic efficacy of Rivaroxaban can be ↓ when used in combination with Dydrogesterone.
Tinzaparin - The therapeutic efficacy of Tinzaparin can be ↓ when used in combination with Dydrogesterone.
Ulipristal - The therapeutic efficacy of Dydrogesterone can be ↓ when used in combination with Ulipristal.
Warfarin - The therapeutic efficacy of Warfarin can be ↓ when used in combination with Dydrogesterone.

Clinical assessment

Liver function tests (LFT), bilirubin during long-term treatment (Abramovitz, 2016).

Overdose

There are no reports of ill-effects from overdosage being reported, however if a large overdosage is discovered within 2–3 hours and treatment seems desirable, gastric lavage[57] is recommended. There are no special antidotes and treatment should be to treat the symptoms only (emc, 2016).

Note

Take with food or milk to decrease/minimise gastrointestinal symptoms (Abramovitz, 2016).

[57] stomach washout or stomach pumped out

Warning

Use with caution with patients with cardiovascular or renal impairment, diabetes mellitus, asthma, epilepsy, and migraine, or side conditions which may be aggravated by fluid retention. Use with care with patients with a history of mental depression (TGC, 2015a).

If you are allergic to lactose then you should tell your doctor, and/or pharmacist, when this drug is prescribed for you (emc, 2016).

Toxicity

No serious or unexpected toxicity has been observed with dydrogesterone. In acute toxicity studies, the LD-50 doses in rats exceeded 4,640mg/kg for the oral route (drugbank, 2014b).

Progesterone

The pharmacological particulars of the product are those of the naturally occurring progesterone with induction of a full secretory endometrium (emc, 2016)

The major progestational steroid that is secreted primarily by the corpus luteum and the placenta. Progesterone acts on the uterus, the mammary glands, and the brain. It is required in embryo implantation, pregnancy maintenance, and the development of mammary tissue for milk production. Progesterone, converted from pregnenolone, also serves as an intermediate in the biosynthesis of gonadal steroid hormones and adrenal corticosteroids (drugbank, 2013j).

Also known as

Cyclogest, Gestone, Utrogestan, Prometrium (USA and Canada), Crinone.

Manufacturer

Crinone - Serono,
Cyclogest - Alpharma,
Gestone - Nordic.
Utrogestan - Besins Healthcare

Contains

Cylcogest - Progesterone 200 mgs, 400 mgs.
Gestone - Progesterone 50 mgs/ml.
Crinone - progesterone 90 mg/application (8%) (BNF, 2016a).

Pharmacokinetics

Absorbed from the gastrointestinal tract, it was believed that progesterone is rapidly inactivated in the liver and thus producing little biological effect when administered by mouth. However, it is now thought to be active after oral administration, but can also be administered buccally [58] and rectally. The half-life in the blood is only a few minutes. It is metabolised in the liver, with about 12% being converted to Pregnanediol which is excreted in the urine conjugated with Glucuronic Acid (TGC, 2015a).

Pharmacodynamics

Progesterone is a naturally occuring progestin or a synthetic form of the naturally occurring female sex hormone, progesterone. In a woman's normal menstrual cycle, an egg matures and is released from the ovaries (ovulation). The ovary then produces progesterone, preventing the release of further eggs and priming the lining of the womb for a possible pregnancy. If pregnancy occurs, progesterone levels in the body remain high, maintaining the womb lining. If pregnancy does not occur, progesterone levels in the body fall, resulting in a menstrual period. Progesterone tricks the body processes into thinking that ovulation has already occurred by maintaining high levels of the synthetic progesterone. This prevents the release of eggs from the ovaries (drugbank, 2013j).

Absorption - Progesterone absorption is prolonged with an absorption half-life of approximately 25–50 hours.
Protein binding - 96%–99%
Metabolism - Progesterone is metabolised primarily by the liver largely to pregnanediols and pregnanolones.
Elimination - The glucuronide and sulfate conjugates of pregnanediol and pregnanolone are excreted in the urine and bile. Progesterone metabolites which are excreted in the bile may undergo enterohepatic recycling or may be excreted in the faeces. Progesterone metabolites are excreted mainly by the kidneys.
Half-life - 34.8–55.13 hours (drugbank, 2013j).

[58] A means of administering a drug where it is held in the mouth against the cheek wall

How it works

Progesterone shares the pharmacological actions of the progestins. Progesterone binds to the progesterone and oestrogen receptors. Target cells include the female reproductive tract, the mammary gland, the hypothalamus, and the pituitary. Once bound to the receptor, progestins like Progesterone will slow the frequency of release of gonadotropin releasing hormone (GnRH) from the hypothalamus and blunt the pre-ovulatory LH (luteinizing hormone) surge. In women who have adequate endogenous oestrogen, progesterone transforms a proliferative endometrium into a secretory one. Progesterone is essential for the development of decidual tissue and is necessary to increase endometrial receptivity for implantation of an embryo. Once an embryo has been implanted, progesterone acts to maintain the pregnancy. Progesterone also stimulates the growth of mammary alveolar tissue and relaxes uterine smooth muscle. It has little oestrogenic and androgenic activity (drugbank, 2013j).

Typical dosage

Pre-op - 100–400 mgs/day (orally)
Post-op - 50–400 mgs/day (unknown, 2005).

Route

Tablets - Utrogestan,
Injection - Gestone, Prometrium,
Pessary - Cyclogest,
Suppository - Cyclogest,
Vaginal gel - Crinone,
Vaginal suppository - Utrogestan.

Contraindications

Known allergy or hypersensitivity to progesterone or to any of the excipients. The capsules contain arachis oil (peanut oil) and should never be used by patients allergic to peanuts. Severe hepatic dysfunction. Mammary or genital tract carcinoma. Thrombophlebitis. Thromboembolic disorders. Cerebral haemorrhage. Porphyria (emc, 2016)

Side-effects

Central Nervous System

- Fatigue,
- **headache -10–31%**,
- **depression - 19%**,
- drowsiness or insomnia,
- **fever**, (WebMD, 2014e)
- **chills**,
- **cold or flu-like symptoms** (drugs.com, 2014c)
- **migraine**,
- **severe dizziness or faintness**,
- **slow or difficult speech**,
- **seizures**,
- **lack of coordination**,
- **loss of balance** (medlineplus, 2015b)
- **dizziness - 15–24%** (Medscape, 2014).

Cardiovascular

- **oedema** (WebMD, 2014e),
- **sharp chest pain** (drugs.com, 2014c)
- **coughing up blood**,
- **fast heartbeat** (medlineplus, 2015b).

Eyes

- **loss of vision**,
- **blurred vision**,
- **bulging eyes**,
- **double vision** (medlineplus, 2015b).

Gastrointestinal

- Stomach upset,
- changes in appetite,
- weight gain (WebMD, 2014e).
- **cough** (drugs.com, 2014c).
- **stomach pain or swelling**,
- **hoarseness** (medlineplus, 2015b).

Genitourinary

- **breast tenderness - 16–27%**, breast discomfort or enlargement,
- PMS-like syndrome, (WebMD, 2014e),
- **problems with urination** (drugs.com, 2014c),
- **breast lumps** (medlineplus, 2015b),
- **breast pain - 6–16%** (Medscape, 2014).

Skin

- **skin rashes**,
- **hives**,
- acne (WebMD, 2014e),
- **itching** (medlineplus, 2015b).

Respiratory

- **shortness of breath**,
- **difficulty breathing**,
- **difficulty swallowing**,
- **swelling of the face, throat, tongue**,
- **lips, eyes, hands**,
- **feet, ankles, or lower legs** (medlineplus, 2015b).

Musculoskeletal

- **leg swelling or pain**,
- **weakness or numbness of an arm or leg** (medlineplus, 2015b).

Interactions/incompatibilities

The metabolism of progesterone by human liver microsomes was inhibited by ketoconazole (IC50 <0.1 M Ketoconazole is a known inhibitor of cytochrome P450 3A4. These data therefore suggest that ketoconazole may ↑ the bioavailability of progesterone. The clinical relevance of the in-vitro findings is unknown (emc, 2016).

Abciximab - The therapeutic efficacy of Abciximab can be ↓ when used in combination with Progesterone.

Acenocoumarol - The therapeutic efficacy of Acenocoumarol can be ↓ when used in combination with Progesterone.

Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Progesterone.

Afatinib - The serum concentration of Afatinib can be ↑ when it is combined with Progesterone.

Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Progesterone.

Apixaban - The therapeutic efficacy of Apixaban can be ↓ when used in combination with Progesterone.

Argatroban - The therapeutic efficacy of Argatroban can be ↓ when used in combination with Progesterone.

Bexarotene - The serum concentration of Progesterone can be ↓ when it is combined with Bexarotene.

Bivalirudin - The therapeutic efficacy of Bivalirudin can be ↓ when used in combination with Progesterone.

Bosentan - The serum concentration of Progesterone can be ↓ when it is combined with Bosentan.

Bosutinib - The serum concentration of Bosutinib can be ↑ when it is combined with Progesterone.

Brentuximab vedotin - The serum concentration of Brentuximab vedotin can be ↑ when it is combined with Progesterone.

Butoconazole - The therapeutic efficacy of Progesterone can be ↓ when used in combination with Butoconazole.

C1 Esterase Inhibitor (Human) - Progesterone may increase the thrombogenic activities of C1 Esterase Inhibitor (Human).

Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Progesterone.

Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Progesterone.

Citric Acid - The therapeutic efficacy of Citric Acid can be ↓ when used in combination with Progesterone.

Colchicine - The serum concentration of Colchicine can be ↑ when it is combined with Progesterone.

Dabigatran etexilate - The serum concentration of the active metabolites of Dabigatran etexilate can be ↑ when Dabigatran etexilate is used in combination with Progesterone.

Dabrafenib - The serum concentration of Progesterone can be ↓ when it is combined with Dabrafenib.

Dalteparin - The therapeutic efficacy of Dalteparin can be ↓ when used in combination with Progesterone.

Danaparoid - The therapeutic efficacy of Danaparoid can be ↓ when used in combination with Progesterone.

Deferasirox - The serum concentration of Progesterone can be ↓ when it is combined with Deferasirox.

Desirudin - The therapeutic efficacy of Desirudin can be ↓ when used in combination with Progesterone.

Dicoumarol - The therapeutic efficacy of Dicoumarol can be ↓ when used in combination with Progesterone.

Doxorubicin - The serum concentration of Doxorubicin can be ↑ when it is combined with Progesterone.

Edetic Acid - The therapeutic efficacy of Edetic Acid can be ↓ when used in combination with Progesterone.

Edoxaban - The serum concentration of Edoxaban can be ↑ when it is combined with Progesterone.

Enoxaparin - The therapeutic efficacy of Enoxaparin can be ↓ when used in combination with Progesterone.

Ethyl biscoumacetate - The therapeutic efficacy of Ethyl biscoumacetate can be ↓ when used in combination with Progesterone.

Everolimus - The serum concentration of Everolimus can be ↑ when it is combined with Progesterone.

Fondaparinux sodium - The therapeutic efficacy of Fondaparinux sodium can be ↓ when used in combination with Progesterone.

Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Progesterone.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Progesterone.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Progesterone.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Progesterone.
Heparin - The therapeutic efficacy of Heparin can be ↓ when used in combination with Progesterone.
Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Progesterone.
Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Progesterone.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Progesterone.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Progesterone.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Progesterone.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Progesterone.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Progesterone.
Ledipasvir - The serum concentration of Ledipasvir can be ↑ when it is combined with Progesterone.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Progesterone.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Progesterone.
Mitotane - The serum concentration of Progesterone can be ↓ when it is combined with Mitotane.
Nadroparin - The therapeutic efficacy of Nadroparin can be ↓ when used in combination with Progesterone.
Naloxegol - The serum concentration of Naloxegol can be ↑ when it is combined with Progesterone.
Pazopanib - The serum concentration of Pazopanib can be ↑ when it is combined with Progesterone.
Phenindione - The therapeutic efficacy of Phenindione can be ↓ when used in combination with Progesterone.
Phenprocoumon - The therapeutic efficacy of Phenprocoumon can be ↓ when used in combination with Progesterone.
Phenytoin - The metabolism of Progesterone can be ↑ when combined with Phenytoin.
Prucalopride - The serum concentration of Prucalopride can be ↑ when it is combined with Progesterone.
Ranolazine - The serum concentration of Ranolazine can be ↑ when it is combined with Progesterone.

Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Progesterone.
Rifaximin - The serum concentration of Rifaximin can be ↑ when it is combined with Progesterone.
Rivaroxaban - The therapeutic efficacy of Rivaroxaban can be ↓ when used in combination with Progesterone.
Saquinavir - The serum concentration of Saquinavir can be ↑ when it is combined with Progesterone.
Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with Progesterone.
Silodosin - The serum concentration of Silodosin can be ↑ when it is combined with Progesterone.
Siltuximab - The serum concentration of Progesterone can be ↓ when it is combined with Siltuximab.
Sulfanilamide - The therapeutic efficacy of Progesterone can be ↓ when used in combination with Sulfanilamide.
Sulodexide - The therapeutic efficacy of Sulodexide can be ↓ when used in combination with Progesterone.
Terconazole - The therapeutic efficacy of Progesterone can be ↓ when used in combination with Terconazole.
Tinzaparin - The therapeutic efficacy of Tinzaparin can be ↓ when used in combination with Progesterone.
Tioconazole - The therapeutic efficacy of Progesterone can be ↓ when used in combination with Tioconazole.
Tocilizumab - The serum concentration of Progesterone can be ↓ when it is combined with Tocilizumab.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Progesterone.
Topotecan - The serum concentration of Topotecan can be ↑ when it is combined with Progesterone.
Treprostinil - The therapeutic efficacy of Treprostinil can be ↓ when used in combination with Progesterone.
Ulipristal - The therapeutic efficacy of Progesterone can be ↓ when used in combination with Ulipristal.
Verapamil - The serum concentration of Verapamil can be ↑ when it is combined with Progesterone.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Progesterone.
Vincristine - The serum concentration of Vincristine can be ↑ when it is combined with Progesterone.
Warfarin - The therapeutic efficacy of Warfarin can be ↓ when used in combination with Progesterone (drugbank, 2013j).

Herbal interactions

St. John's Wort - The serum concentration of Progesterone can be ↓ when it is combined with St. John's Wort (drugbank, 2013j).

Food interactions

- Avoid alcohol.
- Avoid excessive quantities of coffee or tea (Caffeine).
- Increase dietary intake of magnesium, folate, vitamin B6, B12, and/or consider taking a multivitamin.
- Take at the same time everyday.
- Take with food (drugbank, 2013j).

Laboratory test interferences

Utrogestan may affect the results of laboratory tests of hepatic and/or endocrine functions (emc, 2016).

Overdose

Overdosage may produce **euphoria** (emc, 2016).

Shelf life

Cyclogest = 3 years from the date of manufacture.

Crinone = 36 months, (which is 3 years again!) (emc, 2016).

Warning

If unexplained, sudden or gradual,

- **partial or complete loss of vision**,
- **exophthalmos** or
- **diplopia**,
- **papilloedema** [59],
- **retinal vascular lesions** or
- **migraine**

occur during therapy, the drug should be discontinued and appropriate diagnostic and therapeutic measures instituted (emc, 2016).

[59] Papilloedema is an optic disc swelling that is secondary to elevated intracranial pressure. In contrast to side causes of optic disc swelling, vision usually is well preserved with acute papilloedema. Papilloedema almost always presents as a bilateral phenomenon and may develop over hours to weeks (Gossman, 2014)

Chapter 10

Other useful drugs

This section relates to substances that are not hormones, or even anti-androgens, but drugs that are used to provide pain relief for things such as electrolysis.

Ametop

Used as a topical anaesthetic for skin anaesthesia.

Tetracaine (also known as amethocaine; trade name Pontocaine. Ametop and Dicaine) is a potent local anesthetic of the ester group. It is mainly used topically in ophthalmology and as an antipruritic, and it has been used in spinal anesthesia (drugbank, 2015e)

Also known as

Tetracaine, Amethocaine.

Manufacturer

Smith & Nephew Healthcare.

Contains

Ametop = Tetracaine - 4% in a 1.5g tube (BNF, 2016a).

Pharmacology

Amethocaine is a local anaesthetic and is believed to act by blocking nerve conduction mainly by inhibiting sodium ion flux across the axon membrane. Amethocaine achieves this by acting upon specific receptors that control gating mechanisms responsible for conductance changes in specialised proteinaceous sodium channels. Blocking sodium ion flux prevents the setting up of an action potential in the nerve axon, thus preventing pain receptors signalling to the central nervous system (skyscape, 2014).

Indications

Used as a topical anaesthetic for skin anaesthesia prior to venepuncture or venous cannulation (BNF, 2016a).

Pharmacokinetics

It is not necessary to apply Ametop gel for longer than 30–45 minutes and anaesthesia remains for 4–6 hours in most people after a single application (skyscape, 2014).

Typical dosage

Electrolysis 1.5g for no longer than 30–45 minutes (skyscape, 2014).

Route

Topical = Ametop

Contraindications

Hypersensitivity to tetracaine has been reported (BNF, 2016a). Do not apply Ametop gel to broken skin, mucous membranes or to the eyes or ears (skyscape, 2014).

Side-effects

Skin

- **erythema**,
- blanching,
- transient local oedema,
- abnormal sensations,
- urticaria,
- local burning/discomfort (skyscape, 2014).

Slight erythema is frequently seen at the site of application and is due to the pharmacological action of amethocaine in dilating capillary vessels. This may help in delineating the anaesthetised area.

Slight oedema or itching are less frequently seen at the site of application. This may be due to the local release of histamine and 5-HT.

More severe erythema, oedema and/or itching confined to the site of application have rarely been reported (skyscape, 2014).

Usage

Apply the contents of the tube to the centre of the area to be anaesthetised and cover with an occlusive dressing (cling film can also be used). After the appropriate time the gel should be removed prior to treatment (skyscape, 2014).

The contents expellable from 1 tube (approximately 1 gram) are sufficient to cover and anaesthetise an area of up to 30 square centimetres (skyscape, 2014).

Do not apply to broken skin. Not to be taken internally (skyscape, 2014).

Interactions

Hyaluronidase - The risk or severity of adverse effects can be increased when Hyaluronidase is combined with Tetracaine.

Technetium Tc-99m tilmanocept - Tetracaine may decrease effectiveness of Technetium Tc-99m tilmanocept as a diagnostic agent (drugbank, 2015e).

Warning

Repeated exposure to Ametop gel may increase the risk of sensitisation reactions to Amethocaine (skyscape, 2014).

Ametop gel, like other local anaesthetics may be ototoxic and should not be instilled into the middle ear or used for procedures which might involve penetration into the middle ear (skyscape, 2014).

Emla Cream

EMLA stands for 'eutectic mixture of local anaesthetic'.

A local anaesthetic that is similar pharmacologically to lidocaine. Currently, it is used most often for infiltration anesthesia in dentistry (drugbank, 2013i).

Manufacturer

AstraZeneca.

Contains

Emla cream = Lidocaine 2.5%, prilocaine 2.5% (BNF, 2016a).

Pharmacology

Inhibits the conduction of nerve impulses from sensory nerves (emc, 2016).

Indications

Used as a topical anaesthetic for skin anaesthesia, and on the genital mucosa to facilitate the removal of warts in adults (BNF, 2016a).

Pharmacokinetics

At its peak within 2–5 minutes, and with a duration of $\frac{1}{2}$–1 hour (emc, 2016).

Pharmacodynamics

Prilocaine binds to the intracellular surface of sodium channels which blocks the subsequent influx of sodium into the cell. Action potential propagation and never function is, therefore, prevented. This block is reversible and when the drug diffuses away from the cell, sodium channel function is restored and nerve propagation returns (drugbank, 2013i).

Elimination - Prilocaine is metabolised in both the liver and the kidney and excreted via the kidney (drugbank, 2013i).

How it works

Prilocaine acts on sodium channels on the neuronal cell membrane, limiting the spread of seizure activity and reducing seizure propagation. The antiarrhythmic actions are mediated through effects on sodium channels in Purkinje fibres (drugbank, 2013i).

Typical dosage

Electrolysis - 2g for a minimum of 60 minutes, maximum of 5 hours (emc, 2016).

Genitals - Up to 10g for 5–10 minutes before the procedure starts (BNF, 2016a).

Route

Topical = Emla cream.

Contraindications

Hypersensitivity, and secondary bacterial infections.

Side-effects

Skin

Transient paleness, redness, oedema, (BNF, 2016a).

Interactions

Acetaminophen - The risk or severity of adverse effects can be ↑ when Acetaminophen is combined with Prilocaine.

Amyl Nitrite - The risk or severity of adverse effects can be ↑ when Amyl Nitrite is combined with Prilocaine.

Benzocaine - The risk or severity of adverse effects can be ↑ when Benzocaine is combined with Prilocaine.

Butalbital - The risk or severity of adverse effects can be ↑ when Butalbital is combined with Prilocaine.

Celecoxib - The risk or severity of adverse effects can be ↑ when Celecoxib is combined with Prilocaine.

Chloroquine - The risk or severity of adverse effects can be ↑ when Chloroquine is combined with Prilocaine.

Dapsone - The risk or severity of adverse effects can be ↑ when Dapsone is combined with Prilocaine.

Flutamide - The risk or severity of adverse effects can be ↑ when Flutamide is combined with Prilocaine.

Hyaluronidase - The risk or severity of adverse effects can be ↑ when Hyaluronidase is combined with Prilocaine.

Isosorbide - The risk or severity of adverse effects can be ↑ when Isosorbide is combined with Prilocaine.

Isosorbide Dinitrate - The risk or severity of adverse effects can be ↑ when Isosorbide Dinitrate is combined with Prilocaine.

Isosorbide Mononitrate - The risk or severity of adverse effects can be ↑ when Isosorbide Mononitrate is combined with Prilocaine.
Lidocaine - The risk or severity of adverse effects can be ↑ when Lidocaine is combined with Prilocaine.
Mafenide - The risk or severity of adverse effects can be ↑ when Mafenide is combined with Prilocaine.
Metoclopramide - The risk or severity of adverse effects can be ↑ when Metoclopramide is combined with Prilocaine.
Nitric Oxide - The risk or severity of adverse effects can be ↑ when Nitric Oxide is combined with Prilocaine.
Nitrofurantoin - The risk or severity of adverse effects can be ↑ when Nitrofurantoin is combined with Prilocaine.
Nitroglycerin - The risk or severity of adverse effects can be ↑ when Nitroglycerin is combined with Prilocaine.
Nitroprusside - The risk or severity of adverse effects can be ↑ when Nitroprusside is combined with Prilocaine.
Phenazopyridine - The risk or severity of adverse effects can be ↑ when Phenazopyridine is combined with Prilocaine.
Phenobarbital - The risk or severity of adverse effects can be ↑ when Phenobarbital is combined with Prilocaine.
Phenytoin - The risk or severity of adverse effects can be ↑ when Phenytoin is combined with Prilocaine.
Primaquine - The risk or severity of adverse effects can be ↑ when Primaquine is combined with Prilocaine.
Quinine - The risk or severity of adverse effects can be ↑ when Quinine is combined with Prilocaine.
Sodium Nitrite - The risk or severity of adverse effects can be ↑ when Prilocaine is combined with Sodium Nitrite.
Sulfadiazine - The risk or severity of adverse effects can be ↑ when Sulfadiazine is combined with Prilocaine.
Technetium Tc-99m tilmanocept - Prilocaine may ↓ effectiveness of Technetium Tc-99m tilmanocept as a diagnostic agent.
Zopiclone - The risk or severity of adverse effects can be ↑ when Zopiclone is combined with Prilocaine (drugbank, 2013i).

Shelf Life

3 years (emc, 2016).

Notes

Apply thickly, using the spatula provided, and cover with an occlusive dressing at least 1 hour before procedure.

Do not apply to broken skin (emc, 2016).

Warning

Do not use near your eyes (BNF, 2016a).

Minoxidil

Applied to the scalp in the treatment of male-pattern baldness.

Also known as

Regaine, Rogaine.

Manufacturer

Pharmacia.

Pharmacokinetics

On average 1.4% of the total applied dose of Minoxidil is absorbed from intact skin (emc, 2016). Only about 1.4–1.7% absorbed (BNF, 2016a). Following cessation of topical dosing of Regaine Regular Strength, approximately 95% of the systemically absorbed drug is eliminated within 4 days. Minoxidil and its metabolites are excreted principally in the urine (emc, 2016).

Typical dosage

Apply 1ml twice daily to dry hair and scalp (BNF, 2016a).

Route

Solution - Regaine.

Contraindications

Hypersensitivity (Abramovitz, 2016).

Side-effects

Skin

Pruritis, rash (Abramovitz, 2016). Hypertrichosis, local erythema, itching, dry skin/scalp flaking, and exacerbation of hair loss (emc, 2016).

Interactions/incompatibilities

No known drug interactions with the usage of Regaine (emc, 2016).

How it works

Minoxidil is thought to promote the survival of human dermal papillary cells (DPCs) or hair cells by activating both extracellular signal-regulated kinase (ERK) and Akt and by preventing cell death by increasing the ratio of BCl-2/Bax. Minoxidil may stimulate the growth of human hairs by prolonging anagen through these proliferative and anti-apoptotic effects on DPCs. Minoxidil, when used as a vasodilator, acts by opening adenosine triphosphate-sensitive potassium channels in vascular smooth muscle cells. This vasodilation may also improve the viability of hair cells or hair follicles (drugbank, 2013h).

Shelf life

48 months for the regular strength, 24 months for the extra strength (emc, 2016).

Warning

Avoid contact with eyes, mouth and mucous membranes (i.e. nasal passages), broken, infected or inflamed skin. Avoid inhalation of spray mist and use with topical drugs known to enhance absorption (i.e. EMLA cream). Flammable, wash hands after use (BNF, 2016a).

Vaniqa

Eflornithine, an antiprotozoal drug, inhibits the enzyme ornithine decarboxylase in hair follicles and topical application can reduce the growth of unwanted facial hair (BNF, 2016a).

Eflornithine is a prescription drug indicated in the treatment of facial hirsutism (excessive hair growth). Eflornithine hydrochloride cream for topical application is intended for use in women suffering from facial hirsutism and is sold by Allergan, Inc. under the brand name Vaniqa. Besides being a non-mechanical and non-cosmetic treatment, eflornithine is the only non-hormonal and non-systemic prescription option available for women who suffer from facial hirsutism. Eflornithine is on the World Health Organisation's List of Essential Medicines (drugbank, 2015b).

Manufacturer

Shire.

Contains

Each gram of Vaniqa 11.5% w/w cream contains 115 mg eflornithine (as monohydrate chloride) (emc, 2016).

Indications

Used in the treatment of facial hirsutism in women (BNF, 2016a).

Pharmacokinetics

Steady state cutaneous penetration in women from Vaniqa on facial skin of shaving women was 0.8%.

The plasma half-life was approximately 8 hours. Steady state was reached within four days. Excretion was mainly in the urine (emc, 2016).

How it works

Eflornithine prevents hair growth by inhibiting the anagen phase of hair production. This occurs by eflornithine irreversibly binding (also called suicide inhibition) to ornithine decarboxylase (ODC) and physically preventing the natural substrate ornithine from accessing the active site (drugbank, 2015b).

Typical dosage

Apply thinly twice daily (BNF, 2016a).

Route

Topical.

Contraindications

Hypersensitivity (emc, 2016).

Adverse reactions

Skin

Acne, pseudofolliculitis barbae, burning, stinging, dry and/or tingling skin, erythema, rash, pruritus (Medscape, 2014).

Central Nervous System

Alopecia, Headache, Dizziness, Dyspepsia (Medscape, 2014)

Interactions/incompatibilities

None known.

Laboratory test interferences

None known.

Shelf life

3 years (emc, 2016).

Note

Apply a thin layer of the cream to clean and dry affected areas twice daily, at least eight hours apart. Rub in thoroughly (emc, 2016); cosmetics may be applied over treated area 5 minutes after eflornithine; do not wash treated area for 4 hours after application (BNF, 2016a).

Patients may need to continue to use a hair removal method (e.g. shaving) in conjunction with Vaniqa. In that case, the cream should be applied no sooner than five minutes after shaving, as increased stinging or burning may otherwise occur (emc, 2016).

Warning

It must be used indefinitely to prevent regrowth. Continuous use for 8 weeks is required before benefit is seen (BNF, 2016a). The condition may return to pre-treatment levels within eight weeks following discontinuation of treatment (emc, 2016).

Chapter 11

Deprecated Drugs

Ethinylestradiol

This was given FDA approval on 25 June 1943 and was marketed as 'Estinyl' with the manufacturer being Schering Plough Canada Inc. It was marketed by them from the end of 1951 to 11-July 2000 In 2003 it was stated that the reason for the high thrombotic risk of Ethinylestradiol is due to its molecular structure rather than to a first-pass liver effect (Toorians et al., 2003) Due to its high thrombotic risk this hormone is not suitable for use in modern usage, it relates to the time when modern hormones were not available

Ethinylestradiol is a major female sex hormone, a synthetic oestrogen used to make up hormonal deficiencies - sometimes in combination with a progestogen - to treat menstrual, menopausal or other gynaecological problems (such as oestrogen related infertility). It is also a constituent of many oral contraceptives. Administration is oral in the form of tablets. It has the action of the natural hormone, but is some 20 times more potent, and has (reputedly) fewer side effects (unknown, 2005). It is the most potent oestrogen available, and unlike other oestrogens it is only slowly metabolised in the liver (BNF, 2016a).

A semisynthetic alkylated estradiol with a 17-alpha-ethinyl substitution. It has high oestrogenic potency when administered orally and is often used as the oestrogenic component in oral contraceptives (drugbank, 2013c).

Also known as

Ethinylestradiol, Etinilestradiol (Spanish)

Manufacturer

Ethinylestradiol = Norton (unknown, 2015b) and Celltech (emc, 2016).

Contains

Ethinylestradiol 10mcgs, 50mcgs, 1mg (BNF, 2016a). White uncoated tablets, which also contain lactose, starch maize, magnesium stearate, IMS 99%, purified water (emc, 2016).

How it works

Oestrogens diffuse into their target cells and interact with a protein receptor. Target cells include the female reproductive tract, the mammary gland, the hypothalamus, and the pituitary. Oestrogens increase the hepatic synthesis of sex hormone binding globulin (SHBG), thyroid-binding globulin (TBG), and other serum proteins and suppress FSH from the anterior pituitary. This cascade is initiated by initially binding to the oestrogen receptors (drugbank, 2013c).

Pharmacology

3-cyclopentylether of Ethinylestradiol. Ethinylestradiol, is chemically and biologically identical to endogenous human estradiol (emc, 2016).

Absorption - Rapid and complete absorption follows oral intake of ethinylestradiol (bioavailability 43%).

Metabolism - Hepatic. Quantitatively, the major metabolic pathway for ethinylestradiol, both in rats and in humans, is aromatic hydroxylation, as it is for the natural oestrogens.

Half life - 36 +/- 13 hours (drugbank, 2013c).

Indications

Oestrogen replacement therapy in females.

Pharmacokinetics

More potent than endogenous oestrogen because the liver cannot break it down as quickly. Ethinylestradiol is rapidly and completely absorbed from the gut but it undergoes some first pass metabolism in the gut wall.

Ethinylestradiol is rapidly distributed throughout most body tissues with the largest concentration found in adipose tissue.More than 80% of ethinylestradiol in serum is conjugated as the sulphate and almost all the conjugated form is bound to albumin.

Ethinylestradiol is metabolised in the liver. Hydroxylation appears to be the main metabolic pathway. 60% of a dose is excreted in the urine and 40% in the faeces. About 30% is excreted in the urine and bile as the glucuronide or sulphate conjugate (emc, 2016).

It is excreted approximately 60% in the bile and 33% through the kidneys (drugbank, 2013c).

The rate of metabolism of ethinylestradiol is affected by several factors, including enzyme- inducing agents, antibiotics and cigarette smoking.

After oral administration, an initial peak occurs in plasma at 2 to 3 hours, with a secondary peak at about 12 hours after dosing; the second peak is interpreted as evidence for extensive enterohepatic circulation of ethinylestradiol.

The elimination half-life of ethinylestradiol ranges from 5 to 16 hours (emc, 2016).

Quantitatively, the major metabolic pathway for ethinyl estradiol, both in rats and in humans, is aromatic hydroxylation, as it is for the natural oestrogens (drugbank, 2013c)

Typical dosage

Pre-op - 50–150 mcgs/day
Post-op - 50 mcgs/day.

Route

Tablets - Ethinylestradiol.

Contraindications

Active or recent arterial thromboembolic disease, e.g. angina, myocardial infarction; Current or previous idiopathic venous thromboembolism (deep venous thrombosis, pulmonary embolism); Acute liver disease or a history of liver disease as long as liver function tests have failed to return to normal; porphyria; Known hypersensitivity to the active substance or to any of the excipients (emc, 2016).

Side-effects

Central Nervous System

- **Headache**,
- dizziness,
- **depression**,
- lethargy,
- **migraine**,
- **stroke**,
- **cerebral haemorrhage** (Abramovitz, 2016).

Cardiovascular

- **Thromboembolism**,
- **hypertension**,
- **oedema**,
- **pulmonary embolism**,
- **myocardial infarction** (Abramovitz, 2016).

Eyes

- **Worsening myopia or astigmatism**,
- **intolerance of contact lenses**,
- exophthalmos,
- diplopia (Abramovitz, 2016).

Gastrointestinal

- **Nausea**,
- **vomiting**,
- **abdominal cramps**,
- bloating,
- anorexia,
- changes in appetite,
- gallbladder disease,
- **pancreatitis** (Abramovitz, 2016).

Genitourinary

- Granulomatous colitis,
- **vaginal thrush** (Abramovitz, 2016).

Hepatic

- Cholestatic jaundice,
- **liver tumours**,
- gallbladder disease (Abramovitz, 2016).

Metabolic

- **Weight change**,
- additive insulin resistance in diabetics (Abramovitz, 2016).

Skin

- **Rash**,
- acne,
- **erythema multiforme** [60],
- **melasma**,
- **hirsutism** (Abramovitz, 2016).

Other

- **Breast tenderness**,
- **breast enlargement**,
- **anaphylaxis**,
- **haemolytic-uremic syndrome** (Abramovitz, 2016).
- **nausea** and
- **vomiting**, and
- **withdrawal bleeding** may occur in females (drugbank, 2013c).

Cautions

Cardiovascular disease (sodium retention with oedema, thromboembolism), hepatic impairment (jaundice) (BNF, 2016a).

Interactions

Abciximab - ethinylestradiol may ↓ the anticoagulant activities of Abciximab.

Acenocoumarol - ethinylestradiol may ↓ the anticoagulant activities of Acenocoumarol.

Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with ethinylestradiol.

Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with ethinylestradiol.

Anthrax immune globulin - ethinylestradiol may ↑ the thrombogenic activities of Anthrax immune globulin.

Batimastat - The serum concentration of ethinylestradiol can be ↓ when it is combined with Batimastat.

Bexarotene - The serum concentration of ethinylestradiol can be ↓ when it is combined with Bexarotene.

[60] An acute eruption of macules, papules, or subdermal vesicles presenting a multiform appearance, the characteristic lesion being the target or iris form of lesion over the dorsal aspect of the hands and forearms; its origin may be from drug sensitivity, and the eruption, although usually self limited, may be recurrent or may run a severe course, sometimes with fatal termination (Eaton, 2014)

Bortezomib - The metabolism of Bortezomib can be ↓ when combined with ethinylestradiol.
Butabarbital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Butabarbital.
Butethal - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Butethal.
C1 Esterase Inhibitor (Human) - ethinylestradiol may ↑ the thrombogenic activities of C1 Esterase Inhibitor (Human).
Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with ethinylestradiol.
Capromab - ethinylestradiol may ↓ effectiveness of Capromab as a diagnostic agent.
Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with ethinylestradiol.
Citric Acid - ethinylestradiol may ↓ the anticoagulant activities of Citric Acid.
Colesevelam - The serum concentration of ethinylestradiol can be ↓ when it is combined with Colesevelam.
Dalteparin - ethinylestradiol may ↓ the anticoagulant activities of Dalteparin.
Dicoumarol - ethinylestradiol may ↓ the anticoagulant activities of Dicoumarol.
Edetic Acid - ethinylestradiol may ↓ the anticoagulant activities of Edetic Acid.
Enoxaparin - ethinylestradiol may ↓ the anticoagulant activities of Enoxaparin.
Eslicarbazepine acetate - The serum concentration of ethinylestradiol can be ↓ when it is combined with Eslicarbazepine acetate.
Ethyl biscoumacetate - ethinylestradiol may ↓ the anticoagulant activities of Ethyl biscoumacetate.
Fludrocortisone - The serum concentration of Fludrocortisone can be ↑ when it is combined with ethinylestradiol.
Fluvoxamine - The metabolism of Fluvoxamine can be ↓ when combined with ethinylestradiol.
Fondaparinux sodium - ethinylestradiol may ↓ the anticoagulant activities of Fondaparinux sodium.
Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with ethinylestradiol.
Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with ethinylestradiol.
Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with ethinylestradiol.
Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with ethinylestradiol.
Heparin - ethinylestradiol may ↓ the anticoagulant activities of Heparin.
Heptabarbital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Heptabarbital.

Hexobarbital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Hexobarbital.

Icosapent - Icosapent may ↑ the thrombogenic activities of ethinylestradiol.

Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with ethinylestradiol.

Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with ethinylestradiol.

Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with ethinylestradiol.

Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with ethinylestradiol.

Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with ethinylestradiol.

Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with ethinylestradiol.

Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with ethinylestradiol.

Isoflurophate - The serum concentration of ethinylestradiol can be ↓ when it is combined with Isoflurophate.

Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with ethinylestradiol.

Liothyronine - The therapeutic efficacy of Liothyronine can be ↓ when used in combination with ethinylestradiol.

Lumacaftor - The serum concentration of ethinylestradiol can be ↓ when it is combined with Lumacaftor.

Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with ethinylestradiol.

Methohexital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Methohexital.

Pentobarbital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Pentobarbital.

Phenindione - ethinylestradiol may ↓ the anticoagulant activities of Phenindione.

Phenprocoumon - ethinylestradiol may ↓ the anticoagulant activities of Phenprocoumon.

Phenytoin - The metabolism of ethinylestradiol can be ↑ when combined with Phenytoin.

Primidone - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Primidone.

Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with ethinylestradiol.

Rifabutin - The serum concentration of ethinylestradiol can be ↓ when it is combined with Rifabutin.

Rufinamide - The serum concentration of ethinylestradiol can be ↓ when it is combined with Rufinamide.

Saxagliptin - The therapeutic efficacy of Saxagliptin can be ↓ when used in combination with ethinylestradiol.

Secobarbital - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with Secobarbital.
Simeprevir - The serum concentration of ethinylestradiol can be ↓ when it is combined with Simeprevir.
St. John's Wort - The therapeutic efficacy of ethinylestradiol can be ↓ when used in combination with St. John's Wort.
Sulodexide - ethinylestradiol may ↓ the anticoagulant activities of Sulodexide.
Theophylline - The serum concentration of Theophylline can be ↑ when it is combined with ethinylestradiol.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with ethinylestradiol.
Treprostinil - ethinylestradiol may ↓ the anticoagulant activities of Treprostinil.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with ethinylestradiol.
Vitamin C - The serum concentration of ethinylestradiol can be ↑ when it is combined with Vitamin C.
Warfarin - ethinylestradiol may ↓ the anticoagulant activities of Warfarin (drugbank, 2013c).

Anti-infectives - chloramphenicol, fluconazole, griseofulvin, neomycin, nitrofurantoin, penicillins, sulfonamides, tetracyclines - May ↓ contraceptive effect. Advise patient to use another method of contraception.

Atorvastatin - May ↑ norethindrone and ethinylestradiol levels. Monitor patient for adverse effects.
Benzodiazepines - May ↓ or ↑ benzodiazepine levels. Adjust dosage, if necessary.
Beta blockers - May ↑ beta blocker level. Dosage adjustment may be necessary.
Carbamazepine, fosphenytoin, phenobarbital, phenytoin, rifampin - May ↓ oestrogen effect. Use together cautiously.
Corticosteroids - May ↑ corticosteroid effect. Monitor patient closely.
Insulin, sulfonylureas - Glucose intolerance may ↓ antidiabetic effects. Monitor these effects.
NNRTIs, protease inhibitors - May ↓ hormonal contraceptive effect. Avoid using together, if possible.
Oral anticoagulants - May ↓ anticoagulant effect. Dosage adjustments may be needed. Monitor PT[61] and INR[62].
Tamoxifen - May inhibit tamoxifen effect. Avoid using together (Abramovitz, 2016).

[61] prothrombin time

[62] international normalized ratio (unknown, 2013d)

Drug-herb

Black cohosh - May ↑ adverse effects of estrogen. Discourage use together.
Red clover - May interfere with drug. Discourage use together.
Saw palmetto - May have antioestrogenic effect. Discourage use together.
St. John's wort - May ↓ drug effect because of increased hepatic metabolism. Discourage use together, or advise patient to use an additional method of contraception (Abramovitz, 2016).

Drug-food

Caffeine - May ↑ caffeine level. Urge caution.
Grapefruit juice - May ↑ oestrogen level. Advise patient to take with liquid other than grapefruit juice (Abramovitz, 2016).

Drug-lifestyle

Smoking - May ↑ risk of adverse cardiovascular effects. If smoking continues, may need alternative therapy.

Effects on Lab Test Results

May ↑ clotting factors II, VII, VIII, IX, and X; fibrinogen; phospholipid; plasminogen; thyroid-binding globulin; total T4; and triglyceride levels.

May ↑ norepinephrine-induced platelet aggregation and PT.

May ↓ metyrapone test results. May cause false-positive result in nitroblue tetrazolium test (Abramovitz, 2016).

Clinical assessment

Baseline blood pressure, weight, urinalysis (in diabetics).

Notes

Take with food or milk to decrease/minimise gastrointestinal symptoms.

Toxicology

Oral, mouse LD-50: 1737 mg/kg (drugbank, 2013c).

Warning

Ethinylestradiol should not be administered to patients who have cancers proven to be sex hormone linked, who have a history of thrombosis, or who have porphyria or impaired liver function. Caution should be exercised in administering Ethinylestradiol to patients who are diabetic or epileptic, who have heart or kidney disease, or who have high blood pressure or recurrent severe migraine.

See also Ethinylestradiol for further discussion of Ethinylestradiol.

Medroxyprogesterone Acetate

This hormone has several negative side-effects. It is a progestogen with its side-effects including, increasing the risk for depression, irritability, mood disturbances, and/or aggression, which sometimes leads to suicidal thoughts or feelings. Also, it can increase the risk of thrombosis and/or breast cancer due to its glucocorticoid actions. It is only mildly androgenic, and it opposes the oestrogen's beneficial effects on lipids and potentially slows down feminization. Therefore it is on the 'deprecated hormone' list

A synthetic progesterone (TGC, 2015a).

Medroxyprogesterone acetate, also known as 17α-hydroxy-6α-methylprogesterone acetate, and commonly abbreviated as MPA, is a steroidal progestin, a synthetic variant of the human hormone progesterone (drugbank, 2013g).

Also known as

Provera, depo-provera.

Manufacturer

Pharmacia.

Contains

Provera - Medroxyprogesterone acetate 2.5 mgs, 5 mgs, 10 mgs.
Depo-Provera - Medroxyprogesterone acetate 150 mgs/ml

Pharmacology

Medroxyprogesterone acetate has actions and uses similar to those of progesterone, with minimal androgenic activity compared to progesterone and virtually no oestrogenic activity (emc, 2016).

Medroxyprogesterone acetate is a synthetic progestin more potent than progesterone (drugbank, 2013g).

Indications

Uterine bleeding (abnormal), secondary amenorrhoea, endometrial cancer, renal cancer, prevention of endometrial changes associated with oestrogen replacment therapy (Abramovitz, 2016).

Pharmacokinetics

Rapidly absorbed from the gastrointestinal tract with a single oral dose of 10–250 mg. The time taken to reach the peak serum concentration (Tmax) was 2–6 hours and the average peak serum concentration Cmax was 13–46.89 mg/ml. Excreted mainly in the faeces (emc, 2016).

Absorption - Rapidly absorbed from the gastrointestinal tract.
Elimination - Following oral dosing, MPA is extensively metabolised in the liver via hydroxylation, with subsequent conjugation and elimination in the urine. Most MPA metabolites are excreted in the urine as glucuronide conjugates with only minor amounts excreted as sulfates.
Half-life - 50 days!

How it works

Progestins diffuse freely into target cells in the female reproductive tract, mammary gland, hypothalamus, and the pituitary and bind to the progesterone receptor. Once bound to the receptor, progestins slow the frequency of release of gonadotropin releasing hormone (GnRH) from the hypothalamus and blunt the pre-ovulatory LH surge (drugbank, 2013g).

Typical dosage

Pre-op - 2.5–10 mgs/day orally (unknown, 2014a), 150 mg/month intramuscular (Asscheman and LJG Gooren, 1992).
Post-op - Not known at present.

Route

Tablets - Provera.
Intramuscular injection - Depo-provera.

Contraindications

Use in patients with a known sensitivity to medroxyprogesterone acetate. Use in patients with impaired liver function or with active liver disease (emc, 2016).

Side-effects

Central Nervous System

- Anxiety,
- depression,
- fatigue,
- insomnia,
- somnolence,
- dementia,
- **stroke**,
- pain,
- dizziness (Abramovitz, 2016).

Cardiovascular

- Thrombophlebitis,
- **pulmonary embolism**,
- oedema,
- **thromboembolism**,
- fainting (Abramovitz, 2016).

Eyes

- Exophthalmos[63],
- diplopia[64] (Abramovitz, 2016).

Gastrointestinal

- **bloating**,
- abdominal pain (Abramovitz, 2016).

Genitourinary

[63] bulging eyeball out of its socket

[64] double vision

- **breast changes**,
- **gynaecomastia**,
- hot flashes (Abramovitz, 2016).
- **loss of libido** (drugs.com, 2014c).

Hepatic

- Cholestatic jaundice (Abramovitz, 2016).

Metabolic

- **Weight changes** (Abramovitz, 2016).

Musculoskeletal

- Loss of bone mineral density (Abramovitz, 2016). See also Medroxyprogesterone Acetate and osteoporosis

Skin

- Rash,
- induration,
- acne,
- pruritus,
- melasma,
- alopecia,
- hirsutism (Abramovitz, 2016).

Interactions

Aminoglutethimide ↓ plasma concentration (BNF, 2016a).

Abciximab - The therapeutic efficacy of Abciximab can be ↓ when used in combination with Medroxyprogesterone Acetate.

Acenocoumarol - The therapeutic efficacy of Acenocoumarol can be ↓ when used in combination with Medroxyprogesterone Acetate.

Acetohexamide - The therapeutic efficacy of Acetohexamide can be ↓ when used in combination with Medroxyprogesterone Acetate.

Acitretin - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Acitretin.

Alogliptin - The therapeutic efficacy of Alogliptin can be ↓ when used in combination with Medroxyprogesterone Acetate.

Aprepitant - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Aprepitant.

Aripiprazole - The serum concentration of Aripiprazole can be ↓ when it is combined with Medroxyprogesterone Acetate.

Artemether - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Artemether.

Atazanavir - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Atazanavir.

Bexarotene - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Bexarotene.

Boceprevir - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Boceprevir.

Bosentan - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Bosentan.

Butabarbital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Butabarbital.

Butethal - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Butethal.

C1 Esterase Inhibitor (Human) - Medroxyprogesterone Acetate may ↑ the thrombogenic activities of C1 Esterase Inhibitor (Human).

Canagliflozin - The therapeutic efficacy of Canagliflozin can be ↓ when used in combination with Medroxyprogesterone Acetate.

Capromab - Medroxyprogesterone Acetate may decrease effectiveness of Capromab as a diagnostic agent.

Carbamazepine - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Carbamazepine.

Ceritinib - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Ceritinib.

Chlorpropamide - The therapeutic efficacy of Chlorpropamide can be ↓ when used in combination with Medroxyprogesterone Acetate.

Choline C 11 - The therapeutic efficacy of Choline C 11 can be ↓ when used in combination with Medroxyprogesterone Acetate.

Citric Acid - The therapeutic efficacy of Citric Acid can be ↓ when used in combination with Medroxyprogesterone Acetate.

Clarithromycin - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Clarithromycin.

Clobazam - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Clobazam.

Cobicistat - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Cobicistat.

Colesevelam - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Colesevelam.

Dabrafenib - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Dabrafenib.

Dalteparin - The therapeutic efficacy of Dalteparin can be ↓ when used in combination with Medroxyprogesterone Acetate.

Darunavir - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Darunavir.

Deferasirox - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Deferasirox.

Dicoumarol - Medroxyprogesterone Acetate may decrease the anticoagulant activities of Dicoumarol.

Edetic Acid - The therapeutic efficacy of Edetic Acid can be ↓ when used in combination with Medroxyprogesterone Acetate.

Efavirenz - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Efavirenz.

Enoxaparin - The therapeutic efficacy of Enoxaparin can be ↓ when used in combination with Medroxyprogesterone Acetate.

Eslicarbazepine acetate - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Eslicarbazepine acetate.

Ethyl biscoumacetate - The therapeutic efficacy of Ethyl biscoumacetate can be ↓ when used in combination with Medroxyprogesterone Acetate.

Felbamate - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Felbamate.

Flibanserin - The serum concentration of Flibanserin can be ↑ when it is combined with Medroxyprogesterone Acetate.

Fondaparinux sodium - The therapeutic efficacy of Fondaparinux sodium can be ↓ when used in combination with Medroxyprogesterone Acetate.

Fosamprenavir - The serum concentration of the active metabolites of Fosamprenavir can be ↓ when Fosamprenavir is used in combination with Medroxyprogesterone Acetate resulting in a loss in efficacy.

Fosaprepitant - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Fosaprepitant.

Fosphenytoin - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Fosphenytoin.

Gliclazide - The therapeutic efficacy of Gliclazide can be ↓ when used in combination with Medroxyprogesterone Acetate.

Glimepiride - The therapeutic efficacy of Glimepiride can be ↓ when used in combination with Medroxyprogesterone Acetate.

Gliquidone - The therapeutic efficacy of Gliquidone can be ↓ when used in combination with Medroxyprogesterone Acetate.

Glyburide - The therapeutic efficacy of Glyburide can be ↓ when used in combination with Medroxyprogesterone Acetate.

Griseofulvin - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Griseofulvin.

Heparin - The therapeutic efficacy of Heparin can be ↓ when used in combination with Medroxyprogesterone Acetate.

Heptabarbital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Heptabarbital.

Hexobarbital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Hexobarbital.

Hydrocodone - The serum concentration of Hydrocodone can be ↓ when it is combined with Medroxyprogesterone Acetate.

Idelalisib - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Idelalisib.

Indinavir - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Indinavir.

Insulin Aspart - The therapeutic efficacy of Insulin Aspart can be ↓ when used in combination with Medroxyprogesterone Acetate.

Insulin Detemir - The therapeutic efficacy of Insulin Detemir can be ↓ when used in combination with Medroxyprogesterone Acetate.
Insulin Glargine - The therapeutic efficacy of Insulin Glargine can be ↓ when used in combination with Medroxyprogesterone Acetate.
Insulin Glulisine - The therapeutic efficacy of Insulin Glulisine can be ↓ when used in combination with Medroxyprogesterone Acetate.
Insulin Lispro - The therapeutic efficacy of Insulin Lispro can be ↓ when used in combination with Medroxyprogesterone Acetate.
Insulin Regular - The therapeutic efficacy of Insulin Regular can be ↓ when used in combination with Medroxyprogesterone Acetate.
Insulin, isophane - The therapeutic efficacy of Insulin, isophane can be ↓ when used in combination with Medroxyprogesterone Acetate
Itraconazole - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Itraconazole.
Ketoconazole - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Ketoconazole.
Lamotrigine - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Lamotrigine.
Linagliptin - The therapeutic efficacy of Linagliptin can be ↓ when used in combination with Medroxyprogesterone Acetate.
Lopinavir - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Lopinavir.
Lumacaftor - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Lumacaftor.
Metformin - The therapeutic efficacy of Metformin can be ↓ when used in combination with Medroxyprogesterone Acetate.
Methohexital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Methohexital.
Metreleptin - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Metreleptin.
Mifepristone - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Mifepristone.
Mitotane - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Mitotane.
Mycophenolic acid - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Mycophenolic acid.
Nefazodone - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Nefazodone.
Nelfinavir - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Nelfinavir.
Nevirapine - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Nevirapine.
Nimodipine - The serum concentration of Nimodipine can be ↓ when it is combined with Medroxyprogesterone Acetate.
Oxcarbazepine - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Oxcarbazepine.
Pentobarbital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Pentobarbital.

Perampanel - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Perampanel.
Phenindione - The therapeutic efficacy of Phenindione can be ↓ when used in combination with Medroxyprogesterone Acetate.
Phenprocoumon - The therapeutic efficacy of Phenprocoumon can be ↓ when used in combination with Medroxyprogesterone Acetate.
Phenytoin - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Phenytoin.
Posaconazole - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Posaconazole.
Primidone - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Primidone.
Prucalopride - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Prucalopride.
Repaglinide - The therapeutic efficacy of Repaglinide can be ↓ when used in combination with Medroxyprogesterone Acetate.
Rifabutin - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Rifabutin.
Ritonavir - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Ritonavir.
Saquinavir - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Saquinavir.
Saxagliptin - The serum concentration of Saxagliptin can be ↓ when it is combined with Medroxyprogesterone Acetate.
Secobarbital - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Secobarbital.
Selegiline - The serum concentration of Selegiline can be ↑ when it is combined with Medroxyprogesterone Acetate.
Siltuximab - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Siltuximab.
St. John's Wort - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with St. John's Wort.
Sugammadex - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Sugammadex.
Sulodexide - The therapeutic efficacy of Sulodexide can be ↓ when used in combination with Medroxyprogesterone Acetate.
Telaprevir - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Telaprevir.
Telithromycin - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Telithromycin.
Thalidomide - Medroxyprogesterone Acetate may ↑ the thrombogenic activities of Thalidomide.
Tipranavir - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Tipranavir.
Tocilizumab - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Tocilizumab.
Tolbutamide - The therapeutic efficacy of Tolbutamide can be ↓ when used in combination with Medroxyprogesterone Acetate.

Topiramate - The serum concentration of Medroxyprogesterone Acetate can be ↓ when it is combined with Topiramate.
Tranexamic Acid - Medroxyprogesterone Acetate may ↑ the thrombogenic activities of Tranexamic Acid.
Treprostinil - The therapeutic efficacy of Treprostinil can be ↓ when used in combination with Medroxyprogesterone Acetate.
Ulipristal - The therapeutic efficacy of Medroxyprogesterone Acetate can be ↓ when used in combination with Ulipristal.
Vildagliptin - The therapeutic efficacy of Vildagliptin can be ↓ when used in combination with Medroxyprogesterone Acetate.
Voriconazole - The serum concentration of Medroxyprogesterone Acetate can be ↑ when it is combined with Voriconazole.
Warfarin - The therapeutic efficacy of Warfarin can be ↓ when used in combination with Medroxyprogesterone Acetate (drugbank, 2013g).

Effects on Lab Test Results

May ↑ LFT values, thyroid-binding globulin levels, HDL and triglyceride levels, coagulation tests, and prothrombin factors VII, VIII, IX, and X.

May ↓ metyrapone test results. May alter glucose level (Abramovitz, 2016).

Overdose

In animals Provera has been shown to be capable of exerting an adrenocorticoid effect, but this has not been reported in the human, following usual dosages. The oral administration of Provera at a rate of 100 mg per day has been shown to have no effect on adrenal function (emc, 2016).

Overdosage of oestrogen plus progestin therapy may cause

- **nausea** and
- **vomiting**,
- **breast tenderness**,
- **dizziness**,
- **abdominal pain**,
- **drowsiness/fatigue** and withdrawal bleeding may occur in women.

Treatment of overdose consists of discontinuation of CE/MPA together with institution of appropriate symptomatic care (drugs.com, 2014c).

Shelf life

36 months (emc, 2016).

Toxicity

Side effects include loss of bone mineral density, BMD changes in adult women, bleeding irregularities, cancer risks, and thromboembolic disorders (drugbank, 2013g).

Oestrogens, conjugated

This is deprecated because it is in the form of an extract from the urine of pregnant mares containing the effective substances, i.e. oestrogen metabolites. This was one of the earliest commercial preparations available for hormone replacement treatment, which have now been superseded by the use of monosubstances with clearly defined pharmacokinetic and pharmacodynamic features. It is known that the preparation contains oestradiol metabolites as well as equilin metabolites which are specific to horses. However, there is still a lack of knowledge about the exact components of the urine extract. Hitherto unidentified components have been recognised recently in the extract (Bhavnani, 1998). These are delta-8-oestrone and its metabolites; furthermore 16α-hydroxy metabolites and catechol metabolites of equilin are also allegedly present. It is now known that these oestrogen metabolites possess effects other than their oestrogenicity (Lippert, A. O. Mueck, and H. Seeger, 1999). Thus, some have opposing effects: for instance, D-ring metabolites may exert proliferation-stimulating effects on cells, but A-ring metabolites proliferation-inhibiting effects. In general, D-ring metabolites still have an oestrogenic effect, while A-ring metabolites may even show antioestrogenic effects. There has been recent interest in these oestrogen metabolites because there are indications that they can be involved in the development of hormone-dependent tumours, e.g. breast cancer (Lippert, A. O. Mueck, and H. Seeger, 1999). It has been shown that these equilin metabolites have toxic properties with carcinogenic potential through the formation of quinones (Zhang et al., 1999). A special carcinogenic risk factor may be the formation of semiquinone-adducts with DNA (Shen et al., 1998). Equilin metabolites appear to have stronger carcinogenic effects than comparable oestradiol metabolites (Bhavnani, 1998), (Lippert, A. O. Mueck, and H. Seeger, 2000). As this information was established in 1999, to use it in later years is unforgivable.

Conjugated estrogens, a mixture of the water-soluble salts of sulfate esters from estrone, equilin, 17 α-dihydroequilin, and other related steroids, may be derived from pregnant equine urine or yam and soy plants (drugbank, 2015a).

Action

Mimics the actions of endogenous oestrogens; increases synthesis of DNA, RNA, and protein in responsive tissues; reduces release of follicle-stimulating and luteinizing hormones from pituitary gland (Abramovitz, 2016).

Also known as

Premarin, Premarin vaginal cream.

Manufacturer

Wyeth Pharmaceuticals.

Contains

Premarin - 625 mcgs, 1.25 mgs,
Premarin cream - 625mcg/g

Pharmacology

The active ingredients are primarily the sulphate esters of estrone, equilin sulphates, 17α-estradiol and 17β-estradiol. Conjugated oestrogens are soluble in water and are well absorbed from the gastrointestinal tract after release from the drug formulation. The Premarin tablets release conjugated oestrogens slowly over several hours (emc, 2016).

Pharmacodynamics

Conjugated oestrogens, a mixture of the water soluble salts of sulfate esters from estrone, equilin, 17 α-dihydroequilin, and other related steroids, may be derived from pregnant equine urine or yam and soy plants. Oestrogens are important in the development and maintenance of the female reproductive system and secondary sex characteristics. They promote growth and development of the vagina, uterus, and fallopian tubes, and enlargement of the breasts. Indirectly, they contribute to the shaping of the skeleton, maintenance of tone and elasticity of urogenital structures, changes in the epiphyses of the long bones that allow for the pubertal growth spurt and its termination, growth of axillary and pubic hair, and pigmentation of the nipples and genitals. Decline of oestrogenic activity at the end of the menstrual cycle can bring on menstruation, although the cessation of progesterone secretion is the most important

factor in the mature ovulatory cycle. However, in the preovulatory or nonovulatory cycle, oestrogen is the primary determinant in the onset of menstruation. Oestrogens also affect the release of pituitary gonadotropins. The pharmacologic effects of conjugated oestrogens are similar to those of endogenous oestrogens (drugbank, 2015a).

Absorption - Well absorbed.

Elimination - Estradiol, estrone, and estriol are excreted in the urine, along with glucuronide and sulfate conjugates. Exogenous oestrogens are metabolised in the same manner as endogenous oestrogens.

Half-life - 7.4 hours (drugbank, 2015a).

Indications

Inoperable progressing prostate cancer, palliative treatment for metastatic breast cancer, hypogonadism [65], castration, primary ovarian failure, vasomotor menopausal symptoms, moderate to severe menopausal vulvar and vaginal atrophy (Abramovitz, 2016).

Pharmacokinetics

Premarin is metabolised exclusively in the liver, utilises hepatic recirculation, and is excreted in the urine (Abramovitz, 2016).

How it works

Oestrogens enter the cells of responsive tissues (e.g., female organs, breasts, hypothalamus, pituitary) where they interact with a protein receptor, subsequently increasing the rate of synthesis of DNA, RNA, and some proteins. Oestrogens decrease the secretion of gonadotropin-releasing hormone by the hypothalamus, reducing the secretion of FSH and LH from the pituitary (drugbank, 2015a).

Typical dosage

Pre-op - 1.25–7.5 mgs/day (unknown, 2005), 5–10 mgs/day (Asscheman and LJG Gooren, 1992).

Post-op - 0.625–3.75 mgs/day (unknown, 2005).

Route

Oral - tablets - Premarin.

[65] a low testosterone level or sperm count, or both

Vaginal - cream - Premarin vaginal cream.

Contraindications

Oestrogen-dependent cancer, history of breast cancer, active thrombophlebitis, active or recent thromboembolic disease (e.g. angina or myocardial infarction), venous thromboembolism, or history of recurrent venous thromboembolism (unless already on anticoagulant treatment), liver disease (where liver function tests have failed to return to normal), breast feeding (BNF, 2016a).

Adverse reactions

Central Nervous System

- **headache**,
- dizziness,
- chorea,
- depression,
- **stroke**,
- **seizures** (Abramovitz, 2016).

Cardiovascular

- Thrombophlebitis,
- **thromboembolism**,
- hypertension,
- oedema,
- **heart attack**,
- **pulmonary embolism** (Abramovitz, 2016).

Eyes

- Worsening myopia or astigmatism,
- intolerance of contact lenses (Abramovitz, 2016).

Gastrointestinal

- **nausea**,
- **vomiting**,
- **abdominal cramps**,
- bloating,
- anorexia,
- increased appetite,
- **pancreatitis**,
- increased risk of gallbladder disease (Abramovitz, 2016).

Genitourinary

- **Vaginal candidiasis**,
- **testicular atrophy**,
- **impotence** (Abramovitz, 2016).

Hepatic

- Cholestatic jaundice,
- **hepatic adenoma**[66] (Abramovitz, 2016).

Metabolic

- Hypercalcemia,
- weight changes,
- hypertriglyceridemia[67] (Abramovitz, 2016).

Skin

- **melasma**[68],
- **rash**,
- hirsutism or hair loss,
- erythema nodosum[69],
- **erythema multiforme**,
- dermatitis (Abramovitz, 2016).

Other

- **breast tenderness**,
- **breast enlargement**,
- **gynaecomastia**,
- **increased risk of breast cancer** (Abramovitz, 2016).

Interactions

Carbamazepine, fosphenytoin, phenobarbital, phenytoin, rifampin - May ↓ effectiveness of oestrogen therapy. Monitor patient closely.
Clarithromycin, erythromycin, itraconazole, ketoconazole, ritonavir - May ↑ oestrogen plasma levels and side effects. Monitor patient.
Corticosteroids - May ↑ corticosteroid effects. Monitor patient closely.

[66] a benign tumour of the liver, usually occurring in women in association with lengthy oral contraceptive use

[67] elevated triglyceride concentration in the blood

[68] a tan or dark skin discolouration

[69] An inflammation of subcutaneous tissue marked by the sudden formation of painful nodes on the extensor surfaces of the lower extremities, with lesions that are self limiting but tend to recur(unknown, 2013d)

Cyclosporine - May ↑ risk of toxicity. Use together with caution, and monitor cyclosporine level frequently.
Dantrolene, hepatotoxic drugs - May ↑ risk of hepatotoxicity. Monitor liver function closely.
Oral anticoagulants - May ↓ anticoagulant effects. Adjust dosage if needed. Monitor PT and INR.
Tamoxifen - May interfere with tamoxifen effectiveness. Avoid using together (Abramovitz, 2016).

Drug-herb

St. John's wort - May ↓ effects of drug. Discourage use together (Abramovitz, 2016).

Drug-food

Caffeine - May ↑ caffeine level. Urge caution.
Grapefruit, grapefruit juice - May ↑ risk of adverse effects. Discourage use together (Abramovitz, 2016).

Drug-lifestyle

Smoking - May ↑ risk of cardiovascular effects. If smoking continues, may need another form of therapy (Abramovitz, 2016).

Effects on Lab Test Results

May ↑ calcium, thyroid-binding globulin, serum triglyceride, serum phospholipid, and clotting factor VII, VIII, IX, and X levels.

May ↑ norepinephrine-induced platelet aggregation and PT.

May ↓ metyrapone test results and cause impaired glucose tolerance (Abramovitz, 2016).

Shelf Life

Both drugs have a shelf life of 36 months (emc, 2016).

Notes

Take oral dose with food or milk to decrease/minimise gastrointestinal symptoms (Abramovitz, 2016).

With regard to blood levels for this product, useful levels cannot be obtained because the product is a mixture of oestrogens which each have different sensitivities in the sampling machines, so the machine ends up getting confused. It therefore outputs a generalised figure which is not accurate.

This has largely been superseded by better varieties of oestrogen, and it therefore tends to be deprecated, and not used. If a doctor or physician prescribes this for you, I would start to wonder how up-to-date their knowledge actually is!

Toxicity

Nausea and vomiting (drugbank, 2015a).

Spironolactone

Spironolactone should only be prescribed for cardiovascular reasons, and not as an anti-androgen. It is only mildly androgenic, compared to its alternatives, and has life-disturbing side-effects, such as frequent urination, muscle cramps, a lack of energy and potential disruption of electrolytes which can all be avoided if its not taken. There are other better anti-androgens, for example, bicalutamide, flutamide or triptorelin

A potassium sparing diuretic that acts by antagonism of aldosterone in the distal renal tubules. It is used mainly in the treatment of refractory oedema in patients with congestive heart failure, nephrotic syndrome, or hepatic cirrhosis. Its effects on the endocrine system are utilized in the treatments of hirsutism and acne but they can lead to adverse effects (drugbank, 2013k).

Also known as

Aldactone, Spirospare, Spironolacton (German), Espironolactona (Spanish). (BNF, 2016a).

Manufacturer

Aldactone = Pharmacia Ltd, and Searle (BNF, 2016a).

Contains

Spironolactone - tablets - 25 mgs, 50 mgs, 100 mgs
Aldactone - Spironolactone - tablets - 25 mgs, 50 mgs, 100 mgs

Spironolactone - liquid - 5 mg/5 mL, 10 mg/5 mL, 25 mg/5 mL, 50 mg/5 mL and 100 mg/5 mL

Pharmacology

Competes with aldosterone at receptor sites in renal tubule, resulting in excretion of sodium chloride, water, bicarbonate, and calcium, but with retention of potassium, phosphate and hydrogen (Abramovitz, 2016).

Pharmacodynamics

Spironolactone is a synthetic 17-lactone steroid which is a renal competitive aldosterone antagonist in a class of pharmaceuticals called potassium-sparing diuretics. On its own, spironolactone is only a weak diuretic, but it can be combined with other diuretics. Due to its anti-androgen effect, it can also be used to treat hirsutism, and is a common component in hormone therapy for male-to-female transgendered people. Spironolactone inhibits the effect of aldosterone by competing for intracellular aldosterone receptor in the distal tubule cells. This increases the secretion of water and sodium, while decreasing the excretion of potassium. Spironolactone has a fairly slow onset of action, taking several days to develop and similarly the effect diminishes slowly (drugbank, 2013k).

Indications

Oedema and ascites in cirrhosis of the liver, malignant ascites, nephrotic syndrome, congestive heart failure; primary hyperaldosteronism (BNF, 2016a).

Pharmacokinetics

Fairly rapidly absorbed from the gastrointestinal tract, with the extent of its absorption depending on the particle size and formulation. Modern formulations are reported to provide a bioavailability of about 90%, with 90% being bound to the plasma proteins. It is . Orally, onset 24–48 hours, with its peak within 48–72 hours (Abramovitz, 2016).

Absorption - Fairly rapidly absorbed from the gastrointestinal tract. Food increases the bioavailability of unmetabolized spironolactone by almost 100%.

Protein binding - Spironolactone and its metabolites are more than 90% bound to plasma proteins.

Metabolism - Rapidly and extensively metabolised. The metabolic pathway of spironolactone is complex and can be divided into two main routes: those in which the sulphur moiety is retained and those in which the sulphur moiety is removed by dethioacetylation. Spironolactone is transformed to a reactive metabolite that can inactivate adrenal and testicular cytochrome P450 enzymes. It also has anti-androgenic activity.

Elimination - The metabolites are excreted primarily in the urine and secondarily in bile (drugbank, 2013k). Excreted mainly in the urine and also in the faeces in the form of its metabolites (TGC, 2015a).

Half-life - 10 minutes.

How it works

Spironolactone is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule. Spironolactone causes increased amounts of sodium and water to be excreted, while potassium is retained. Spironolactone acts both as a diuretic and as an antihypertensive drug by this mechanism. It may be given alone or with other diuretic agents which act more proximally in the renal tubule. Aldosterone interacts with a cytoplasmic mineralocorticoid receptor to enhance the expression of the Na+, K+-ATPase and the Na+ channel involved in a Na+ K+ transport in the distal tubule. Spironolactone bind to this mineralcorticoid receptor, blocking the actions of aldosterone on gene expression. Aldosterone is a hormone; its primary function is to retain sodium and excrete potassium in the kidneys (drugbank, 2013k).

Typical dosage

Pre-op - 100–400 mg/day (unknown, 2005), 100–200 mg/day (Asscheman and LJG Gooren, 1992).

Post-op - 50 mg/day (unknown, 2005).

Route

Tablets - Spironolactone, Aldactone.

Suspension - Spironolactone.

Contraindications

Hypersensitivity, anuria[70], severe renal disease, hyperkalaemia[71] (Abramovitz, 2016), hyponatraemia[72], Addisons disease (BNF, 2016a).

Side-effects

Central Nervous System

- Headache,
- confusion,
- drowsiness,
- lethargy,
- ataxia (Abramovitz, 2016).

Gastrointestinal

- Diarrhoea,
- cramps,
- bleeding,
- gastritis,
- vomiting,
- anorexia,
- nausea (Abramovitz, 2016).

Skin

- Rash,
- pruritis,
- urticaria (Abramovitz, 2016).

Genitourinary

- Impotence,
- gynaecomastia,
- hirsutism,
- deepening voice (Abramovitz, 2016).

Haematological

Agranulocytosis [73] (Abramovitz, 2016).

[70] complete suppression of urine formation and excretion (medical-dictionary, 2014)

[71] An excess of potassium in the blood. If left untreated it can lead to cardiac arrest

[72] A deficiency of sodium in the blood

[73] An acute condition marked by severe depression of the bone marrow, which produces white blood cells, neutropenia results, whereby the body is severely depleted in its ability to defend itself. Fever, malaise, and bleeding ulcers of the rectum, mouth, and vagina may be present

Skeletal

Osteomalacia (BNF, 2016a).

Interactions

- Aspirin - ↓ action of spironolactone.
- Digoxin - ↑ digoxin action.
- Lithium - ↑ action, toxicity.
- ACE inhibitors, diuretics (potassium-sparing), potassium products, salt substitute: ↑ hyperkalaemia.
- Anticoagulants: ↓ effects of anticoagulants.
- Antihypertensives: ↑ action (Abramovitz, 2016).

Abiraterone - The therapeutic efficacy of Abiraterone can be ↓ when used in combination with Spironolactone.

Acetylsalicylic acid - The risk or severity of adverse effects can be ↑ when Acetylsalicylic acid is combined with Spironolactone.

Aldesleukin - The risk or severity of adverse effects can be ↑ when Aldesleukin is combined with Spironolactone.

Alfentanil - The risk or severity of adverse effects can be ↑ when Alfentanil is combined with Spironolactone.

Alfuzosin - Alfuzosin may ↑ the hypotensive activities of Spironolactone.

Amifostine - Spironolactone may ↑ the hypotensive activities of Amifostine.

Amiloride - Amiloride may ↑ the hyperkalaemic activities of Spironolactone.

Ammonium chloride - The risk or severity of adverse effects can be ↑ when Spironolactone is combined with Ammonium chloride.

Ardeparin - Ardeparin may ↑ the hyperkalaemic activities of Spironolactone.

Atorvastatin - The risk or severity of adverse effects can be ↑ when Atorvastatin is combined with Spironolactone.

Atracurium besylate - Spironolactone may ↑ the neuromuscular blocking activities of Atracurium besylate.

Brimonidine - Brimonidine may ↑ the antihypertensive activities of Spironolactone.

Buprenorphine - The risk or severity of adverse effects can be ↑ when Buprenorphine is combined with Spironolactone.

Butabarbital - Butabarbital may ↑ the hypotensive activities of Spironolactone.

Butethal - Butethal may ↑ the hypotensive activities of Spironolactone.

Butorphanol - The risk or severity of adverse effects can be ↑ when Butorphanol is combined with Spironolactone.

Caffeine - The risk or severity of adverse effects can be ↑ when Caffeine is combined with Spironolactone.

Canagliflozin - Canagliflozin may ↑ the hyperkalaemic activities of Spironolactone.

Chlorphenamine - The risk or severity of adverse effects can be ↑ when Chlorphenamine is combined with Spironolactone.
Cholestyramine - The risk or severity of adverse effects can be ↑ when Cholestyramine is combined with Spironolactone.
Ciprofloxacin - Spironolactone may ↑ the arrhythmogenic activities of Ciprofloxacin.
Cisatracurium besylate - Spironolactone may ↑ the neuromuscular blocking activities of Cisatracurium besylate.
Codeine - The risk or severity of adverse effects can be ↑ when Codeine is combined with Spironolactone.
Cyclosporine - Spironolactone may ↑ the hyperkalaemic activities of Cyclosporine.
Diazoxide - Diazoxide may ↑ the hypotensive activities of Spironolactone.
Digoxin - The serum concentration of Digoxin can be ↑ when it is combined with Spironolactone.
Dihydrocodeine - The risk or severity of adverse effects can be ↑ when Dihydrocodeine is combined with Spironolactone.
Dipivefrin - Spironolactone may ↓ the vasoconstricting activities of Dipivefrin.
Dopamine - Spironolactone may ↓ the vasoconstricting activities of Dopamine.
Drospirenone - Drospirenone may ↑ the hyperkalaemic activities of Spironolactone.
Duloxetine - Spironolactone may ↑ the orthostatic hypotensive activities of Duloxetine.
Ephedrine - Spironolactone may ↓ the vasoconstricting activities of Ephedrine.
Epinephrine - Spironolactone may ↓ the vasoconstricting activities of Epinephrine.
Eplerenone - Eplerenone may ↑ the hyperkalaemic activities of Spironolactone.
Fentanyl - The risk or severity of adverse effects can be ↑ when Fentanyl is combined with Spironolactone.
Heparin - Heparin may ↑ the hyperkalaemic activities of Spironolactone.
Heptabarbital - Heptabarbital may ↑ the hypotensive activities of Spironolactone.
Hexobarbital - Hexobarbital may ↑ the hypotensive activities of Spironolactone.
Hydrocodone - The risk or severity of adverse effects can be ↑ when Hydrocodone is combined with Spironolactone.
Hydromorphone - The risk or severity of adverse effects can be ↑ when Hydromorphone is combined with Spironolactone.
Infliximab - Infliximab may ↓ the antihypertensive activities of Spironolactone.
Levodopa - Spironolactone may ↑ the orthostatic hypotensive activities of Levodopa.
Levorphanol - The risk or severity of adverse effects can be ↑ when Levorphanol is combined with Spironolactone.

Methadone - The risk or severity of adverse effects can be ↑ when Methadone is combined with Spironolactone.
Methohexital - Methohexital may ↑ the hypotensive activities of Spironolactone.
Methylphenidate - Methylphenidate may ↓ the antihypertensive activities of Spironolactone.
Mitotane - The therapeutic efficacy of Mitotane can be ↓ when used in combination with Spironolactone.
Molsidomine - Molsidomine may ↑ the hypotensive activities of Spironolactone.
Morphine - The risk or severity of adverse effects can be ↑ when Morphine is combined with Spironolactone.
Moxonidine - Moxonidine may ↑ the hypotensive activities of Spironolactone.
Nalbuphine - The risk or severity of adverse effects can be ↑ when Nalbuphine is combined with Spironolactone.
Nicorandil - Nicorandil may ↑ the hypotensive activities of Spironolactone.
Nitrofurantoin - Nitrofurantoin may ↑ the hyperkalaemic activities of Spironolactone.
Norepinephrine - Spironolactone may ↓ the vasoconstricting activities of Norepinephrine.
Obinutuzumab - Spironolactone may ↑ the hypotensive activities of Obinutuzumab.
Oxycodone - The risk or severity of adverse effects can be ↑ when Oxycodone is combined with Spironolactone.
Oxymorphone - The risk or severity of adverse effects can be ↑ when Oxymorphone is combined with Spironolactone.
Pancuronium - Spironolactone may ↑ the neuromuscular blocking activities of Pancuronium.
Pentazocine - The risk or severity of adverse effects can be ↑ when Pentazocine is combined with Spironolactone.
Pentobarbital - Pentobarbital may ↑ the hypotensive activities of Spironolactone.
Pentoxifylline - Pentoxifylline may ↑ the hypotensive activities of Spironolactone.
Perindopril - Spironolactone may ↑ the hyperkalaemic activities of Perindopril.
Pethidine - The risk or severity of adverse effects can be ↑ when Pethidine is combined with Spironolactone.
Phenelzine - Phenelzine may ↑ the orthostatic hypotensive activities of Spironolactone.
Primidone - Primidone may ↑ the hypotensive activities of Spironolactone.
Pseudoephedrine - Spironolactone may ↓ the vasoconstricting activities of Pseudoephedrine.
Quinidine - The therapeutic efficacy of Quinidine can be ↓ when used in combination with Spironolactone.
Quinine - Quinine may ↑ the hypotensive activities of Spironolactone.

Racepinephrine - Spironolactone may ↓ the vasoconstricting activities of Racepinephrine.
Remifentanil - The risk or severity of adverse effects can be ↑ when Remifentanil is combined with Spironolactone.
Risperidone - Spironolactone may ↑ the hypotensive activities of Risperidone.
Rituximab - Spironolactone may ↑ the hypotensive activities of Rituximab.
Rocuronium - Spironolactone may ↑ the neuromuscular blocking activities of Rocuronium.
Secobarbital - Secobarbital may ↑ the hypotensive activities of Spironolactone.
Sufentanil - The risk or severity of adverse effects can be ↑ when Sufentanil is combined with Spironolactone.
Tacrolimus - Spironolactone may ↑ the hyperkalaemic activities of Tacrolimus.
Tadalafil - Tadalafil may ↑ the antihypertensive activities of Spironolactone.
Tapentadol - The risk or severity of adverse effects can be ↑ when Tapentadol is combined with Spironolactone.
Tolvaptan - Tolvaptan may ↑ the hyperkalaemic activities of Spironolactone.
Tramadol - The risk or severity of adverse effects can be ↑ when Tramadol is combined with Spironolactone.
Tranylcypromine - Tranylcypromine may ↑ the orthostatic hypotensive activities of Spironolactone.
Treprostinil - Treprostinil may ↑ the hypotensive activities of Spironolactone.
Triamterene - Triamterene may ↑ the hyperkalaemic activities of Spironolactone.
Trimethoprim - Trimethoprim may ↑ the hyperkalaemic activities of Spironolactone.
Triprolidine - Spironolactone may ↓ the vasoconstricting activities of Triprolidine.
Valsartan - Valsartan may ↑ the hyperkalaemic activities of Spironolactone.
Vardenafil - Vardenafil may ↑ the antihypertensive activities of Spironolactone.
Vecuronium - Spironolactone may ↑ the neuromuscular blocking activities of Vecuronium.
Yohimbine - Yohimbine may ↓ the antihypertensive activities of Spironolactone (drugbank, 2013k).

Food interactions

- Avoid alcohol,
- Food increases the bioavailability of spironolactone by almost 100%,
- Spironolactone may decrease the excretion of potassium. Salt substitutes containing potassium increase the risk of hyperkalaemia (drugbank, 2013k).

Laboratory test interferences

False: ↑ Urinary catecholamines (Abramovitz, 2016). Interference: Glucose, insulin tolernace tests (Abramovitz, 2016).

Clinical assessment

Monitor electrolytes: potassium, sodium, calcium, magnesium; also include blood urea nitrogen, arterial blood gas, uric acid, complete blood cell count, blood glucose (Abramovitz, 2016).

Overdose

Acute overdosage may be manifested by -

- **drowsiness**,
- **mental confusion, nausea**,
- **vomiting**,
- **dizziness** or
- **diarrhoea**.

Hyponatraemia, or hyperkalaemia may be induced, but these effects are unlikely to be associated with acute overdosage. Symptoms of hyperkalaemia may manifest as paraesthesia, weakness, flaccid paralysis or muscle spasm and may be difficult to distinguish clinically from hypokalaemia. Electrocardiographic changes are the earliest specific signs of potassium disturbances. No specific antidote has been identified. Improvement may be expected after withdrawal of the drug. General supportive measures including replacement of fluids and electrolytes may be indicated. For hyperkalaemia, reduce potassium intake, administer potassium-excreting diuretics, intravenous glucose with regular insulin or oral ion-exchange resins (emc, 2016).

Shelf life

The shelf life of Aldactone tablets is 5 years (emc, 2016).

Caution

Spironolactone has been shown to produce tumours in rats when administered at high doses over a long period of time (emc, 2016).

Warning

You should be aware that drowsiness, ataxia, and mental confusion may occur; you should therefore be careful whilst driving.

You should notify your doctor if you get any of these -

- **muscle cramps, weakness**,
- **nausea, dizziness**, or
- **numbness** (Abramovitz, 2016).

Toxicity

The oral LD-50 of spironolactone is greater than 1,000 mg/kg in mice, rats, and rabbits. Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats (drugbank, 2013k).

Chapter 12

Potential problems

This section is included not to frighten or scare people but to highlight some of the potential problems, their possible causes and what you can do about them. Again, I would also refer you to the disclaimer and also point out that there is no substitute for good medical advice.

These subjects are not in any particular order, except alphabetical order.

Allergic reactions

Seek medical attention right away if any of these SEVERE side effects occur -

- **rash**,
- **hives**,
- **itching**,
- **difficulty breathing**,
- **tightness in the chest**,
- **swelling of the mouth, face, lips, or tongue**,
- **difficulty swallowing**,
- **unusual hoarseness**.

Breast Self Examination

It is recommended by healthcare professionals that all women over the age of 20 examine their breasts once a month. By examining your breasts regularly, you will know how your breasts normally feel. If a change should happen in your breasts, you will be able to identify it and let your doctor know. Most lumps are found by women themselves. If you find any lumps, thickenings or changes, tell your doctor right away. Remember, most breast lumps are not cancerous, but you don't know if you don't ask. Breast cancer

can be successfully treated if you find it and treat it early. Delaying the diagnosis of breast cancer does not change the diagnosis, it only worsens the outcome. This is not to say that we are at risk of breast cancer as there are very few known cases, extremely few, only four in total (Kanhai and Hage, 2000), but I believe it is in our best interests to self-examine our breasts. See also Breast Self-Exam.

When to Do a Breast Self-Examination

You should do a Breast Self-Examination (Breast self-examination (BSE)) every month 2 or 3 days after your period. If you do not have regular periods, just do it the same day every month... like the first... or the tenth... or the day that matches your birthday. (Note: just before your period or during pregnancy, your breasts may be somewhat lumpy or more tender.) If you are taking HRT, talk with your doctor about when to do BSE.

How to do your Breast Self-Examination

1. Lie down. Flatten your right breast by placing a pillow under your right shoulder. Place your right arm behind your head.
2. Use the sensitive finger pads (where your fingerprints are, not the tips) of the middle three fingers on your left hand. Feel for lumps using a circular, rubbing motion in small, penny-sized circles without lifting the fingers. Powder, oil or lotion can be applied to the breast to make it easier for the fingers to glide over the surface and feel changes.
3. Press firmly enough to feel different breast tissues, using three different pressures. First, light pressure to just move the skin without jostling the tissue beneath, then medium pressure pressing midway into the tissue, and finally deep pressure to probe more deeply down to the ribs or to the point just short of discomfort.
4. Completely feel all of the breast and chest area up under your armpit, and up to the collarbone and all the way over to your shoulder to cover breast tissue that extends toward the shoulder.
5. Use the same pattern to feel every part of the breast tissue. Choose the method that you find easiest:

Figure 12.1 – Feel your breasts whilst lying down

Figure 12.2 – Lines examination

Figure 12.3 – Circle examination

Figure 12.4 – Wedges examination

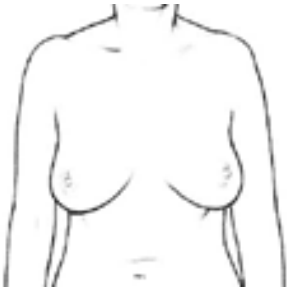

Figure 12.5 – Examine your breasts while standing

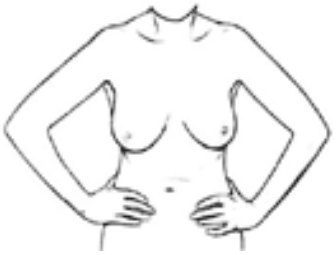

Figure 12.6 – Examine your breasts whilst turning

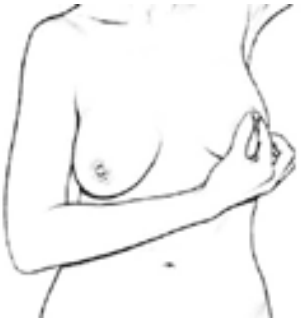

Figure 12.7 – Look for dimples or bulges

Figure 12.8 – Flex your chest muscles

Lines - Start in the underarm area and move your fingers downward little by little until they are below the breast. Then move your fingers slightly toward the middle, and slowly move back up. Go up and down until you cover the whole area.

Circles - Beginning at the outer edge of your breast, move your fingers slowly around the breast in a circle. Move around the breast in smaller and smaller circles, gradually working toward the nipple. Dont forget to check the armpit and upper chest areas, too.

Wedges - Starting at the outer edge of the breast, move your fingers toward the nipple and back to the edge. Check your whole breast, covering one small wedge-shaped section at a time. Be sure to check the armpit and the upper chest.

- After you have completely examined your right breast, then examine your left breast using the same method and your right hand, with a pillow under your left shoulder.
- You may want to examine your breasts or do an extra examination whilst showering. Its very easy to slide soapy hands over your skin, and to feel anything unusual.

- You should also check your breasts while looking in a mirror looking for any change in size or contour, dimpling of the skin or spontaneous nipple discharge.
- When standing upright in front of the mirror look at your breasts carefully. Look for any recent changes in the size or shape of your breasts.
- Turn slowly from side to side, so that you can see all parts of your breasts.
- Next put your hands on your head and look for any dimples or bulges in your breasts, particularly underneath. Dimples which are equal in size and shape and occur in both breasts are normally harmless.
- Finally rest the palms of your hands on your hips and press down firmly while holding your shoulders back, this flexes your chest muscles.

Again, look for any changes in appearance. By regular inspection you will see what is normal for you (Kimble, 2014).

Deep Vein Thrombosis

I have already mentioned DVT's but I'm also aware that some people don't know what a 'DVT' is or how serious it may be. See also Blood clots.

Deep vein thrombosis occurs when a blood clot forms in a vein lying beneath the deep tissue of the leg and obstructs the normal flow of the blood back to the heart. It can occur spontaneously or in association with other risk factors such as;-

Age - the risk appears to increase significantly after the age of 60.
Immobilisation - This may be permanent or a temporary risk. Examples include after a stroke, people in plaster casts following fractures, long-distance travel and postoperative recovery. Major surgery, especially if there was an operation on the abdomen or lower limb, is a common preventable cause.
Surgery - most especially hip and knee replacements.
Cardiac disease - increased in people who have cardiac disease.
Previous history of DVT - A previous episode of DVT is the strongest risk factor for DVT with a five-fold increase over baseline risk.
Family history of VTE
Cancer
Smoking
BMI over 30 kg/m^2
Male gender
Acquired or familial thrombophilia
Heart failure
Varicose veins
Trauma to the vein or chronic low-grade injury (vasculitis, stasis, chemotherapy)

Dehydration

To give an idea of it's prevalence it affects about 1 in 1000 in the UK, and therefore a typical health authority (with a population of 750,000) is likely to see about 750 cases a year. Pulmonary embolism is an acute complication of deep vein thrombosis and is a major cause of mortality, estimated to be responsible for around 10% of hospital deaths each year (Brough, 1998).

Risk factors for venous thromboembolism

Family history of venous thromboembolism - in first-degree relative aged under 45 years.

Obesity - body mass index greater than 30kg/m^2. (Avoid if body mass index above 39kg/m^2).

Long-term immobilisation - e.g. in a wheelchair (avoid if confined to bed or leg in a plaster cast).

Varicose veins - (avoid during sclerosing treatment or where definite history of thrombosis).

Signs

Not all of these will be seen in every case. There may be calf tenderness and a mild fever. There may be pitting oedema, increased warmth and distended veins at the site. There may also be swelling at the site and/or local skin discolouration compared to the other limb. If any combination of these are seen then you ought to contact your G.P., or whoever is standing in for them. Meanwhile you should sit down as much as possible and rest your lower legs on something about the same height as you are sitting on i.e. lie/sit on the sofa with your legs raised off the floor.

If DVT is suspected, a venous ultrasound (Duplex Doppler) will usually be performed to confirm the presence of blood clots in deep veins. A blood test known as a D-dimer test may also be performed if necessary (unknown, 2013a).

A venous thrombus most often occurs in the deep veins of the legs or pelvis and is then called a deep vein thrombosis (DVT). The clot may dislodge and travel to the lungs to cause a pulmonary embolism (PE) (NICE, 2012), (patientinfo, 2015).

A DVT can be very difficult to diagnose but early recognition and appropriate treatment can save many lives. A thrombus either arises spontaneously or is predisposed by such conditions as surgery, trauma or prolonged bed rest. They usually form in the deep veins of the lower limbs but may extend higher and into the pelvic veins. The close relationship between DVT and pulmonary PE is such that the term venous thromboembolism (Venous thromboembolism (VTE)) is often used to cover both conditions (patientinfo, 2015).

Epidemiology

- DVT has an annual incidence of about 1 in 1,000 people (NICE, 2013).
- Major risk factors for VTE include a prior history of DVT, age over 60 years, surgery, obesity, prolonged travel, acute medical illness, cancer, immobility, thrombophilia and pregnancy (NICE, 2012).
- One study found that 50–70% of patients had readily identifiable risk factors (Ageno, Agnelli, and Imberti, 2008).

The clinical diagnosis of DVT can be very difficult. Many DVTs progress to PE without DVT being clinically apparent. In those with classic clinical signs, only about a third have DVT. Classical features are a result of obstruction to venous drainage -

- Limb pain and tenderness along the line of the deep veins.
- Swelling of the calf or thigh (usually unilateral). Involvement of the iliac bifurcation, the pelvic veins or the vena cava produces leg oedema that is usually bilateral.
- Pitting oedema.
- Distension of superficial veins.
- Increase in skin temperature.
- Skin discoloration (erythema or occasionally purple or cyanosed).
- A palpable cord (hard, thickened palpable vein) (patientinfo, 2015).

Cellulitis adds to the problem -

- Severe signs of DVT can resemble cellulitis.
- Secondary cellulitis may develop with primary DVT.
- Primary cellulitis may be followed by a secondary DVT.
- Superficial thrombophlebitis may hide an underlying DVT (patientinfo, 2015).

If it is diagnosed as a DVT

The treatment may well take several months and there is a possibility that you may be hospitalised, but it seems that the trend in most cases is not to admit to hospital.

The following measures can be taken as part of the treatment, but should also be discussed with your doctor

- You should avoid standing for long periods of time. Where this is not possible i.e. on a busy train, then leg movements or walking around should be used.
- The feet should be raised whenever possible when sitting down.
- Gentle exercise (with the emphasis on gentle, which means no contact sports) until given the go-ahead by the doctor.
- Moisturise both legs daily to keep the skin supple, as it will have a tendency to get very dry.

- See if any medications or supplements contain Vitamin K, and if so, stop taking them. This is because Vitamin K is an antidote to anticoagulant therapy.
- Moderate any drinking of alcohol as this may enhance the effects of anticoagulants.
- Avoid dental treatment whilst taking anticoagulants. If it is unavoidable, then discuss it with your dentist and your doctor.
- Avoid non-steroidal anti-inflammatory drugs (i.e. Ibuprofen, and Aspirin) because they will enhance the anticoagulant effect.
- Above all, dont panic! Think carefully and discuss the situation with your doctor (Brough, 1998).

The incidence of venous thrombosis associated with oestrogen treatment in male-to-female (M–>F) transsexuals is considerably higher with administration of oral ethinylestradiol than with transdermal 17β-estradiol. To find an explanation for the different thrombotic risks of oral ethinylestradiol and transdermal 17β-estradiol use, we compared the effects of treatment of M–>F transsexuals with cyproterone acetate only, and with cyproterone acetate in combination with transdermal 17β-estradiol, oral ethinylestradiol, or oral E(2) on a number of hemostatic variables [activated protein C (APC) resistance and plasma levels of protein S, protein C, and prothombin], all of which are documented risk factors for venous thrombosis. APC resistance was determined by quantification of the effect of APC on the amount of thrombin generated during tissue factor-initiated coagulation; plasma levels of total and free protein S were determined by standard ELISA; and levels of prothrombin and protein C were determined with functional assays after complete activation of the zymogens with specific snake venom proteases. Cyproterone acetate-only, transdermal 17β-estradiol+cyproterone acetate, or oral-E(2)+cyproterone acetate treatment produced rather small effects on hemostatic variables, whereas oral ethinylestradiol treatment resulted in a large increase in APC resistance from 1.2 +/- 0.8 to 4.1 +/- 1 (P <0.001), a moderate increase in plasma protein C (9%; P = 0.012), and a large decrease in both total and free plasma protein S (30%; P <0.005). *The large differential effect of oral ethinylestradiol and oral E(2) indicates that the prothrombotic effect of ethinylestradiol is due to its molecular structure rather than to a first-pass liver effect (which they share). Moreover, these differences may explain why M–>F transsexuals treated with oral ethinylestradiol are exposed to a higher thrombotic risk than transsexuals treated with transdermal 17β-estradiol*. Testosterone administration to female-to-male transsexuals had an antithrombotic effect (Toorians et al., 2003).

Treating a DVT

Treatment of DVT usually involves hospitalization and treatment with injections of a low molecular weight heparin, also known as low molecular weight heparin (LMWH), an anticoagulant that thins the blood and reduces the possibility of a clot. LMWHs include dalteparin (Fragmin), enoxaparin (Lovenox), and tinzaparin. Daily injections of a LMWH may also be given to prevent the formation of DVT in patients considered to be at risk following surgery.

Other anticoagulants such as standard heparin may also be given by injection to break down blood clots. Fondaparinux (Arixtra) is another drug that may be used as an alternative to LMWHs or standard heparin in the initial treatment of DVT. Following treatment with injections (or sometimes in combination treatment), anticoagulants such as warfarin will be prescribed. The dosage of these tablets is usually adjusted according to blood tests that show the blood clotting time; treatment needs to be continued for several months (unknown, 2013a).

Osteoporosis

Osteoporosis is a silent disease which can develop over many years and usually becomes apparent in the over-60 age group, affecting (on average) 1 in 3 women and 1 in 12 men. It is a systemic skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture (WHO, 1994). The lifetime risk of a 50-year-old women in the UK sustaining an osteoporotic fracture of the wrist, vertebra or hip is 14%, 11% and 13% respectively, while the lifetime risk of a 50-year-old man is 5% at each site (Cooper, 1996). Osteoporosis and it's sequelae of fractures may have serious effects on the individual in terms of pain, disability and increased morbidity and mortality. It also has a major impact on health service expenditure and in 1998 accounted for £942 million in the UK health budget (Torgerson and Dolan, 1998). The commonest fracture sites in post-menopausal women are the forearm, neck of femur (where the thigh bone joints at the hip) and the lumbar spine. Fractures can occur spontaneously, such as when having a coughing fit (fractured ribs), or picking up a child or lifting a heavy object (fractured vertebra). Crush fractures of the vertebras can lead to a loss of height of up to 25cms and involve an increased curvature of the spine over time the head sinks into the chest, causing pressure on the lungs which often leads to lung disease which may then become the primary cause of death (unknown, 1997).

There is overwhelming evidence that oestrogen can prevent bone loss and there is less good but convincing evidence that oestrogen prevents fractures. Oestrogen use of between 5 and 10 years is associated with a 50% reduction in risk of fracture. There is good evidence that in established osteoporosis, oestrogen prevents further bone loss and reduces the incidence of fractures. Oestrogen use leads to lasting skeletal benefits and will prevent bone loss at whatever age it is started. Prior to fracture there are no symptoms associated with osteoporosis and few patients will be diagnosed at a time when effective treatment could be instigated. It is apparent that the risk of developing osteoporosis cannot be deduced from clinical data alone and bone mineral measurements provide the single best test for future risk. Bone mass can be measured directly and there is no need for guess work. The most important potential application for oestrogen is in preventive therapy, and the efficient use of oestrogen in this situation depends upon the diagnosis of low bone mass. Who to treat remains the issue. For any age group the median value of bone density and a range of percentiles can be generated, thus facilitating therapeutic decisions (Fogelman, 1991).

Postmenopausal osteoporosis affects millions of women, with oestrogen deficiency being the key factor in the development of osteoporosis. Fracture prevention is one of the public health priorities worldwide. Different treatments for osteoporosis are available, with the various options being aimed at maintaining bone health and decreasing the risk of fractures. The majority of these drugs are antiresorptive agents, i.e., drugs that lower bone turnover, inhibiting osteoclastic bone resorption. Dietary sources of calcium intake and vitamin D are ideal, while pharmacological supplements should be used if diet alone cannot provide the recommended daily intake. Bisphosphonates are the first-line therapy for patients with established osteoporosis at high risk of fracture. In climacteric [74] women, in different stages of menopausal transition, and beyond, hormone replacement therapy at different doses rapidly normalizes turnover, preventing and/or treating osteoporosis. Hormone replacement therapy is able to preserve and even increase bone mass density at all skeletal sites, leading to a significant reduction in vertebral and non-vertebral fractures.

Studies investigating the actions of phytoestrogens on bone mass density or bone turnover are largely contradictory, making them inconclusive. At the present time, phytoestrogens cannot be recommended for postmenopausal osteoporosis (Gambacciani, 2014).

Risk factors for osteoporosis

Unchangeable risks

Some risk factors for osteoporosis are out of your control, including -

[74] the period during which women gradually lose their reproductive capabilities as a result of aging. Also used as an adjective to describe this period

Your sex - Women are much more likely to develop osteoporosis than are men.

Age - The older you get, the greater your risk of osteoporosis.

Race - You're at greatest risk of osteoporosis if you're white or of Asian descent.

Family history - Having a parent or sibling with osteoporosis puts you at greater risk, especially if your mother or father experienced a hip fracture.

Body frame size - Men and women who have small body frames tend to have a higher risk because they may have less bone mass to draw from as they age.

Hormone levels

Osteoporosis is more common in people who have too much or too little of certain hormones in their bodies. Examples include -

Sex hormones - Lowered sex hormone levels tend to weaken bone. The reduction of oestrogen levels at menopause is one of the strongest risk factors for developing osteoporosis. Women may also experience a drop in oestrogen during certain cancer treatments. Men experience a gradual reduction in testosterone levels as they age. And some treatments for prostate cancer reduce testosterone levels in men.

Thyroid problems - Too much thyroid hormone can cause bone loss. This can occur if your thyroid is overactive or if you take too much thyroid hormone medication to treat an underactive thyroid.

Other glands - Osteoporosis has also been associated with overactive parathyroid and adrenal glands.

Dietary factors

Osteoporosis is more likely to occur in people who have -

Low calcium intake - A lifelong lack of calcium plays a major role in the development of osteoporosis. Low calcium intake contributes to diminished bone density, early bone loss and an increased risk of fractures.

Eating disorders - People who have anorexia are at higher risk of osteoporosis. Low food intake can reduce the number of calories and amount of protein and calcium ingested. In women, anorexia can stop menstruation, leading to weaker bones. In men, anorexia lowers the amount of sex hormones in the body and can weaken bone.

Gastrointestinal surgery - A reduction in the size of your stomach or a bypass or removal of part of the intestine limits the amount of surface area available to absorb nutrients, including calcium.

Lifestyle choices

Some bad habits can increase your risk of osteoporosis. Examples include -

Sedentary lifestyle - People who spend a lot of time sitting have a higher risk of osteoporosis than do those who are more active. Any weight-bearing exercise and activities that promote balance and good posture are beneficial for your bones, but walking, running, jumping, dancing and weightlifting seem particularly helpful.

Excessive alcohol consumption - Regular consumption of more than two alcoholic drinks a day increases your risk of osteoporosis.

Tobacco use - The exact role tobacco plays in osteoporosis isn't clearly understood, but it has been shown that tobacco use contributes to weak bones (M. C. Staff, 2014b).

Prevention and management of osteoporosis

The mainstays of prevention are -

- An adequate lifetime calcium intake,
- Weight-bearing exercise.
- Stopping smoking, as smoking doubles the risk of osteoporosis developing and is also known to have an adverse effect on women, reducing body weight and thus reducing bone density.

The mainstays of slowing down bone loss and osteoporosis management are -

- Eating a diet rich in calcium (1,000–1,200 mgs daily). Calcium is found in milk, cheese, and green vegetables.
- Moderating alcohol consumption.
- Maintaining regular weight-bearing activity such as dancing, walking, cycling, running or riding because the load-bearing exercise stresses bone, thereby stimulating bone strength.
- Maintaining exposure to sunlight throughout life (for adequate vitamin D production). However, vitamin D is also found in eggs, sardines, milk, salmon and cereals such as bran flakes (unknown, 1997)(Sutcliffe, 1999).

N.B. Postmenopausal women absorb dietary calcium less efficiently than premenopausal women and require an average of 1500 mg/day of elemental calcium to remain in neutral calcium balance. By comparison, premenopausal women require about 1000 mg/day, and the average calcium intake in the USA is 400–600 mg/day. Therefore, if not contraindicated, calcium supplementation may be considered helpful.

Height loss and osteoporosis

Nurses are being encouraged to measure the height of their older female patients as a screening tool for osteoporosis. US researchers issued the advice after finding that the risk of osteoporosis in the hip increased four-fold in women who had lost two inches in height and nine-fold in those who had lost more than three inches. In the study 2,108 women with an average age of 60 who had had bone mineral density scans were asked to recall how tall they were at 21. The researchers then measured the women and used the recorded height loss and bone mineral density data to calculate risk values for osteoporosis. They concluded that evaluation of height loss should be routine in the outpatient setting (unknown, 2004b)

The use of hormone replacement therapy for osteoporosis prevention is based on biology, epidemiology, animal and preclinical data, observational studies and randomized, clinical trials. Osteoporosis prevention can actually be considered as a major additional effect in climacteric women who use hormone replacement therapy for treatment of climacteric symptoms. Bone protection is one of the major benefits of hormone replacement therapy. The possibility that low dose hormone replacement therapy causes a decrease in fracture risk is not demonstrated but the scientific evidence is compelling. Conversely, established osteoporosis, often occurring in elderly women, can better be treated with specific treatments, such as bisphosphonates or, in more severe and selected cases, anabolic agents (Gambacciani, 2014).

Prostate cancer

The prostate shrinks considerably when testosterone is removed and oestrogens take it's place. The occurrence of prostate cancer is very rare in transsexuals, but it can occur. This may be due to problems that exist before significant hormone replacement therapy has begun. It is important that transsexuals get their prostate examined, particularly if they start hormone replacement therapy later in life and regardless if they are pre or post op. Having the testicles removed earlier in life helps a lot, but in middle-age MTFs the protection may not be there. The prostate is not removed in the SRS operation, as it can add to the natural lubrication of the neo-vaginal area, and is also a source of stimulation (unknown, 2014a).

Prostate cancer is a common cancer among men. There is usually no symptom at the early stage. If you have symptoms, it suggests the cancer has spread out of the prostate gland. Main symptoms include urgent urination, painful urination, blood in urine, weak urine flow, interrupted urine flow, urine retention, night urine, painful ejaculation pain, lower abdominal pain, lower back pain and thigh pain. Prostate cancer usually grows slowly. At the beginning it is confined to the prostate and it is

not very serious. When it spread to other parts of the body, it can cause serious consequences. For some patients, combination of multiple treatment methods, such as surgery plus radiotherapy or radiotherapy plus hormone therapy may be the best option (diseaseandsymptom, 2016a).

Pulmonary Embolism

Pulmonary embolism occurs when lung arteries are clogged. In most cases, embolisation is due to one or more clots of other parts of the body fall and flow into the lungs with the blood. Symptoms of pulmonary embolism are various, including sudden shortness of breath, chest pain, coughing up blood or blood stained sputum and rapid heartbeat. In most cases it is not fatal if treated timely. Anticoagulants can significantly reduce the risk of death (diseaseandsymptom, 2016b). A lung scan can be used to detect a pulmonary emboli (unknown, 2013a).

Testicular Self Examination

Testicular self-exam is an examination of the testicles that you do on yourself. See also Testicular Self Exam.

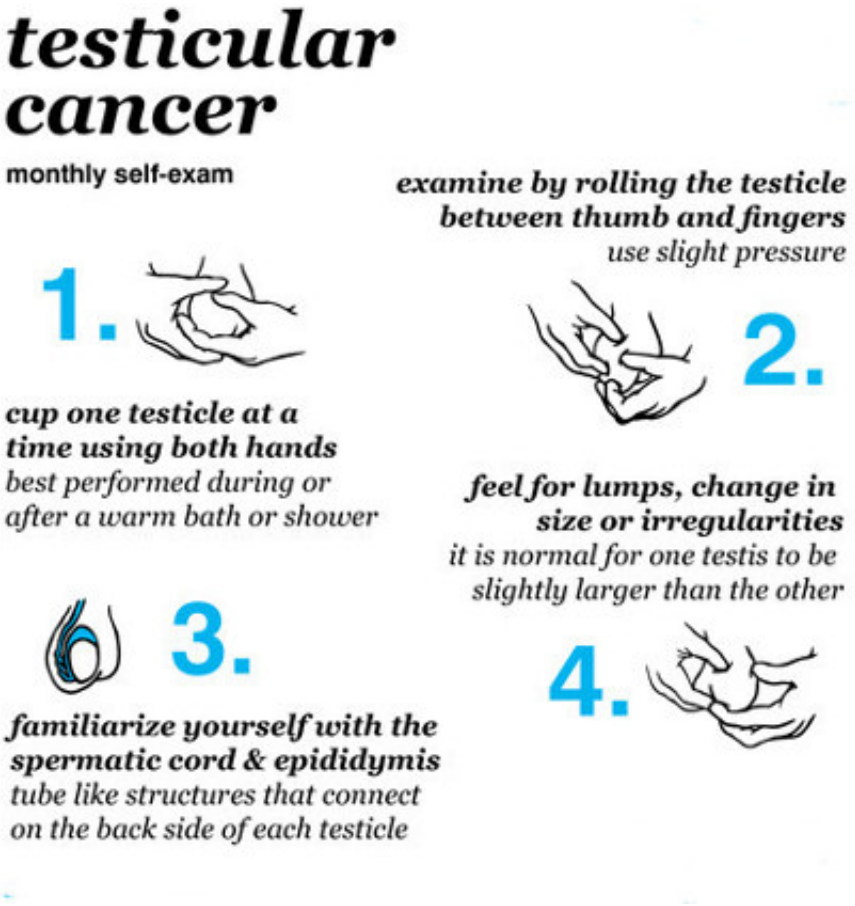

Figure 12.9 – How to do testicular self examination

How the Test is Performed

The testicles (also called the testes) are the male reproductive organs that produce sperm and the hormone testosterone. They are located in the scrotum under the penis.

You can do this test during or after a shower. This way, the scrotal skin is warm and relaxed. It is best to do the test while standing.

- Gently feel your scrotal sac to locate a testicle.
- Use one hand to stabilize the testicle. Use your fingers and thumb on the other hand to firmly but gently feel the testicle. Feel the entire surface.
- Check the other testicle in the same way.

Why the Test is Performed

A testicular self-exam may be done to check for testicular cancer.

Testicles have blood vessels and other structures that can make the exam confusing.

If you notice any lumps or changes in a testicle, contact your GP right away.

Doctors may recommend that you do a testicular self-exam every month if you have any of the following risk factors -

- Family history of testicular cancer,
- Past testicular tumour,
- Undescended testicle.

Some, but not all expert organizations, recommend self-exam if you are a teenager or young adult (to about 35 years old). It is not clear that performing this exam when you have no symptoms would decrease the risk of dying from testicular cancer.

Normal Results

Each testicle should feel firm, but not rock hard. One testicle may be lower or slightly larger than the other.

Talk to your health care provider if you have questions.

What Abnormal Results Mean

If you find a small, hard lump (like a pea), have an enlarged testicle, or notice any other differences that do not seem normal, see your health care provider right away.

Call your GP if -

- You cannot find one or both testicles — the testicles may not have descended properly in the scrotum
- There is a soft collection of thin tubes above the testicle — this may be a varicocele[75].
- You have pain or swelling in the scrotum — this may be an infection or a hydrocele[76] causing a blockage of blood flow to the area
- Sudden, severe (acute) pain in the scrotum or testicle that lasts for more than a few minutes is an emergency. If you have this type of pain, seek medical attention right away.

A lump in the testicle is often the first sign of testicular cancer. If you find a lump, see a health care provider right away. Most testicular cancers are very treatable. Keep in mind that some cases of testicular cancer do not show symptoms until they reach an advanced stage.

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[75] collection of widened veins

[76] fluid-filled sac

Signs of testicular cancer

- Any enlargement of a testicle,
- A significant loss of size in one of the testicles,
- A feeling of heaviness in the scrotum,
- A dull ache in the lower abdomen or in the groin,
- A sudden collection of fluid in the scrotum,
- Pain or discomfort in a testicle or in the scrotum,
- Enlargement or tenderness of the breasts.

Please be aware that your testicles **are** affected by the hormones that we take, and you may find that what you consider is a sign of testicular cancer is actually a change due to the hormones.

If you find a lump on your testicle or any of the other signs of testicular cancer, please see a doctor right away. The abnormality may not be cancer, but if it is testicular cancer, it will spread if it is not stopped by treatment. Even if it is something else like an infection, you are still going to need to see a doctor. Waiting and hoping will not fix anything. Please note that free floating lumps in the scrotum that are not attached in any way to a testicle are not testicular cancer. When in doubt, get it checked out - if only for peace of mind!

Please note that anything out of the ordinary down there should prompt a visit to the doctor, but you should be aware that the following symptoms are not normally signs of testicular cancer.

- A pimple, ingrown hair or rash on the scrotal skin,
- A free floating lump in the scrotum, seemingly not attached to anything,
- A lump on the epidiymis or tubes coming from the testicle that kind of feels like a third testicle,
- Pain or burning during urination,
- Blood in the urine or semen.

Remember, only a doctor can make a positive diagnosis! For that matter, only a doctor can make a negative diagnosis too. If you think something feels strange, go see the doctor!

Finally, embarassment is a poor excuse for not having any problem examined by a doctor. If you think there is something wrong or something has changed, please see your doctor!

To show how important Testicular self-examination (TSE) is, a testicular cancer tumour can double in size every 90 days! That is not scare-mongering, that is a fact! So if you think you have testicular cancer please see a doctor and get it checked out.

Thrombophlebitis

Thrombophlebitis is a condition in which blood clots form abnormally in veins, usually the veins of the legs. The condition may be inherited in people with a family history of disorders of the blood-clotting mechanism. The blood clots are usually superficial (ie, close to the surface of the skin). Deep clots can cause DVT, which is more dangerous, see also Deep Vein Thrombosis.

Superficial thrombophlebitis causes a painful swelling along the course of the veins close to the surface of the skin. The pain may vary from moderate discomfort to a cramp-like pain. The pain gradually subsides over a period of one to two weeks, leaving hard clots that can be felt along the course of the veins.

Superficial thrombophlebitis is rarely associated with deep venous disease and it is not thought to be a risk factor for pulmonary embolism.

A blood test can confirm if a person has inherited a familial clotting disorder.

For superficial thrombophlebitis, the affected leg should be elevated regularly and heat applied to the area involved. Anti-inflammatory medications may be prescribed — either oral or topical creams or gels (unknown, 2013a).

Urinary Tract Infections - UTI's

The urinary tract is the name given to the group of internal organs that collect, store and remove urine from the body. The most common part of the urinary tract to get infection is the bladder. Infection here is called cystitis. Cystitis is more common in women than men, which is probably due to the female urethra (the tube leading from the bladder to the outside (known as the urethra)) being shorter in women than in men, and being, on average, only 3cms long. Cystitis in men is often associated with infection and inflammation of the prostate gland (prostatitis). A urinary infection that involves the urine collecting system of the kidney is called pyelitis. It has usually spread up the tubes that run from the kidneys to the bladder (known as the ureters). When the infection also involves the substance of the kidney, it is called pyelonephritis. Up to 60% of women have a urinary tract infection at some point in their lives and at least a third of these will have a recurrence within the next year. Women in the 25–29 age group and the over 55s are at most risk of urinary tract infection.

Causes

Urinary infections are generally caused by differing varieties of bacteria. The most common bacteria is *Escherichia coli* (found in 65–80% of all Urinary Tract Infection (UTI's)), which normally lives in the bowel without causing harm. The infection may also be caused by other germs, including those acquired during sexual intercourse such as *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Haemophilus vaginalis* or *Candida albicans*.

Cystitis is commonly caused when bacteria on the skin from the vagina or from the rectum enter the urinary tract. Cystitis may result from sexual activity, including intercourse, especially if you have only recently become sexually active or have not had sex for a long time.

Usually the bladder is flushed by the frequent passage of newly produced urine. However if for some reason there is bladder stasis (perhaps due to immobility or dehydration caused by not drinking enough fluids, for whatever reason) then the bacteria can multiply.

Faecal organisms may also enter the bladder via spread from the bloodstream. This is particularly true of elderly or immobilised people (LGBT, 2014a)

Bladder function

The normal bladder has a dual function. For most of the time it acts as a highly compliant receptacle for urine that has been produced in the kidneys (storage phase). It also acts as a contracting organ, expelling urine via the urethra (emptying phase). As the bladder fills there should be an absence of contractile activity, allowing the bladder to expand. Bladder capacity is approximately 500ml (Rigby, 2003). It has been suggested that the sensation of bladder distension originates in tension receptors in the bladder wall (Cardozo, 1997). The first desire to void is usually experienced at approximately 300ml (Norton, 1996) (Rigby, 2005).

Symptoms

Cystitis causes a frequent desire to urinate. Often only a small amount of urine is passed but there is a burning or scalding pain whilst urinating, and there may also be a sensation that the bladder does not completely empty. This is a very common symptom. It sometimes includes the involuntary passing of a small squirt of urine on coughing or laughing (which is known as 'stress incontinence'). Sometimes a little blood is passed in the urine, and affected people often have to get up during the night to pass water.

Sometimes there are other symptoms which may include fever, shivering, pain in the groin and a general feeling of being unwell. This may mean that the infection has spread to the kidneys (when it is then known as 'Pyelonephritis').

Cystitis or urethritis cause acute retention because of the reduced contractility of the detrusor[77] muscle (Cardozo, 1997).

The symptoms of cystitis usually begin with a burning sensation when you urinate. This is followed by a frequent need to urinate in small amounts and a feeling of pressure in the abdomen. As the infection progresses, the urine may become cloudy, contain blood or have an unpleasant odour. Sometimes this is accompanied by cramps, a low-grade fever or back pain (LGBT, 2014c).

If you are asked for a urine sample, then please see Getting a urine sample.

Treatment

Mild cystitis will usually go away by itself within 2–4 days without any treatment. You can use OTC[78] painkillers like paracetamol to help cope with the symptoms (but always read the drugs informational leaflet to see if there are any interactions with your current medications).

More serious forms of urinary tract infection may need treatment with antimicrobial drugs, either under the care of your G.P. or a hospital. However, you may need to have some tests to rule out other possible causes before a treatment is prescribed. The drugs Trimethoprim, Nitrofurantoin and Cefalexin are often used to treat urinary tract infections.

Other commonly recommended treatments such as drinking more fluid have not been proven. However, drinking at least two litres of plain water each day is generally good for your health.

While on medication, drink plenty of liquids, at least 10–12 glasses a day. Avoid alcohol and any liquids containing caffeine, such as coffee, tea and cola. It is advised that you abstain from sexual activity while being treated for cystitis. In the future, if you have sex, you may use additional lubricant, such as KY Jelly or Astroglide with lubricated condoms, to help prevent irritation or friction (LGBT, 2014a).

Prevention

1. Get in the habit of drinking lots of water and juice every day, 8 to 10 glasses (8 oz.), or 2 litres, are recommended daily.

[77] the smooth muscle of the bladder

[78] over-the-counter, meaning easily purchased from drug stores and supermarkets

2. Always wipe from the front to the back after urination or a bowel movement.
3. Urinate at least every 2–3 hours while awake, or whenever you feel the need to go. Avoid "holding" urine for long periods.
4. If you are sexually active, urinate before and after sex. This helps flush out any bacteria that might become lodged in the urethral opening during sex.
5. Use additional lubrication, if needed, for intercourse.
6. A daily bath or shower is recommended. Use of a mild soap is preferred. Avoid scented bath products.
7. Good hand washing is very important. Make sure your partner's hands are clean prior to any sexual contact (LGBT, 2014a).

Self-help

Although I've said that the UTI normally goes away in two to three days, that period of time is damned uncomfortable and seemingly never-ending.

So what can you do meanwhile? Here is what works for me, totally getting rid of a UTI within about six hours!

- The usual route of infection is faecal ->oral, so to break it wash your hands **every time** you go to the toilet.
- Drink plenty of fluids, squash, tea, water, but no alcohol. As soon as one cup/mug/glass is empty, get a refill, so that you are constantly drinking, and constantly urinating getting rid of this extra fluid.
- Urinate when you need to, not according to the clock.
- Take two paracetamol, and take two more four hours later if necessary.
- Rest as much as possible, allow your body time and space to fight the infection.

Very simple guidance, some might say common-sense, but it works every time for me. Using these steps I have totally got rid of an UTI without ever seeing my GP.

Chapter 13

Blood tests and their results

What To Expect With Blood Tests

What To Expect Before Blood Tests

Many blood tests don't require any special preparation and take only a few minutes.

Other blood tests require fasting (not eating any food) for 8 to 12 hours before the test. Your doctor will tell you how to prepare for your blood test(s).

What To Expect During Blood Tests

Blood usually is taken from a vein in your arm or other part of your body using a needle. It also can be taken using a finger prick.

The person who takes your blood might tie a band around the upper part of your arm or ask you to make a fist. Doing this can make the veins in your arm stick out more, which makes it easier to insert the needle.

The needle that goes into your vein is attached to a small test tube. The person who takes your blood removes the tube when it's full, and the tube seals on its own. The needle is then removed from your vein. If you're getting a few blood tests, more than one test tube may be attached to the needle before it's withdrawn.

Some people get nervous about blood tests because they're afraid of needles. Others may not want to see blood leaving their bodies.

If you're nervous or scared, it can help to look away or talk to someone to distract yourself. You might feel a slight sting when the needle goes in or comes out.

Taking blood usually takes less than 3 minutes.

What To Expect After Blood Tests

Once the needle is withdrawn, you'll be asked to apply gentle pressure with a piece of gauze, cotton-wool ball,or bandage to the place where the needle was inserted. This helps stop bleeding. It also helps prevent swelling and bruising.

Most of the time, you can remove the pressure after a minute or two. You may want to keep the pressure bandage/cotton-wool ball on for a few hours.

Usually, you don't need to do anything else after a blood test. Results can take anywhere from a few minutes to a few weeks to come back. Your doctor should get the results. It's important that you follow up with your doctor to discuss your test results (nhlbi, 2012e).

Blood testing

Blood testing is what health tracking devices always wanted to be.

They all show you aspects of what's happening in your body so you could make better lifestyle choices to be healthier, but blood testing tells a deeper story than a mobile app or wristband could tell on their own. With all these devices and services becoming more accessible, healthcare is finally shifting from your doctor's hands to your own, and advancements in blood testing are opening even greater doors.

Most of us have had our blood taken at some point, whether it was a doctor's appointment or a donation with the Blood Transfusion Service, so you probably have a general idea of how it happens. But, have you ever wondered what happens from the moment the needle pricks your arm to the time you get your results?

It turns out, it is quite an intricate process. Blood needs to be collected, stored, packaged, transported, and analysed with very particular, nuanced methods. Read on to learn everything you never realised you wanted to know about the wonderful complexity of blood testing.

What is Blood Testing?

Blood tests reveal how our health is doing by showing what is in our blood. That deep red fluid is packed with different substances, like proteins, nutrients, and hormones. Analysing them requires a fresh blood sample, a very careful and sterile process, and fancy tools and machinery

at specialised labs. Giving a blood sample normally takes less than 3 minutes (nhlbi, 2012f) and is painless, though some people may experience temporary discomfort and bruising from the needle shortly after the blood is taken (nhlbi, 2012c).

Why Get Blood Tests?

Blood tests can uncover the risk or development of health problems that would otherwise go unnoticed. This is crucial for preventing disease or stopping it in its tracks. If you use any medication, blood tests also let you know how well the treatments are working (nhlbi, 2012b).

Blood Basics

There are four to six litres (7 to 10.5 pints) of blood circulating throughout the human body at all times, keeping us alive and functioning properly. Blood provides oxygen and nutrients to tissue, and removes waste. Approximately 45% of our blood consists of red blood cells, less than 1% consists of white cells and platelets, and the remaining 55% is made up of clear yellowish fluid called plasma (ARC, 2015).

Each substance has a unique, essential role -

Plasma

The liquid component of blood is called plasma, a mixture of water, sugar, fat, protein, and salts. The main job of the plasma is to transport blood cells throughout your body along with nutrients, waste products, antibodies, clotting proteins, chemical messengers such as hormones, and proteins that help maintain the body's fluid balance (ASH, 2015).

Plasma is a fluid, composed of about 92% water, 7% vital proteins such as albumin, gamma globulin, anti-haemophiliac factor, and other clotting factors, and 1% mineral salts, sugars, fats, hormones and vitamins (ARC, 2015).

Red blood cells

Known for their bright red colour, red cells are the most abundant cell in the blood, accounting for about 40–45% of its volume. The shape of a red blood cell is a biconcave disk with a flattened centre - in other words, both faces of the disc have shallow bowl-like indentations (a red blood cell looks like a doughnut).

Production of red blood cells is controlled by erythropoietin, a hormone produced primarily by the kidneys. Red blood cells start as immature cells in the bone marrow and after approximately seven days of maturation are released into the bloodstream. Unlike many other cells, red blood cells have no nucleus and can easily change shape, helping them fit through the various blood vessels in your body. However, while the lack of a nucleus makes a red blood cell more flexible, it also limits the life of the cell as it travels through the smallest blood vessels, damaging the cell's membranes and depleting its energy supplies. The red blood cell survives on average only 120 days.

Red cells contain a special protein called haemoglobin, which helps carry oxygen from the lungs to the rest of the body and then returns carbon dioxide from the body to the lungs so it can be exhaled. Blood appears red because of the large number of red blood cells, which get their colour from the haemoglobin. The percentage of whole blood volume that is made up of red blood cells is called the haematocrit and is a common measure of red blood cell levels (ASH, 2015).

White Blood Cells

(also called leukocytes) White blood cells protect the body from infection. They are much fewer in number than red blood cells, accounting for about 1% of your blood.

The most common type of white blood cell is the neutrophil, which is the "immediate response" cell and accounts for 55–70% of the total white blood cell count. Each neutrophil lives less than a day, so your bone marrow must constantly make new neutrophils to maintain protection against infection. Transfusion of neutrophils is generally not effective since they do not remain in the body for very long.

The other major type of white blood cell is a lymphocyte. There are two main populations of these cells. T-lymphocytes help regulate the function of other immune cells and directly attack various infected cells and tumours. B-lymphocytes make antibodies, which are proteins that specifically target bacteria, viruses, and other foreign materials (ASH, 2015).

Platelets

(also called thrombocytes) Unlike red and white blood cells, platelets are not actually cells but rather small fragments of cells. Platelets help the blood clotting process (or coagulation) by gathering at the site of an injury, sticking to the lining of the injured blood vessel, and forming a platform on which blood coagulation can occur. This results in the formation of a fibrin clot, which covers the wound and prevents blood from leaking out. Fibrin also forms the initial scaffolding upon which new tissue forms, thus promoting healing.

A higher than normal number of platelets can cause unnecessary clotting, which can lead to strokes and heart attacks; however, thanks to advances made in antiplatelet therapies, there are treatments available to help prevent these potentially fatal events. Conversely, lower than normal counts can lead to extensive bleeding (ASH, 2015).

Abnormal platelet levels may be a sign of a bleeding disorder (not enough clotting) or a thrombotic disorder (too much clotting) (nhlbi, 2012a).

There are many different types of tests and procedures to analyse the various substances in blood. The right preparation for your donated blood depends on what is being tested.

Preparing for Your Blood Test

While some tests do not need any special preparation, other blood tests require fasting for 12 hours before your blood donation. A blood sample from a fasting state better represents your natural, baseline blood levels. Substances from food temporarily change your blood levels and can interfere with analyses (quest, 2015a), so a sample taken in a non-fasting state may render misleading results.

Exercise also alters your blood levels, so you shouldn't take part in any exercise or unusual physical activity during the 24 hours before the donation unless you are specifically testing how this activity affects you.

Blood Test Preparation

We recommend drinking a lot of water during the 24 hours before your test as this will help the blood to flow more freely during the blood donation.

Out of the 5 litres of blood in your body, even 3–5 full vials are a safe quantity and unsubstantial, so don't worry! This ensures that enough samples are available for back-up in case some samples are compromised. It also allows for any confirmatory tests that may be needed after the initial tests.

Preparing Blood for Analyses

Your blood samples must be handled very precisely to maintain their integrity and protect the blood analyst from any possible infection. Lab technicians and everyone else who handle the samples follow specific guidelines to avoid contaminating the samples, keep cells alive, and prevent too much from changing, which happens naturally the longer the blood is removed from its host. There's even a method to proper labeling so your blood samples are tracked securely while keeping your personal information private.

Proper handling of the blood sample starts with choosing the right test tube to contain it; there are various types of tubes designed for specific types of tests. Tubes are capped with a vacuum seal so, if the cap is punctured with a special needle to collect blood, the pressure effortlessly pushes blood into the needle without risking contamination.

Blood collection tubes

For certain tests, it is important that blood does not clot. In these cases, the samples go in test tubes lined with Ethylenediaminetetraacetic acid (EDTA), a chemical that prevents clotting.

Blood samples also need to be kept at the right temperature, which will vary according to what is being tested. Storage temperature usually ranges between room temperature (15 - 30'C), refrigerated (2 to 10'C), or frozen (-20'C or colder) (quest, 2015a).

Specific components of the blood may need to be isolated for certain tests. In these cases, whole blood needs to be separated into its three main components: plasma, white blood cells and platelets, and red blood cells. This separation is achieved through centrifugation, the method of separating lighter and denser portions of a mixture by centrifugal force. If the tests call for it, the test tube with your blood sample will be placed in a device called a "centrifuge." This device spins very quickly to separate heavy and lighter components of the blood. After centrifugation, you can see the blood separated into three layers. The lighter components (plasma) naturally end up on top. Specific components of the blood can now be isolated, transferred into another container, and analysed individually.

Transferring blood components is also a delicate process. Biosafety practices have been established to protect blood samples and the people handling them. To prevent contamination, test tubes typically should be opened in a biological safety cabinet (BSC), or biosafety cabinet, an enclosed and ventilated desk space designed for working with materials that have the potential to contaminate or be contaminated with pathogens. There are three types of biosafety cabinets for different types of tests. Air circulates in these cabinets as it flows from the bottom and gets sucked up at the top, so no air can enter or escape. This protects the interior of the cabinet from external contaminators and prevents any pathogens from escaping the cabinet.

A Long Journey

Once the blood samples have been centrifuged and transferred to a proper container, as needed, they are transported to a lab for analysis. As you can imagine, the commute will possibly expose blood samples to all sorts of bumps, shocks, and temperature fluctuations, so proper packaging is essential to keep the blood samples secure.

Packaging blood samples for transport may involve details like using the right containers, tight caps and lids, special transport bags and boxes, and proper labels and seals. Frozen samples should be transported in plastic screw-cap containers only, and will be shipped with ice to remain frozen until they reach the laboratory (quest, 2015a). This is important because analysis cannot be done on thawed samples. Dry ice is used for longer distances.

I've known some blood has been carried by motorbike riders who can generally get to a hospital quicker than a van, but obviously they are limited in what they can carry on their bike.

Analysing Blood

Different tests are designed to analyse various components of your blood and assess certain aspects of your health. Whole blood is used to count red blood cells, while plasma is separated from blood cells by centrifugation to undergo other tests (nhlbi, 2012b). Some tests require serum, which is what remains in place of plasma after blood clots so no clotting factors are present. Blood is left to clot for sixty minutes and then centrifuged for 15 minutes to separate the serum (quest, 2015b).

Blood analysis method

Plasma is more commonly used for tests because its components are believed to better reflect a patient's pathological situation than those in serum (hset, 2012). For these analyses, test tubes are lined with the chemical anticoagulant EDTA to prevent clotting.

Now What?

Blood test results are generally available in three to seven days, depending on which markers are being tested. If you had a standard blood test at your doctor's and no signs of disease were found, then there are no next steps.

Blood groups

There are four main blood groups (types of blood) - A, B, AB and O. Your blood group is determined by the genes you inherit from your parents.

Each group can be either RhD positive or RhD negative, which means your blood group can be one of the eight types shown below -

Antigens and antibodies

Your blood group is identified by antigens and antibodies in the blood. Antibodies are part of your body's natural defences against invading substances such as germs.

Antigens are protein molecules found on the surface of red blood cells. Antibodies are proteins found in plasma. Antibodies recognise anything foreign in your body and alert your immune system to destroy it.

The ABO system

There are four main blood groups defined by the ABO system -

blood group A - has A antigens on the red blood cells with anti-B antibodies in the plasma,
blood group B - has B antigens with anti-A antibodies in the plasma,
blood group O - has no antigens, but both anti-A and anti-B antibodies in the plasma,
blood group AB - has both A and B antigens, but no antibodies,

Almost half (48%) of the UK population has blood group O, making this the most common blood group.

Receiving blood from the wrong ABO group can be life threatening. For example, the anti-A antibodies in a recipient with group B blood will attack the group A cells if transfused to them. This is why group A blood must never be given to a group B person.

As group O red blood cells don't have any A or B antigens, it can safely be given to any other group.

The Rh system

Red blood cells sometimes have another antigen, a protein known as the RhD antigen. If this is present, your blood group is RhD positive. If it's absent, your blood group is RhD negative. This means you can be one of eight blood groups -

- A RhD positive (A+),
- A RhD negative (A-),
- B RhD positive (B+),
- B RhD negative (B-),
- O RhD positive (O+),
- O RhD negative (O-),
- AB RhD positive (AB+),
- AB RhD negative (AB-).

About 85% of the UK population is RhD positive (36% of the population has O+, the most common type).

In most cases, O RhD negative blood (O-) can safely be given to anyone. It's often used in medical emergencies when the blood type isn't immediately known. It's safe for most users because it doesn't have any A, B or RhD antigens on the surface of the cells, and is compatible with every other ABO and RhD blood group.

Reference ranges

The normal values listed here - called a reference range - are just a guide. These ranges vary from lab to lab, and your lab may have a different range for what's normal. Your lab report should contain the range your lab uses. Also, your doctor will evaluate your results based on your health and other factors. This means that a value that falls outside the normal values listed here may still be normal for you or your lab.

But what are they testing for? Following are the reference ranges for (in alphabetical order) -

- Alkaline phosphate - ALP,
- Bilirubin,
- Blood Glucose,
- Low-density lipoprotein - LDL,
- High-density lipoprotein - HDL,
- Dehydroepiandrosterone sulphate - DHEAS,
- Dihydrotestosterone - DHT,
- Follicle stimulating hormone - FSH,
- Liver function tests,
- Luteinizing hormone - LH,
- Oestrogen,
- Prolactin - PRL
- Sex hormone binding globulin - SHBG,
- Testosterone,
- Thyroxine, free - T4.

Alkaline phosphate - ALP

	Male	Female
≥20 Years	40–115 U/L	
20–49 Years		33–115 U/L
≥50 Years		33–130 U/L (quest, 2016)
17–23 years		52–144 U/L
18 years	52–222 U/L	

	Male	Female
> 18 years	39–117 IU/L	39–117 IU/L (labcorp, 2016b)
> or = 19 years	45–115 U/L	
24–45 years		37–98 U/L
46–50 years		39–100 U/L
51–55 years		41–108 U/L
56–60 years		46–118 U/L
61–65 years		50–130 U/L
> or = 66 years		55–142 U/L (mayomedical, 2015)
	Conventional units	**SI units**
	36–92 U/L	0.5–1.5 μkat/L (merck, 2015)
	25–100 U/L	0.43–1.70 mckat/L (WebMD, 2014b)

Table 13.1 – Reference ranges for Alkaline Phosphate - ALP

An Alkaline phosphate (ALP) test measures the amount of the enzyme[79] ALP in the blood. ALP is made mostly in the liver and in bone with some made in the intestines and kidneys.

Normal alkaline phosphate levels

Normal values may vary slightly from laboratory to laboratory. They also can vary with age and gender. High levels of ALP are normally seen in children undergoing growth spurts and in pregnant women (medlineplus, 2015a).

Low alkaline phosphate levels

- Hypophosphatasia[80],
- Malnutrition,

[79] An enzyme is a protein produced by the body to speed up a specific chemical reaction in the body. The body produces many different kinds of enzymes for many different body processes, such as digestion and blood clotting. Some inherited diseases are caused by problems with the production of certain enzymes. Doctors may measure the levels of certain enzymes in a person's blood to help diagnose certain types of disease, such as liver problems

[80] This is an inherited disorder that affects the development of bones and teeth

- Protein deficiency,
- Wilson disease (medlineplus, 2015a).

Some drugs (clofibrate, azathioprine, oestrogens and oestrogens in combination with androgens) lower serum ALP activity (labcorp, 2016b).

High alkaline phosphate levels

- Biliary obstruction,
- Bone conditions,
- Osteoblastic bone tumours, osteomalacia, a fracture that is healing,
- Liver disease or hepatitis,
- Eating a fatty meal if you have blood type O or A [81],
- Gilbert syndrome - increase in intestinal alkaline phosphatase is seen (Butch et al., 1989),
- Hyperparathyroidism,
- Hypervitaminosis D, (labcorp, 2016b),
- Leukemia,
- Lymphoma,
- Paget disease,
- Rickets,
- Sarcoidosis, (medlineplus, 2015a).

Drugs - oestrogens (large doses), birth control agents, methyltestosterone, phenothiazines, oral hypoglycaemic agents, erythromycin, or any drug producing hypersensitivity or toxic cholestasis. Many commonly and uncommonly used drugs elevate alkaline phosphatase, and tenfold increases may be seen with drug cholestasis (labcorp, 2016b).

Bilirubin

Test	Conventional units	SI units
	$\leq$0.2 mg/dL	(quest, 2016)
	0.0–1.2 mg/dL	(labcorp, 2016b)
Direct	0–0.3 mg/dL	0–5.1 μmol/L
Total	0.3–1.2 mg/dL	5.1–20.5 μmol/L (merck, 2015)

Table 13.2 – Reference ranges for Bilirubin

[81] Serum ALP activity of intestinal origin occurs only in individuals of ABO blood type O or A. They are secretors of ABH RBC antigens and also carry the Lewis red cell antigen. Serum intestinal ALP level increases in these individuals about two hours following consumption of a fatty meal (labcorp, 2016b)

High bilirubin levels

Liver disease - hepatitis, cholangitis, cirrhosis, other types of liver disease (including primary or secondary neoplasia),

alcoholism - (usually with high AST (SGOT), Gamma glutamyl transpeptidase (GGT), molluscum contagiosum virus (MCV), or some combination of these findings),

biliary obstruction - (intrahepatic or extrahepatic),

infectious mononucleosis - (look also for increased LD (LDH), lymphocytosis),

Gilbert disease - (familial hyperbilirubinemia) is encountered as a moderate elevation with otherwise unremarkable chemistries (Ohkubo and Okuda, 1984).

Nicotinic acid increases the formation of bilirubin in the spleen, leading to a rise in unconjugated bilirubin. This can be used as a test for Gilbert disease (Ohkubo and Okuda, 1984) in which there is a decreased hepatic clearance of unconjugated bilirubin. Although the indirect bilirubin level is increased in normal controls when nicotinic acid is given, the increase is much greater in patients with Gilbert disease (Ohkubo and Okuda, 1984).

Blood Glucose

This table shows the ranges for blood glucose levels after 8 to 12 hours of fasting (not eating). It shows the normal range and the abnormal ranges that are a sign of prediabetes or diabetes.

	Results
Normal	70–99 mg/dL
Prediabetes	100–125 mg/dL
Diabetes [82]	126 mg/dL and above (nhlbi, 2012d)

Table 13.3 – Glucose reference ranges

[82] The test is repeated on another day to confirm the results

Cholesterol

Cholesterol is a waxy substance that comes from two sources - your body and food. Your body, and especially your liver, makes all the cholesterol you need and circulates it through the blood. But cholesterol is also found in foods from animal sources, such as meat, poultry and full-fat dairy products. Your liver produces more cholesterol when you eat a diet high in saturated and trans fats (heart.org, 2014)

Excess cholesterol can form plaque between layers of artery walls, making it harder for your heart to circulate blood. Plaque can break open and cause blood clots. If a clot blocks an artery that feeds the brain, it causes a stroke. If it blocks an artery that feeds the heart, it causes a heart attack.

There are two types of cholesterol: "good" and "bad." Too much of one type - or not enough of another - can put you at risk for coronary heart disease, heart attack or stroke. It's important to know the levels of cholesterol in your blood so that you and your doctor can determine the best strategy to lower your risk.

Making healthy eating choices and increasing exercise are important first steps in improving your cholesterol. For some people, cholesterol-lowering medication may also be needed to reduce the risk for heart attack and stroke.

Cholesterol can't dissolve in the blood. It must be transported through your bloodstream by carriers called lipoproteins, which got their name because theyre made of fat (lipid) and proteins.

The two types of lipoproteins that carry cholesterol to and from cells are LDL, and HDL. LDL cholesterol and HDL cholesterol, along with one fifth of your triglyceride level, make up your total cholesterol count, which can be determined through a blood test. See LDL (Bad) Cholesterol and also HDL (Good) Cholesterol.

LDL (Bad) Cholesterol

LDL cholesterol is considered the "bad" cholesterol because it contributes to plaque, a thick, hard deposit that can clog arteries and make them less flexible. This condition is known as atherosclerosis. If a clot forms and blocks a narrowed artery, heart attack or stroke can result. Another condition called peripheral artery disease can develop when plaque buildup narrows an artery supplying blood to the legs (heart.org, 2014).

HDL (Good) Cholesterol

HDL cholesterol is considered "good" cholesterol because it helps remove LDL cholesterol from the arteries. Experts believe HDL acts as a scavenger, carrying LDL cholesterol away from the arteries and back to the liver, where it is broken down and passed from the body. One-fourth to one-third of blood cholesterol is carried by HDL. A healthy level of HDL cholesterol may also protect against heart attack and stroke, while low levels of HDL cholesterol have been shown to increase the risk of heart disease (heart.org, 2014).

Triglycerides

Triglycerides are another type of fat, and they're used to store excess energy from your diet. High levels of triglycerides in the blood are associated with atherosclerosis. Elevated triglycerides can be caused by overweight and obesity, physical inactivity, cigarette smoking, excess alcohol consumption and a diet very high in carbohydrates (more than 60% of total calories). Underlying diseases or genetic disorders are sometimes the cause of high triglycerides. People with high triglycerides often have a high total cholesterol level, including a high LDL cholesterol (bad) level and a low HDL cholesterol (good) level. Many people with heart disease or diabetes also have high triglyceride levels (heart.org, 2014).

Reference	Total cholesterol
Desirable	< 200 (nhlbi, 2001)
Desirable	200 mg/dL (healthcare.uiowa, 2015)
Borderline high	200–239 (nhlbi, 2001)
Increased risk	200–240 mg/dL (healthcare.uiowa, 2015)
High, greater than or equal to	240 (nhlbi, 2001)
Significant increased risk	> 240 mg/dL (healthcare.uiowa, 2015)

Table 13.4 – Reference ranges for cholesterol

Results

Keeping your cholesterol levels healthy is a great way to keep your heart healthy - and lower your chances of getting heart disease or having a stroke.

But first, you have to know your cholesterol numbers.

The American Heart Association recommends all adults age 20 or older have their cholesterol, and other traditional risk factors, checked every four to six years.

Your test report will show your cholesterol levels in milligrams per deciliter of blood (mg/dL). Your total cholesterol and HDL (good) cholesterol are among numerous factors your doctor can use to predict your lifetime or 10-year risk for a heart attack or stroke.

Your test report will show your cholesterol levels in milligrams per deciliter of blood (mg/dL). To determine how your cholesterol levels affect your risk of heart disease, your doctor will also take into account other risk factors such as age, family history, smoking and high blood pressure (heart.org, 2014).

A complete fasting lipoprotein profile will show the following for -

Total blood (or serum) cholesterol - Your total cholesterol score is calculated using the following equation: HDL + LDL + 20 percent of your triglyceride level.

HDL (good) cholesterol - With HDL cholesterol, higher levels are better. Low HDL cholesterol puts you at higher risk for heart disease. People with high blood triglycerides usually also have lower HDL cholesterol. Genetic factors, type 2 diabetes, smoking, being overweight and being sedentary can all result in lower HDL cholesterol.

LDL (bad) cholesterol - A low LDL cholesterol level is considered good for your heart health. However, your LDL number should no longer be the main factor in guiding treatment to prevent heart attack and stroke, according to new guidelines from the American Heart Association. For patients taking statins, the guidelines say they no longer need to get LDL cholesterol levels down to a specific target number. A diet high in saturated and trans fats raises LDL cholesterol.

Triglycerides - Triglyceride is the most common type of fat in the body. Normal triglyceride levels vary by age and sex. A high triglyceride level combined with low HDL cholesterol or high LDL cholesterol is associated with atherosclerosis, the buildup of fatty deposits in artery walls that increases the risk for heart attack and stroke (heart.org, 2014).

Cholesterol and lifestyle

Your body needs cholesterol to work well. But cholesterol levels that are too high can harm you.

Cholesterol is measured in milligrams per deciliter (mg/dL). Extra cholesterol in your blood builds up inside the walls of your blood vessels. This buildup is called plaque, or atherosclerosis. Plaque reduces or stops blood flow. This can cause a -

- Heart attack,

- Stroke,
- Serious heart or blood vessel disease,
- Your cholesterol numbers (medlineplus, 2014a).

All men should have their blood cholesterol levels tested every 5 years, starting at age 35. All women should do the same, starting at age 45. Many people should have their blood cholesterol levels tested at a younger age, possibly as early as age 20, if they have risk factors for heart disease. Have your cholesterol checked more often (probably every year) if you have -

- Diabetes,
- Heart disease,
- Blood flow problems to your feet or legs,
- A history of stroke (medlineplus, 2014a).

A blood cholesterol test measures the level of total cholesterol. This includes HDL (good) cholesterol and LDL (bad) cholesterol.

Your LDL level is what doctors watch most closely. You want it to be low. If it gets too high, you will need to treat it.

Treatment includes -

- Eating a healthy diet,
- Losing weight (if you are overweight),
- Exercising,
- You may also need medicine to lower your cholesterol.

You want your HDL cholesterol to be high. Exercise can help raise it (medlineplus, 2014a).

Eating right

It is important to eat right, keep a healthy weight, and exercise, even if -

- You do not have heart disease or diabetes,
- Your cholesterol levels are in the normal range (medlineplus, 2014a).

These healthy habits may help prevent future heart attacks and other health problems.

Eat foods that are low in fat. These include whole grains, fruits, and vegetables. Using low-fat toppings, sauces, and dressings will help.

Look at food labels. Avoid foods that are high in saturated fat. Eating too much of this type of fat can lead to heart disease (medlineplus, 2014a).

- Choose lean protein foods, such as soy, fish, skinless chicken, very lean meat, and fat-free or 1% dairy products.
- Look for the words "hydrogenated", "partially hydrogenated", and "trans fats" on food labels. DO NOT eat foods with these words in the ingredients lists.
- Limit how much fried food you eat.

- Limit how many prepared baked goods (donuts, cookies, and crackers) you eat. They may contain a lot of fats that are not healthy.
- Eat fewer egg yolks, hard cheeses, whole milk, cream, ice cream, and butter.
- Eat less fatty meat and smaller portions of meat, in general.
- Use healthy ways to cook fish, chicken, and lean meats, such as broiling, grilling, poaching, and baking.
- Eat foods that are high in fibre. Good fibres to eat are oats, bran, split peas and lentils, beans (kidney, black, and navy beans), some cereals, and brown rice (medlineplus, 2014a).

Learn how to shop for, and cook, foods that are healthy for your heart. Learn how to read food labels to choose healthy foods. Stay away from fast foods, where healthy choices can be hard to find.

Get plenty of exercise. And talk with your doctor about what kinds of exercises are best for you (medlineplus, 2014a).

Dehydroepiandrosterone sulphate - DHEAS

	Male	Female
22–30 years	85–690 mcg/dL	18–391 mcg/dL (quest, 2016)
31–40 years	106–464 mcg/dL	23–266 mcg/dL (quest, 2016)
41–50 years	70–495 mcg/dL	19–231 mcg/dL (quest, 2016)
20–24 years	164.3–530.5 µg/dL	110.0–431.7 µg/dL (labcorp, 2016b)
20–40 years		0.7–11.5 mol/l (College, 2010)
25–34 years	138.5–475.2 µg/dL	84.8–378.0 µg/dL (labcorp, 2016b)
31–50 years	3.4–16.7	(Eaton, 2014)
35–44 years	102.6–416.3 µg/dL	57.3–279.2 µg/dL (labcorp, 2016b)
45–54 years	71.6–375.4 µg/dL	41.2–243.7 µg/dL (labcorp, 2016b)
40–60 years		0.8–6.9 mol/l (College, 2010)
51–60 years	38–313 mcg/dL	8–188 mcg/dL (quest, 2016)

	Male	Female
55–64 years	48.9–344.2 μg/dL	29.4–220.5 μg/dL (labcorp, 2016b)
20–50 years		0.7–11.5 (Eaton, 2014)
> 60 years		0.4–4.7 mol/l (College, 2010)
61–70 years	24–244 mcg/dL	12–133 mcg/dL (quest, 2016)
65–74 years	30.9–295.6 μg/dL	20.4–186.6 μg/dL (labcorp, 2016b)
$\geq$ 71 years	5–253 mcg/dL	7–177 mcg/dL (quest, 2016)
$\geq$ 75 years	20.8–226.4 μg/dL	13.9–142.8 μg/dL (labcorp, 2016b)
post-menopausal		0.5–5.6 (Eaton, 2014)

Table 13.5 – Reference ranges of dehydroepiandrosterone sulphate - DHEAS

DHEA-S is a steroid hormone which is produced from the precursor cholesterol in the zona reticularis and broad fascia of the adrenal cortex (Gronowski and Landau-Levine, 1999). The determination of elevated DHEA-S values is an important aid in the diagnosis of hirsutism and virilism (Goldfien and Monroe, 1994), (Hatch et al., 1981). DHEA-S exhibits only a weak androgenic activity but can be metabolized to more active androgens, such as androstenedione and testosterone, which can indirectly cause hirsutism and virilism (Goldfien and Monroe, 1994), (Mooradian, Morley, and Korenman, 1987).

The rate of secretion of DHEA-S into the blood stream is only slightly more than the rate observed for DHEA. As a consequence of the DHEA-S half-life of approximately one day, the DHEA-S level is, however, about a thousand-fold greater (Haning, 1981). DHEA-S is relatively strongly bound to albumin, only a small portion is nonprotein bound, and none appears to be bound to sex hormone-binding globulin (SHBG) (Longcope, 1996). Due to its high concentration and low inter- and intra-day variability, DHEA-S is an excellent indicator of adrenal cortex androgen production (Haning, 1981), (Lobo, Paul, and Goebelsmann, 1981).

Together with testosterone, DHEA-S assays represent the assay of choice for initial screening tests to determine whether androgen values are elevated in hirsutism.

Dehydroepiandrosterone (DHEA) is the principal human C-19 steroid. DHEA has very low androgenic potency, but serves as the major direct or indirect precursor for most sex steroids. DHEA is secreted by the adrenal gland and production is at least partly controlled by adrenocorticotropic hormone. The bulk of DHEA is secreted as a 3-sulfoconjugate (DHEA-S). Both hormones are albumin bound, but binding of DHEA-S is much tighter. In gonads and several other tissues, most notably skin, steroid sulphatases can convert DHEA-S back to DHEA, which can then be metabolized to stronger androgens and to oestrogens.

During pregnancy, DHEA-S and its 16-hydroxylated metabolites are secreted by the foetal adrenal gland in large quantities. They serve as precursors for placental production of the dominant pregnancy oestrogen, estriol. Within weeks after birth, DHEA-S levels fall by 80% or more and remain low until the onset of adrenarche[83]. Adrenarche is a poorly understood phenomenon peculiar to higher primates, which is characterised by a gradual rise in adrenal androgen production. It precedes puberty but is not causally linked to it. Early adrenarche is not associated with early puberty or with any reduction in final height or overt androgenization and is generally regarded as a benign condition, not needing intervention. However, girls with early adrenarche may be at increased risk of polycystic ovarian syndrome as adults, and some boys may develop early penile enlargement.

Following adrenarche, DHEA-S levels increase until the age of 20 to a maximum level roughly comparable to that observed at birth. Levels then decline over the next 40 to 60 years to around 20% of peak levels. The clinical significance of this age-related drop is unknown and trials of DHEA-S replacement in the elderly have not produced convincing benefits. However, in young and old patients with primary adrenal failure, the addition of DHEA-S to corticosteroid replacement has been shown in some studies to improve mood, energy, and sex drive.

Elevated DHEA-S levels can cause symptoms or signs of hyperandrogenism in women. Men are usually asymptomatic, but through peripheral conversion of androgens to oestrogens can occasionally experience mild oestrogen excess. Most mild to moderate elevations in DHEA-S levels are idiopathic [84]. However, pronounced elevations of DHEA-S may be indicative of androgen-producing adrenal tumours. In small children, congenital adrenal hyperplasia (CAH) due to 3 beta-hydroxysteroid deficiency is associated with excessive DHEA-S production. Lesser

[83] Adrenarche is known to be an ordinary bodily process that happens to boys and girls as they begin to make the transition to being a teenager. It is a development that happens before puberty, usually between the ages of 6 and 8. During this time certain hormones (biological messengers) begin to increase and may either go unnoticed or can cause changes in the body like new hair growth (Leach, 2013)

[84] of unknown cause (Dictionary.com, 2014)

elevations may be observed in 21-hydroxylase deficiency (the most common form of CAH) and 11 beta-hydroxylase deficiency. By contrast, steroidogenic acute regulatory protein or 17 alpha-hydroxylase deficiencies are characterized by low DHEA-S levels.

An initial panel in adults might also include total and bioavailable testosterone (TTBS / Testosterone, Total and Bioavailable, Serum) measurements. Depending on results, this may be supplemented with measurements of sex hormone-binding globulin (SHBG / Sex Hormone-Binding Globulin [SHBG], Serum) and, occasionally other androgenic steroids (eg, 17-hydroxyprogesterone) (Medical, 2014).

Dihydrotestosterone - DHT

Dihydrotestosterone measurement is used to diagnose 5α-reductase deficiency and for the evaluation of androgen utilization. Dihydrotestosterone is produced by the reduction of testosterone by 5α-reductase in the target organs. Circulating dihydrotestosterone is tightly bound to sex hormone-binding globulin. The free fraction represents the dihydrotestosterone available to act on tissues (labcorp, 2016a).

Low levels of DHT indicate general androgen deficiency or poor 5α-reductase activity. Low levels of testosterone, DHEA and androstenedione can be causative factors of reduced DHT levels. This may result in diminished sex drive and poor muscle tone (gdx, 2008).

This is a more potent form of testosterone that is metabolized by the body from other androgens. In men most is made from testosterone, while in women the main source is androstenedione (which is first converted INTO testosterone). Current research indicates that DHT is responsible for male-pattern balding and excessive, unwanted hair in both sexes. In males it is also responsible for non-cancerous prostate swelling (BPH).

The principal prostatic androgen is dihydrotestosterone (DHT). Levels of DHT remain normal with aging, despite a decrease in the plasma testosterone, and are not elevated in benign prostatic hyperplasia (BPH) (S, Levine, and Chow, 1979).

DHT is generated by reduction of testosterone by 5α-reductase. Two isoenzymes of 5α-reductase have been discovered. Type 1 is present in most tissues in the body where 5α-reductase is expressed, and is the dominant form in sebaceous glands. Type 2 is the dominant isoenzyme in genital tissues, including the prostate.

DHT should serve as the primary marker of peripheral androgen production. However, because it is metabolised rapidly and has a very high affinity for sex hormone-binding globulin (SHBG), DHT does not reflect peripheral androgen action. Instead, its distal metabolite, 3α, 17β-androstanediol glucuronide, serves as a better marker of peripheral androgen action (mayomedical, 2016).

Gender	Reference Range
Females	0.4–1.5 nmol/L (Director, 2013)
Female	3.0–28.0 ng/dL (gdx, 2008)
20–55 years	< or = 300 pg/mL (mayomedical, 2016)
> 55 years	< or = 128 pg/mL (mayomedical, 2016)
- Premenopausal	24–368 pg/mL (hemingways, 2004b)
- Premenopausal	80–1270 pmol/L (Eaton, 2014)
- Postmenopausal	10–181 pg/mL (hemingways, 2004b)
- Postmenopausal	30–620 pmol/L (Eaton, 2014)
Males	1.3–2.5 nmol/L (Director, 2013)
Males	29.0–90.0 ng/dL (gdx, 2008)
Males	860–3400 pmol/L (Eaton, 2014)
Males	250–990 pg/mL (hemingways, 2004b)
> 19 years	112–955 pg/mL (mayomedical, 2016)

Table 13.6 – Reference ranges for dihydrotestosterone - DHT

Follicle stimulating hormone - FSH

Test	Conventional Units	SI Units
FSH - adult females		
Follicular or luteal phase	5–20 mU/mL	5–20 U/l (**0368**)

Test	Conventional Units	SI Units
Follicular phase		2.5–10.2 mIU/ml (quest, 2016)
"		1.5–10.0 U/l (College, 2010)
"		3.1–8.1 IU/L (Director, 2013)
"		3.5–12.5 IU/L (Dr. Lamb, 2014)
"		3.5–12.5 iu/mL (Eaton, 2014)
"		3.5–12.5 mIU/mL (labcorp, 2016b)
Luteal phase		1.5–9.1 mIU/ml (quest, 2016)
"		1.5–8.0 U/l (College, 2010)
"		1.0–5.5 IU/L (Director, 2013)
"		1.7–7.7 IU/L (Dr. Lamb, 2014)
"		1.7–7.7 iu/mL (Eaton, 2014)
"		1.7–7.7 mIU/mL (labcorp, 2016b)
Midcycle peak	30–50 mU/mL	30–50 U/l (merck, 2015)
"		3.1–17.7 mIU/ml (quest, 2016)
"		7.0–20.0 U/l (College, 2010)
"		2.6–16.7 IU/L (Director, 2013)
"		4.7–21.5 IU/L (Dr. Lamb, 2014)
"		4.7–21.5 iu/mL (Eaton, 2014)
"		4.7–21.5 mIU/mL (labcorp, 2016b)
Postmenopausal	> 35 mU/mL	> 35 U/l (merck, 2015)
"		23.0–116.3 mIU/ml (quest, 2016)
"		>20 U/l (College, 2010)

Test	Conventional Units	SI Units
"		> 27 IU/L (Director, 2013)
"		25.8–34.8 IU/L (Dr. Lamb, 2014)
"		25.8–134.8 iu/mL (Eaton, 2014)
"		25.8–134.8 mIU/mL (labcorp, 2016b)
FSH - adult males		
	5–15 mU/mL	5–15 U/l (merck, 2015)
		1.6–8.0 mIU/ml (quest, 2016)
		1.7–8.0 U/l (College, 2010)
		1.0–12.0 IU/L (Director, 2013)
		1.5–12.4 IU/L (Dr. Lamb, 2014)
		1.5–12.0 iu/mL (Eaton, 2014)
		1.5–12.4 mIU/mL (labcorp, 2016b)

Table 13.7 – Reference ranges of follicle stimulating hormone

FSH together with **??**, belongs to the gonadotropin family. FSH and LH regulate and stimulate the growth and function of the gonads (ovaries and testes) synergistically (M. R. Johnson et al., 1993).

FSH and LH are released in pulses from the gonadotropic cells of the anterior pituitary. The levels of the circulating hormones are controlled by steroid hormones via negative feedback to the hypothalamus. In the ovaries, FSH, together with LH, stimulates the growth and maturation of the follicle and hence also the biosynthesis of oestrogens in the follicles.

In women, the gonadotropins act within the hypothalamus-pituitary-ovary regulating circuit to control the menstrual cycle (Runnebaum and Rabe, 1994), (Beastall et al., 1987). The FSH level shows a peak at midcycle, although this is less marked than with LH. Due to changes in ovarian function and reduced estrogen secretion, high FSH concentrations occur during menopause (Runnebaum and Rabe, 1994). The determination of FSH in conjunction with LH is utilised for the following indications - congenital diseases with chromosome aberrations, polycystic ovaries (PCO), amenorrhea (causes), and menopausal syndrome.

In men, FSH serves to induce spermatogonium development. Determination of the FSH concentration is used in the elucidation of dysfunctions within the hypothalamus-pituitary-gonads system. Depressed gonadotropin levels in men occur in azoospermia (Runnebaum and Rabe, 1994), (M. R. Johnson et al., 1993), (Schmidt-Mathiesen, 1992), (Scott et al., 1989).

High-density lipoprotein - HDL

HDL cholesterol is used in the assessment of coronary or other vascular pathology risk (medscape, 2014b).

Instructions

You should fast at least 12–14 hours before the blood is taken (medscape, 2014b).

Gender	Ranges
Males	> 55 mg/dL
Females	> 65 mg/dL

Table 13.8 – Reference ranges for high-density lipoprotein

Interpretation

Increased levels

High-density lipoprotein cholesterol (High-density lipoprotein cholesterol (HDL-C)) levels are increased in the following conditions -

- Hyperalphalipoproteinemia,
- Regular physical activity or exercise,
- Chronic liver disease,
- Weight loss (Williamson, Snyder, and Wallach, 2011).

HDL-C levels are increased in association with moderate ethanol consumption, insulin, and oestrogen (Williamson, Snyder, and Wallach, 2011). Additionally, regular aerobic exercise, smoking cessation, decrease in body mass index, and statin therapy (mild) increase HDL-C levels. Statins or HMG-CoA reductase inhibitors modestly increase HDL-C levels. The mild rise in HDL-C levels from these drugs may be related to inhibition of rho-

signaling pathways with activation of peroxisome proliferator-activated receptor (PPAR)alpha. Increases in HDL-C levels may also be attributable to decreasing plasma cholesteryl ester transfer protein (CETP) activity by statins (Rader, 2012).

Decreased levels

HDL-C levels are decreased in the following conditions -

- Obesity,
- Uncontrolled diabetes mellitus,
- Hepatocellular disease,
- Cholestasis,
- Chronic renal failure,
- Metabolic syndrome (insulin resistance, hypertriglyceridemia),
- Malnutrition,
- Sedentary lifestyle,
- Cigarette smoking,
- Familial abetalipoproteinemia,
- Beta-blocker therapy (short-term effect) (Williamson, Snyder, and Wallach, 2011).

HDL-C levels are decreased in association with recent illness; starvation and stress; smoking; obesity and lack of exercise; medications such as thiazide diuretics, steroids, and beta-blockers; hypertriglyceridemia; and in elevated immunoglobin levels (medscape, 2014b).

Background

HDL-C, which consists mostly of cholesterol, phospholipid, and protein, is produced and secreted by the liver and intestine (Botham, 2009).

HDL-C transports cholesterol from tissues to the liver. In this reverse cholesterol transport process, it performs a "clean-up" function. This process is called reverse cholesterol transport because cholesterol synthesized in peripheral tissues is eventually returned to the liver for its disposal from the body.

HDL-Cs have many surface proteins. Apo-A1 and apo-A2 proteins on HDL-C are derived by direct secretion from the liver (L. et al., 2008). ApoA-I synthesis is necessary to produce HDL-C. Mutations in the apoA-I gene that cause HDL-C deficiency are associated with accelerated atherogenesis. Overexpression of apoA-I in the mouse model protects against experimentally induced atherogenesis (Tp, 2011). Additionally, HDL-C may protect against atherogenesis by mechanisms not directly

related to reverse cholesterol transport. These functions include putative anti-inflammatory, anticoagulant, antioxidative, platelet anti-aggregatory, and profibrinolytic activities (E. M. deGoma, R. L. deGoma, and Rader, 2008).

High levels of HDL-C are desirable because of their inverse relation with coronary risk. HDL-C is called good cholesterol because it is inversely related with the incidence of atherosclerosis (medscape, 2014b).

Low-density lipoprotein - LDL

The standard lipid profile, as recommended by the Adult Treatment Panel III (ATP III), consists of direct measurement of total cholesterol, HDL-C, and triglycerides, with a calculated Low-density lipoprotein cholesterol (LDL-C) (medscape, 2014c).

Instructions

You should fast at least 9–12 hours before the blood is taken (medscape, 2014c).

Status	Ranges
Normal	< 100 mg/dL (healthcare.uiowa, 2012)
Optimal	< 100 mg/dL (nhlbi, 2001)
Above normal	100–129 mg/dL (healthcare.uiowa, 2012)
Near optimal/Above optimal	100–129 mg/dL (nhlbi, 2001)
Borderline high	130–159 mg/dL (healthcare.uiowa, 2012)
Borderline high	130–159 mg/dL (nhlbi, 2001)
High	160–189 mg/dL (healthcare.uiowa, 2012)
High	160–189 mg/dL (nhlbi, 2001)
Very high	≥ 190 mg/dL (healthcare.uiowa, 2012)
Very high	≥ 190 mg/dL (nhlbi, 2001)

Table 13.9 – Reference ranges for low-density lipoprotein

Interpretation

LDL-C is one of the major culprits in the development of atherosclerotic heart disease.

Goal LDL (to prevent atherosclerotic plaque formation) is between 50–70 mg/dL. A higher value confers increasing risk for the development of coronary artery disease and needs to be remedied. This is based on The Framingham Heart Study, which was the first study to reveal a positive association between total cholesterol and Coronary artery disease (CAD) (Kannel, 1971).

Achieving the LDL value of less than 100mg/dL is especially important in patients who have other risk factors that will accelerate the development of CAD. These risk factors are cigarette smoking, hypertension, low HDL, and a family history of CAD (medscape, 2014c).

Collection

LDL-C is a calculated value and is part of the lipid profile recommended by the ATP III of the National Cholesterol Education Program (2001).

Blood is drawn after a 9-hour to 12-hour fast. The rationale behind fasting is to eliminate chylomicrons in the blood. If a patient doesn't fast, it can cause an underestimation of the LDL value.

Early morning specimens are preferable. Patients should have been on a stable diet for 3 weeks for the results to be accurate (medscape, 2014c).

Background

About 60–70% of cholesterol in the body is carried as LDL-C in the blood.

The standard lipid profile, as recommended by the ATP III, consists of direct measurement of total cholesterol, HDL-C, and triglycerides, with a calculated LDL-C, obtained after a 9-hour to 12-hour fast. The Friedewald formula used to calculate the LDL level in the blood is as follows:

- LDL = Total cholesterol - HDL - (Triglycerides/5)

Lipoproteins are required for the transportation of cholesterol ,which in turn is required for the biosynthesis of bile acids, steroid hormones, and vitamin D.

Two main sources of cholesterol exist: One is dietary intake and the other is endogenous hepatic production.

Metabolism of ingested cholesterol yields very-low-density lipoprotein (VLDL) and intermediate density lipoprotein (IDL). Further metabolism of the VLDL results in the cholesterol rich LDL, which is the key ingredient for the development of an atherosclerotic plaque (medscape, 2014c).

Indications

This test is indicated to monitor the LDL levels in order to prevent the progression of CAD (medscape, 2014c).

Liver function tests

The liver is a large organ located in the upper right-hand part of the abdomen behind the lower ribs. It takes up drugs and toxic substances from the blood and renders them harmless. It produces proteins, including enzymes and blood clotting factors, helps maintain hormone balance and stores vitamins. The liver produces bile, a fluid that is transported through ducts to the gallbladder to be stored and then to the small intestine to help digest fats (medrevise, 2010).

A liver function test is a blood test that gives an indication of whether the liver is functioning properly. The test is also very useful to see if there is active damage in the liver (hepatitis) or sluggish bile flow (cholestasis).

Liver function tests measure the amount of particular chemicals in the blood. This gives a gauge of possible damage to liver cells - damage that can be caused by many things including HCV. So a more correct term for a liver test would actually be a liver dysfunction test (mydr, 2015).

Liver disease is detected, evaluated and monitored by combinations of up to five tests measured at the same time on a blood sample. These may include -

Alanine Transaminase (ALT) - An enzyme found in liver cells. When liver cells are damaged, they leak this out, so its a marker of liver damage (medrevise, 2010), this is an enzyme produced in hepatocytes (the major type of liver cells). ALT level in the blood is increased when hepatocytes are damaged or die all types of hepatitis (viral, alcoholic, drug-induced etc) cause hepatocyte damage. Levels of ALT may equate to the degree of cell damage but this is not always the case, particularly with hepatitis C. An accurate estimate of liver cell damage can only be made by liver biopsy (mydr, 2015).

Aspartate Transaminase (AST) - Similar to ALT, but less specific to the liver - can go up in heart damage too (medrevise, 2010), an enzyme found in the liver and a few other places, particularly the heart and other muscles in the body, The main use for AST is that when AST and ALT are both raised, and ALT is higher, it points to viral hepatitis. When AST is higher, it points to alcoholic hepatitis (medrevise, 2010), this is similar to ALT above, but less specific for liver disease because it is also produced in body muscle cells. It does tend to be higher than ALT in cases of alcohol-related liver disease (mydr, 2015).

Bilirubin - Bilirubin is a by-product of the breakdown of red blood cells. It is the yellowish pigment responsible for jaundice. Bilirubin levels can be raised due to many different liver diseases, as well as conditions other than liver disease, e.g. gallstones. In cases of long-term liver illness (chronic hepatitis), the level usually stays within the normal range until significant liver damage has occurred and cirrhosis is present. In cases of short-term liver illness (acute hepatitis), elevated bilirubin levels indicate the severity of the acute illness (mydr, 2015).

- **Total bilirubin - TBIL** - measures all the yellow bilirubin pigment in the blood,
- **Direct bilirubin (Conjugated BR)** - amount of conjugated bilirubin, enabling you to work out what type of jaundice is going on, measures the form made only in the liver (medrevise, 2010).

Alkaline phosphate - ALP - is an enzyme found in the ducts of the biliary tree. Thus when there is damage or obstruction in the bile ducts, more of it gets released and goes into the blood. Also goes up in Paget's disease of bone, due to increased bone turnover (medrevise, 2010), this is a family of enzymes produced in the bile ducts, intestine, kidneys, placenta and bones. These levels may rise when disease of the bile ducts or bone disorders occur (mydr, 2015),

Total protein - this is simply a combined measure of the concentrations of proteins in the blood. This information can provide clues to several diagnostic possibilities. There are 2 major types of protein: albumin and globulin (mydr, 2015),

- **Albumin - ALB** - This provides a gauge of nutritional status. It can be reduced due to liver damage and kidney disease. Because albumin is made in the liver, levels tend to drop with cirrhosis (mydr, 2015). It's the main protein in blood, produced by the liver. Low albumin is seen in nephrotic syndrome (where its leaked out) and liver failure (where it's not produced) (medrevise, 2010).
- **Globulin** - This describes the specific level of globulins - which include antibodies. This measure can be raised when liver cells are damaged due to autoimmune liver damage or to long-standing liver disease of many types, particularly when cirrhosis exists (mydr, 2015).

Gamma glutamyl transpeptidase - GGT - mostly used because it is raised in chronic alcohol abuse (medrevise, 2010). This is an enzyme produced in bile ducts that may be elevated due to bile duct illness. The GGT test is extremely sensitive and may be elevated due to any type of liver disease or by different drugs, including alcohol, even when liver disease is minimal. GGT levels are sometimes elevated even in the case of a normally functioning liver (mydr, 2015).

Platelet count - Platelets are the smallest of all blood cells and are involved in promoting clotting of the blood - normally a process of healing. In cases of chronic liver disease where cirrhosis exists, the platelet count can be lowered - although this can occur due to many conditions other than liver disease (mydr, 2015).

Other tests that can help to assess liver function include 5′-nucleotidase (5′-NT) and Prothrombin - PT, together with bilirubin and urobilinogen in urine.

Luteinizing hormone - LH

Analyte	Reference range
Male	
"	1.1–8.8 IU/L (Director, 2013)
"	1.7–8.6 IU/L (Dr. Lamb, 2014)
"	1.7–8.6 IU/mL (Eaton, 2014)
"	2–12 U/L (College, 2010)
"	1.7–8.6 mIU/mL (labcorp, 2016b)
Female	
Follicular	2.4–6.6 IU/L (Director, 2013)
"	2.4–12.6 IU/L (Dr. Lamb, 2014)
"	2.4–12.6 iu/mL (Eaton, 2014)
"	2–10 U/L (College, 2010)
"	2.4–12.6 mIU/mL (labcorp, 2016b)
Ovulatory phase	14.0–95.6 IU/L (Dr. Lamb, 2014)
	9.1–74 IU/L (Director, 2013)
	14.0–95.6 iu/mL (Eaton, 2014)
	20–60 U/L (College, 2010)
	14.0–95.6 mIU/mL (labcorp, 2016b)
Luteal	0.9–9.3 IU/L (Director, 2013)
"	1.0–11.4 IU/L (Dr. Lamb, 2014)
"	1.0–11.4 iu/mL (Eaton, 2014)
"	4–14 U/L (College, 2010)
"	1.0–11.4 mIU/mL (labcorp, 2016b)

Analyte	Reference range
Post-menopause	7.7–58.5 IU/L (Dr. Lamb, 2014)
"	7.7–58.8 iu/mL (Eaton, 2014)
"	> 20 (College, 2010)
"	7.7–58.5 mIU/mL (labcorp, 2016b)

Table 13.10 – Reference ranges of luteinizing hormone - LH

LH (luteinizing hormone), together with FSH (follicle-stimulating hormone), belongs to the gonadotropin family. LH and FSH regulate and stimulate the growth and function of the gonads (ovaries and testes) synergistically (Beastall et al., 1987), (M. R. Johnson et al., 1993).

In women, the gonadotropins act within the hypothalamus-pituitary-ovary regulating circuit to control the menstrual cycle (Runnebaum and Rabe, 1994), (Scott et al., 1989). LH and FSH are released in pulses from the gonadotropic cells of the anterior pituitary and pass via the bloodstream to the ovaries. Here the gonadotropins stimulate the growth and maturation of the follicle and hence the biosynthesis of oestrogens and progesterones. The highest LH-concentrations occur during the midcycle peak and induce ovulation and formation of the corpus luteum, the principal secretion product of which is progesterone.

Determination of LH concentration is used in the elucidation of dysfunctions within the hypothalamus-pituitary-gonads system. In the Leydig cells of the testes, LH stimulates the production of testosterone (Beastall et al., 1987), (Runnebaum and Rabe, 1994), (Scott et al., 1989).

Oestrogen

Test	Conventional Units	SI Units
Estradiol, females -		
Day 1–10 of menstrual cycle	14–27 pg/mL	50–100 pmol/l
Day 11–20 of menstrual cycle	14–54 pg/mL	50–200 pmol/l
Day 21–30 of menstrual cycle	19–40 pg/mL	70–150 pmol/l (merck, 2015)
Early follicular		< 300 pmol/l (College, 2010)
Follicular	90–590 pg/mL	(quest, 2016)

Test	Conventional Units	SI Units
	12.5–166.0 pg/mL	(labcorp, 2016b)
Luteal		250–1000 pmol/l (College, 2010)
	130–460 pg/mL	(quest, 2016)
	43.8–211.0 pg/mL	(labcorp, 2016b)
Pre-ovulatory		400–1200 pmol/l
Postmenopausal		< 190 pmol/l (College, 2010)
	50–170 pg/mL	(quest, 2016)
	< 6.0–54.7 pg/mL	(labcorp, 2016b)
Estradiol, males -		
	10–30 pg/mL	37–110 pmol/l (merck, 2015)
		< 190 pmol/l (College, 2010)
	60–190 pg/mL	(quest, 2016)
	7.6–42.6 pg/mL	(labcorp, 2016b)

Table 13.11 – Reference ranges of estradiol

Estradiol plays a key role in germ cell maturation and numerous other, nongender-specific processes, including growth, bone metabolism, nervous system maturation, and endothelial responsiveness. Oestrogens are crucial for the normal development and maintenance of the breasts. However, excessive oestrogen levels can promote cell proliferation and may increase the risk of developing breast and uterine cancer as well as uterine endometriosis (Stocco, 2012).

The three major naturally occurring oestrogens in women are estrone (E1), estradiol (E2), and estriol (E3). E2 is the predominant oestrogen during reproductive years, both in terms of absolute serum levels as well as in terms of oestrogenic activity (Kronenberg and H. R. Williams, 2008). During menopause, a dramatic drop in E2 production leaves estrone as the predominant circulating oestrogen. Estriol is the main pregnancy oestrogen, but it does not play a significant role in nonpregnant women or men (Kronenberg and H. R. Williams, 2008)[3]. The concentration of E2 in men is much lower than in women of reproductive age. All oestrogens are synthesized from androgen precursors by the enzyme aromatase (Kronenberg and H. R. Williams, 2008), (Stocco, 2012). Aromatase converts the androgenic substrates androstenedione, testosterone, and 16-hydroxytestosterone to the corresponding oestrogens: estrone, estradiol, and estriol (Stocco, 2012). E2 is produced primarily in ovaries and testes

by aromatization of testosterone (Kronenberg and H. R. Williams, 2008). A lesser amount of E2 is produced in the adrenal glands and some peripheral sites, most notably adipose tissue. Most of the circulating estrone is derived from peripheral aromatization of androstenedione (mainly in the adrenal gland). E2 and E1 can be converted to each other, and both are inactivated via hydroxylation and conjugation. E2 demonstrates two to five times the biological potency of E1 (Kronenberg and H. R. Williams, 2008).

The main site of oestrogen biosynthesis in the nonpregnant premenopausal woman is the ovarian granulosa cells; however, the adipose tissue becomes a major source of circulating estradiol in postmenopausal women (Kronenberg and H. R. Williams, 2008). After menopause, androstenedione, secreted by the adrenal gland, is converted into estrone in the adipose tissue (Kronenberg and H. R. Williams, 2008). The conversion of plasma androstenedione to estrone increases with excess body weight in both pre- and postmenopausal women (Kronenberg and H. R. Williams, 2008). Estrone is then eventually converted to estradiol by 17-β-hydroxysteroid dehydrogenase enzymes present in peripheral tissues (Kronenberg and H. R. Williams, 2008).

Postmenopausal women with lower E2 levels are at increased risk of osteoporotic fractures, while higher estradiol levels are associated with increased risk of malignancy and cardiovascular disease (Taylor and J. E. Manson, 2011), (Yager and N. E. Davidson, 2006).

Oestrogens (and androgens) play an important role in the normal physiology of the skeleton in both sexes (Kronenberg and H. R. Williams, 2008). Males with diminished oestrogen levels (due to congenital aromatase deficiency) or insensitivity to oestrogens (due to oestrogen receptor deficiency) have a characteristic phenotype with regard to bone development (Kronenberg and H. R. Williams, 2008), (Santen et al., 2009). These males exhibit significant increased overall height due to lack of estrogen-induced epiphyseal closure (Santen et al., 2009). The importance of estradiol in bone health is further supported by the fact that estradiol levels correlate better with bone mineral density than do testosterone levels in aging men (Santen et al., 2009). The Endocrine Society has recently reported that low estradiol levels are associated with increased fracture risk and accelerated bone loss in older men (Bulun, 2014).

Normal oestrogen level

The range of normal varies widely depending on a person's age. For those between 20–29, the average is 149 pg/ml and will increase to 210 pg/ml for females 30–39. The level falls back to 152 pg/ml for women over 40 who are not yet in menopause. These levels are generalisations as the exact level varies on a daily basis and is closely tied to the various phases of the menstrual cycle (newhealthguide, 2014).

Low oestrogen levels

Severe deficiency of oestrogen can result in levels as low as 10–20 pg/ml and produce a variety of symptoms including fatigue, night sweats, vaginal dryness, and memory impairment. Some women will experience irritability, mood swings and feel drained and exhausted. Oestrogen deficiency can result from eating disorders such as anorexia, menopause, surgical removal of the ovaries and congenital conditions. Turner syndrome and congenital adrenal hyperplasia are two such congenital disorders that result in profound hormonal abnormalities as well as unique physical characteristics (newhealthguide, 2014).

High oestrogen levels

Excess oestrogen levels are typically noted when oestrogen is in excess of 200 pg/ml. Causes include obesity, exogenous intake (medications), stress, cardiovascular disease and lifestyle. Excessive alcohol intake also influences oestrogen levels. Common symptoms include mood swings, anxiety, depression and insomnia. Excess oestrogen exposure is clearly linked to an increase in breast and uterine cancer (newhealthguide, 2014).

Prolactin - PRL

	Male	Female
Adult	2.0–18.0 ng/mL	(quest, 2016)
	<700 mIU/L	<1000 mIU/L (Director, 2013)
	86–324 mU/L	102–496 mU/L (Dr. Lamb, 2014)
	86–324 mU/L	102–496 mU/L (Eaton, 2014)
Non-pregnant		3.0–30.0 ng/mL (quest, 2016)
Pregnant		10.0–209.00 ng/mL (quest, 2016)
Postmenopausal		2.0–20.0 ng/mL (quest, 2016)
	75–375 mIU/l	125–625 mIU/l (College, 2010)
	4.0–15.2 ng/mL	4.8–23.3 ng/mL (labcorp, 2016b)

Table 13.12 – Reference ranges of prolactin - PRL

Elevated prolactin may be associated with corpus luteum insufficiency or anovulation. Sequelae of hyperprolactinemia include amenorrhea, anovulation, and decreased bone density.

When determining prolactin, it should be remembered that the measured concentration is dependent upon when the blood sample was taken, since the secretion of prolactin occurs in episodes and is also subject to a 24-hour cycle.

The release of prolactin is promoted physiologically by suckling and stress. In addition, elevated serum prolactin concentrations are caused by a number of pharmaceuticals (eg, dibenzodiazepines, phenothiazine), TRH, and oestrogen (Frantz, 1978), (Müller et al., 1983), (Pontiroli, Falsetti, and Bottazzo, 1987). The release of prolactin is inhibited by dopamine, L-dopa, and ergotamine derivatives.

Antipsychotic drugs may elevate serum prolactin. Antipsychotics block dopamine, thereby elevating serum prolactin levels. Hyperprolactinemia is present in many patients receiving neuroleptics with an occasional patient developing amenorrhea, galactorrhea, and/or decreased libido. Amoxapine, a dibenzoxazepine type of tricyclic with antidepressant and antipsychotic characteristics, has been found to cause galactorrhea and oligomenorrhea with hyperprolactinemia. Amoxapine may have a dopamine blocking action (Gelenberg et al., 1979). The prolactin level may rise significantly but only briefly.

Persistent elevations of plasma prolactin levels may be observed with, and after withdrawal from, chronic cocaine abuse, and may reflect a cocaine-induced derangement in the neural dopaminergic regulatory systems (Mendelson et al., 1988).

Prothrombin - PT

A prothrombin time test measures how quickly your blood clots. Sometimes called a PT or pro time test, a prothrombin time test uses a sample of your blood.

Prothrombin is a protein produced by your liver. It is one of many factors in your blood that help it to clot appropriately (mayoclinic, 2015a).

Results

Prothrombin time test results can be presented in two ways.

In seconds

The average time range for blood to clot is about 10 to 14 seconds. A number higher than that range means it takes blood longer than usual to clot. A number lower than that range means blood clots more quickly than normal (mayoclinic, 2015a).

As INR

This ratio - which allows for easier comparisons of test results from different laboratories - is used if you take blood-thinning medications (mayoclinic, 2015a).

See also International Normalised Ratio - INR.

Sex hormone binding globulin - SHBG

	Male	Female
18–55 years	10–50 nmol/L	17–124 nmol/L (quest, 2016)
> 55 years	22–77 nmol/L	14–73 nmol/L (quest, 2016)
	20–40 nmol/L	40–80 nmol/L (College, 2010)
20–50 years	16.5–55.9 nmol/L	24.6–122.0 nmol/L (Director, 2013)
> 50 years	19.3–76.4 nmol/L	17.3–125.0 nmol/L (Director, 2013)
17–65 years	15–48 nmol/L	(Dr. Lamb, 2014)
17–50 years		26–110 nmol/L (Dr. Lamb, 2014)
post-menopausal		14–70 nmol/L (Dr. Lamb, 2014)
	10–80 nmol/L	20–130 nmol/L (Eaton, 2014)

Table 13.13 – Reference ranges of SHBG

Levels of SHBG are under the positive control of oestrogens and thyroid hormones, and are suppressed by androgens. These influences dynamically control the liver synthesis of this carrier protein. Decreased levels of SHBG are frequently seen in hirsutism, virilization, obese postmenopausal women, and in women with diffuse hair loss. Increased levels may be present in cases of hyperthyroidism, testicular feminization, cirrhosis, male hypogonadism, pregnancy, women using oral contraceptives, and prepubertal children.

Sex hormone-binding globulin (SHBG) is the blood transport protein for testosterone and estradiol.

Planar C18 and C19 steroids with a 17α-hydroxyl group bind particularly well (Avvakumov et al., 2001), (Hammond and Bochinfuso, 1995) whereas C19 17-ketosteroids, such as dehydroepiandrosterone (DHEA) and androstenedione, do not bind so easily. SHBG has a high binding affinity to dihydrotestosterone (DHT), medium affinity to testosterone and estradiol, and only a low affinity to estrone, DHEA, androstenedione, and estriol. SHBG binds reversibly to sexual steroids.

SHBG has a half-life of about seven days and is produced mainly by the liver. Its synthesis and secretion are regulated by oestrogen (Burger, 2002), (S. Davis, 2001). SHBG serum concentrations depend on the extent, duration, and the kind of oestrogen applied, and how regulation takes place. Androgens and gestagens with androgenic residual action have the opposite effect.

In serum, SHBG mainly takes over the transportation of steroids and the reduction/regulation of the effect of androgen (Rosner et al., 1999), (Burger and S. R. Davis, 2003). Decreased SHBG serum levels are associated with conditions in which elevated androgen levels are present or in which the effect of androgen on its target organs is excessive. This explains the gender-related differences seen between men and women, especially during puberty.

Elevated SHBG levels can be seen in elderly men, and are often found in patients with hyperthyroidism and cirrhosis of the liver. SHBG levels also increase when oral contraceptives or antiepileptic drugs are taken. Decreased SHBG concentrations are often seen with hypothyroidism, polycystic ovarian syndrome (PCOS), obesity, hirsutism, elevated androgen levels, alopecia, and acromegaly.

Testosterone

Test	Conventional Units	SI Units
Testosterone, adults -		

Test	Conventional Units	SI Units
Females	20–75 ng/dL	0.7–2.6 nmol/L (merck, 2015)
Females		< 3.0 nmol/l (College, 2010)
Females		0.0–2.0 nmol/L (Director, 2013)
Females		0.2–2.9 nmol/l (Dr. Lamb, 2014)
Females		0.29–1.67 nmol/L (Eaton, 2014)
Females		0.2–2.9 nmol/L (Hornsby, 2013)
Males	300–1200 ng/dL	10–42 nmol/L (merck, 2015)
Males		10–30 nmol/l (College, 2010)
Males		>12 nmol/L (Director, 2013)
Males		10–28 nmol/l (Dr. Lamb, 2014)
Males		10–30 nmol/L (Eaton, 2014)
Males		9.9–27.8 nmol/L (Hornsby, 2013)
Free testosterone		
Male		
18–69 Years	46.0–224.0 pg/ml	
> 69 Years	6.0–73.0pg/ml	(quest, 2016)
Bioavailable testosterone		
Male		
18–69 Years	110.0–575.0 ng/dl	
> 69 Years	15.0–150.0 ng/dl	(quest, 2016)

Table 13.14 – Reference ranges of testosterone - T

The Leydig cells of the testes produce between 5 and 10 mg of testosterone daily. Testosterone levels are highest in early morning and lowest during the evening hours; however, in older men, this diurnal pattern may be reduced.

Testosterone is synthesized from cholesterol through several intermediate compounds, including dehydroepiandrosterone (DHEA) and androstenedione. Circulating testosterone is mostly protein-bound, about 40% avidly bound to sex hormonebinding globulin (SHBG) and 58% loosely bound to albumin. Thus, only about 2% of circulating testosterone is bioavailable as free testosterone.

In target tissues, about 4 to 8% of testosterone is converted to a more potent metabolite, dihydrotestosterone (DHT), by the enzyme 5α-reductase. DHT has important trophic effects in the prostate and mediates androgenic alopecia. In adults, spermatogenesis requires adequate intratesticular testosterone, but the role of DHT in spermatogenesis is unclear.

Testosterone and DHT have metabolic and other effects, including -

- Stimulating protein anabolism (increasing muscle mass and bone density),
- Stimulating renal erythropoietin production (increasing red blood cell mass),
- Stimulating bone marrow stem cells (modulating the immune system),
- Causing cutaneous effects (ie, sebum production, hair growth),
- Causing neural effects (ie, affecting cognition, increasing libido and possibly aggression).

Testosterone undergoes conversion to estradiol as well as to DHT, with estradiol mediating most of testosterone's action on organs such as bones and the brain.

Testosterone is important for -

- Keeping bones and muscles strong,
- Making sperm,
- Maintaining sex drive,
- Making red blood cells,
- Feeling well and having energy in general (medlineplus, 2013).

As you become older, testosterone levels slowly drop. This can lead to signs and symptoms, including -

- Low sex drive,
- Problems having an erection,
- Low sperm count,
- Sleep problems such as insomnia,
- Decrease in muscle size and strength and in bone density,
- Increase in body fat,
- Depression,
- Trouble concentrating (medlineplus, 2013).

Signs

Low testosterone levels

- Early or late puberty (in boys),
- Infertility, erectile dysfunction, low level of sexual interest, infertility, thinning of the bones (in men) (medlineplus, 2014b).

Raised testosterone levels

- Acne, oily skin,
- Change in voice,
- Decreased breast size,
- Excess hair growth (thick, dark hair in the area of the moustache, beard, sideburns, chest, buttocks, inner thighs),
- Increased size of the clitoris,
- Irregular or absent menstrual periods,
- Male-pattern baldness or hair thinning (medlineplus, 2014b).

Abnormal results

Increased testosterone

- Resistance to the action of male hormones (androgen resistance),
- Tumour of the ovaries,
- Cancer of the testes,
- Congenital adrenal hyperplasia,
- Taking medications or drugs that increase testosterone levels (medlineplus, 2014b).

Decreased testosterone

- Chronic illness,
- Condition in which the pituitary gland does not produce normal amounts of some or all of its hormones,
- Injury or disease of the hypothalamus,
- Delayed puberty,
- Diseases of the testicles (trauma, infection, immune),
- Noncancerous tumour of the pituitary cells that produce too much of the hormone prolactin (medlineplus, 2014b).

Thyroxine, free - T4

This test is used in the diagnosis of Hypothyroidism or Hyperthyroidism

Analyte	Reference range
Thyroxine, free	9–19 pmol/L (Director, 2013)
Thyroxine, free	12–22 pmol/l (Dr. Lamb, 2014)
Thyroxine, free	10–24 pmol/L (Eaton, 2014)

Analyte	Reference range
Thyroxine, free	8–21 pmol/L (Hornsby, 2013)

Table 13.15 – Reference ranges of thyroxine, free - T4

Note

Many medicines including oestrogen, certain types of contraceptive birth control pills, those drugs used to help control epilepsy and large doses of aspirin can interfere with total T4 test results, so tell your doctor about any drugs you are taking. In general, free T4 levels are not affected by these medications.

In addition, total T4 levels may be affected by contrast material used for certain X-ray imaging tests. Total T4 is now rarely measured in the UK having been replaced by Free T4 (FT4) (labtestsonline, 2011).

Further blood tests

You may hear requests being done as FBC, U & E's, Thyroid function test (TFT), LFT, ESR, BUN, and INR. These are the tests that they refer to -

FBC - Full Blood Count - FBC,
U & E's - Urine and electrolytes - Sodium, Potassium, Urea, Creatinine.
TFT - Thyroid function test - TFT,
LFT - Liver function tests,
ESR - Erythrocyte sedimentation rate - ESR,
PSA - Prostate specific antigen - PSA,
BUN - Blood, urea and nitrogen - BUN,
INR - International Normalised Ratio - INR.

Blood, urea and nitrogen - BUN

A common blood test, the BUN test reveals important information about how well your kidneys and liver are working. A BUN test measures the amount of urea nitrogen that's in your blood.

Here's how your body typically forms and gets rid of urea nitrogen -

- Your liver produces ammonia - which contains nitrogen - after it breaks down proteins used by your body's cells.
- The nitrogen combines with other elements, such as carbon, hydrogen and oxygen, to form urea, which is a chemical waste product.

- The urea travels from your liver to your kidneys through your bloodstream.
- Healthy kidneys filter urea and remove other waste products from your blood.
- The filtered waste products leave your body through urine.

A BUN test can reveal whether your urea nitrogen levels are higher than normal, suggesting that your kidneys or liver may not be working properly (mayoclinic, 2013a).

Why it's done

You may need a blood urea nitrogen test -

- If your doctor suspects that you have kidney damage,
- If your kidney function needs to be evaluated,
- To help determine the effectiveness of dialysis treatment if you're receiving hemodialysis or peritoneal dialysis,
- As part of a blood test group to help diagnose a number of other conditions, such as liver damage, urinary tract obstruction, congestive heart failure or gastrointestinal bleeding - although an abnormal BUN test result alone doesn't confirm any of these conditions (mayoclinic, 2013a).

If kidney problems are the main concern, when your blood is tested for urea nitrogen levels, it's likely it will also be tested for creatinine levels. Creatinine is another waste product that healthy kidneys filter out of your body through urine. High levels of creatinine may be a sign of kidney damage (mayoclinic, 2013a).

Results

Results of the blood urea nitrogen test are measured in milligrams per deciliter (mg/dL) in the United States and in millimoles per liter (mmol/L) internationally. In general, 7 to 20 mg/dL (2.5 to 7.1 mmol/L) is considered normal. But normal ranges may vary, depending on the reference range used by the lab, and your age. Ask your doctor to explain your results.

Urea nitrogen levels tend to increase with age. Infants have lower levels than other people do, and the range in children varies.

Generally, a high blood urea nitrogen level means your kidneys aren't working well. But elevated urea nitrogen can also be due to -

- Urinary tract obstruction
- Congestive heart failure or recent heart attack
- Gastrointestinal bleeding
- Dehydration, resulting from not drinking enough fluids or for other reasons

- Shock
- Severe burns
- Certain medications, such as corticosteroids and some antibiotics
- A high protein diet (mayoclinic, 2013a).

If kidney damage is a concern, ask your doctor what factors may be contributing to the damage and what steps you can take to try to control them.

Full Blood Count - FBC

This is a test to check the types and numbers of cells in your blood, including red blood cells, white blood cells and platelets.

This can help give an indication of your general health, as well as provide important clues about certain health problems you may have.

White blood cell (WBC) - count is a count of the actual number of white blood cells per volume of blood. Both increases and decreases can be significant.

White blood cell differential - looks at the types of white blood cells present. There are five different types of white blood cells, each with its own function in protecting us from infection. The differential classifies a person's white blood cells into each type - neutrophils (also known as PMNs), lymphocytes, monocytes, eosinophils, and basophils.

Red blood cell (RBC) count - is a count of the actual number of red blood cells per volume of blood. Both increases and decreases can point to abnormal conditions.

Haemoglobin - measures the amount of oxygen-carrying protein in the blood.

Haematocrit - measures the amount of space red blood cells take up in the blood. It is reported as a percentage (0 to 100) or a proportion (0 to 1).

The platelet count - is the number of platelets in a given volume of blood. Both increases and decreases can point to bleeding or bone marrow disorders.

Mean platelet volume (MPV) - is a machine-calculated measurement of the average size of your platelets. New platelets are larger, and an increased MPV occurs when increased numbers of platelets are being produced.

Mean corpuscular volume (MCV) - is a measurement of the average size of your RBCs. The MCV is elevated when your RBCs are larger than normal (macrocytic), for example in anaemia caused by vitamin B12 deficiency or folic acid deficiency. When the MCV is decreased, your RBCs are smaller than normal (microcytic), which may indicate iron deficiency anaemia, inflammation or occasionally thalassaemias.

Mean corpuscular haemoglobin (MCH) - is a calculation of the amount of oxygen-carrying haemoglobin inside your RBCs. Since macrocytic RBCs are larger than either normal or microcytic RBCs, they would also tend to have higher MCH values.

Mean corpuscular haemoglobin concentration (MCHC) - is a calculation of the concentration of haemoglobin inside the RBCs. Decreased MCHC values (hypochromia) are seen in conditions where the haemoglobin is abnormally diluted inside the red cells, such as in iron deficiency anaemia, long standing inflammation or thalassaemia. Increased MCHC values (hyperchromia) are seen in conditions where the haemoglobin is abnormally concentrated inside the red cells, such as in hereditary or autoimmune spherocytosis.

Red cell distribution width (RDW) - is a calculation of the variation in the size of your RBCs. In some anaemias, such as iron deficiency or pernicious anaemia, the amount of variation (anisocytosis) in RBC size (along with variation in shape poikilocytosis) causes an increase in the RDW (labtestsonline, 2016a).

White blood cell

An elevated number of white blood cells is called leucocytosis. This can result from bacterial infections, inflammation, leukaemia, trauma, medication, or stress. A WBC count of 11.0–17.0x109/L cells would be considered mild to moderate leucocytosis.

A decreased WBC count is called leucopenia. It can result from many different situations, such as -

- medication, especially chemotherapy, or radiotherapy,
- bone marrow disorder,
- vitamin deficiency, such as B12 or folic acid,
- liver disease,
- an enlarged spleen,
- occasionally in inflammatory conditions such as rheumatoid arthritis or SLE,
- some infections,
- diseases of the immune system.

A count of 3.0–4.0x109/L cells would be considered mild leucopenia.

The WBC count tends to be lower in the morning and higher in the late afternoon. WBC counts change with age with normal newborns and infants typically have a higher WBC counts than adults. It is not uncommon for the elderly to fail to develop leucocytosis (a high WBC) as a response to infection.

There are many drugs that cause both increased and decreased WBC counts (labtestsonline, 2016f).

White blood cell differential

The results indicate the relative percentage and actual numbers of each type of white blood cell that is present.

Neutrophils can increase in response to bacterial infection, inflammatory disease, steroid medication, or more rarely leukaemia. Decreased neutrophil levels may be the result of severe infection, liver disease, enlarged spleens or other conditions, such as responses to various medications or chemotherapy.

Eosinophils can increase in response to allergic disorders, inflammation of the skin, and parasitic infections. They can also occur in response to some infections or to various bone marrow malignancies.

Basophils can increase in cases of leukaemia, long-standing inflammation, the presence of a hypersensitivity reaction to food, or radiation therapy.

Lymphocytes can increase in cases of bacterial or especially viral infection, leukaemia, lymphoma and in people with underactive or absent spleens. Decreased lymphocyte levels are common in later life but can also be due to steroid medication, stress, lupus, and human immunodeficiency virus (HIV) infection.

Monocyte levels can increase in certain leukaemias, in response to infection of all kinds as well as to inflammatory disorders. Decreased monocyte levels can indicate bone marrow injury or failure and some forms of leukaemia - especially "hairy cell leukaemia" .

Neutrophils

- engulf bacteria and cellular debris. An increase in the number of neutrophils occurs in acute infections, certain malignant neoplastic diseases, and some other disorders.

Eosinophils

- normally about 1–3% of the total white blood cell count, are believed to function in allergic responses and in resisting some infections.

Basophils

- normally constitute 1% or less of the total white blood cell count but may increase or decrease in certain diseases.

Lymphocytes

- White blood cell (leucocyte) containing no granules that normally makes up about 25% of the total white blood cell count but increases in the presence of infection. Lymphocytes occur in two forms: B cells, the chief agents of the humoral immune system, which recognize specific antigens and produce antibodies against them; and T cells, the agents of the cell-mediated immune system, which secrete immunologically active compounds and assist B cells in their function.

Monocyte

- Leucocyte (white blood cell) which ingests bacteria and other foreign particles. Monocytes are usually larger then other peripheral blood leucocytes, have a large central oval or indented nucleus and make up 5–10% of the total white blood cell count.

Red blood cell (RBC) count

A high RBC count may indicate congenital heart disease, dehydration, obstructive lung disease, or bone marrow over-production. A low RBC count may indicate anaemia, bleeding, kidney disease, bone marrow failure (for instance, from radiation or a tumour), malnutrition, or other causes. A low count may also indicate nutritional deficiencies of iron, folate and vitamin B12 (labtestsonline, 2016e).

Haemoglobin

Normal values in an adult are approximately 120 to 180 grams per litre (12 to 18 g/dL) of blood but are influenced by the age, sex and ethnic origin in the person.

High haemoglobin

Above-normal haemoglobin levels may be the result of -

- dehydration,
- excess production of red blood cells in the bone marrow,
- severe lung disease, or
- several other conditions.

Low haemoglobin

Below-normal haemoglobin levels may be the result of -

- iron deficiency,
- vitamin deficiencies,
- bleeding,
- kidney disease,
- inflammatory disorders such as rheumatoid arthritis or infections,
- haemolysis (accelerated loss of red blood cells through destruction),
- inherited haemoglobin defects such as thalassaemia or sickle cell anaemia,
- bone marrow failure,
- cirrhosis of the liver (during which the liver becomes scarred),
- bone marrow failure,
- cancers that affect the bone marrow (labtestsonline, 2016b).

Haematocrit

A decreased haematocrit indicates anaemia. Further testing may be necessary to determine the exact cause of the anaemia.

Low haematocrit

Conditions that can result in a low haematocrit include -

- Bleeding,
- Nutritional - iron, vitamin (e.g. B12 or folate) or other mineral deficiencies,
- Inflammatory conditions such as rheumatoid arthritis,
- Kidney disease (healthy kidneys secrete a hormone erythropoietin or epo which stimulates red blood cell production in the bone marrow),
- Cirrhosis of the liver
- Haemolysis, where the red cells are being destroyed prematurely either due to attack by the bodys immune system, due to organ damage or due to inherited abnormalities of the red cells or the haemoglobin they contain,
- Bone marrow disorders such as aplastic anaemia, myelodysplastic syndrome, leukaemia, lymphoma or myeloma.
- Some medicines - including chemotherapy

High haematocrit

The most common cause of increased haematocrit is dehydration, and with adequate fluid intake, the haematocrit returns to normal. However, it may reflect a condition called polycythaemia where there are too many red cells.

Primary polycythaemia (polycythaemia rubra vera or PRV) - means the bone marrow is overproducing red blood cells of its own accord.

More commonly polycythaemia is a due to factors outside the bone marrow (secondary polycythaemia).

Causes of secondary polycythaemia include -

- Some lung or heart diseases where the bone marrow manufacturers more red blood cells in order to carry enough oxygen throughout your body,
- Excessive alcohol consumption,
- Smoking,
- Liver or kidney disease,
- Some tumours which can secrete erythropoietin ("epo"), stimulating the production of red blood cells,
- Rare inherited haemoglobins, which don't release enough oxygen to the body (labtestsonline, 2016c).

The platelet count

The result is compared to a "normal" range, which represents the platelet count found in 95% of healthy individuals. In adults the platelet count is usually between 150 and 450 x 109/L, which means there are 150,000 to 450,000 platelets per microlitre of blood.

Low platelet count

A low platelet count (less than 150x19/L) may also be referred to as 'thrombocytopenia'. Thrombocytopenia may be caused by either of two different processes that cause a reduction in the count; the bone marrow is not producing enough platelets, or the bone marrow is producing normal amounts but the platelets are being consumed (used) or destroyed faster than they should in the blood.

Reduced platelet counts can be found in the following conditions -

Immune thrombocytopenia - an immune condition that causes platelets to be destroyed faster than they should be due. This is one of the most common causes of thrombocytopenia, diagnosis involves ruling out any other potential cause of a low platelet count,

B12 or folate deficiency - severe deficiency of these B complex vitamins is associated with x and, if severe, can also result in reduced platelet and white cell counts,

Drugs/medication - some medications (such as penicillin, gold used to treat arthritis, furosemide, valproic acid and others) can affect platelet production. Heparin (an anticoagulant drug) can cause a sudden fall in platelet numbers, this is a rare condition called heparin-induced thrombocytopenia or HIT ,

Infection and viruses - several infections and viruses can result in a reduced platelet count (e.g. parvovirus, cytomegalovirus, infectious mononucleosis),

Liver disease - established liver disease is associated with a low platelet count, among other changes to blood cells and proteins,

Autoimmune disorders - such as lupus, can cause increased destruction of platelets,

Gestational thrombocytopenia - up to 1 in 10 women experience a fall in platelet count to below the normal range during pregnancy. If no underlying cause is found then a diagnosis of gestational thrombocytopenia (low platelets caused by pregnancy) is made,

Chronic bleeding - where there is long-term bleeding, such as from a stomach ulcer, platelet counts may be found to be low,

Leukaemia or lymphoma - cancers of the white blood cells affect the function of the bone marrow and platelet numbers will be reduced,

Rare inherited platelet disorders - such as Bernard-Soulier syndrome, Glanzmann Thrombasthenia and MYH9-related thrombocytopenias are associated with a reduction in circulating platelets and an increased platelet size (giant platelets),

Bone marrow disorders/invasion - other diseases affecting the bone marrow (such as myelodysplasia, aplastic anaemia, or other haematological conditions), or invasion of the bone marrow by other cancer cells (metastasis) can affect platelet production,

Chemotherapy and radiotherapy - chemotherapy and/or radiotherapy will affect the function of the bone marrow and result in reduced production of all blood cells, including platelets,

Systemic disorders - some serious disorders can result in multiple abnormalities of the blood cell counts and characteristics. Haemolytic uraemic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP) and disseminated intravascular coagulation (DIC) are examples of syndromes in which patients will have reduced platelet counts alongside other clinical symptoms and blood cell changes.

The degree of thrombocytopenia (how low the platelet count is), the presence or absence of associated bleeding symptoms and the individual clinical situation will determine the course of action to be taken. Thrombocytopenia may be monitored closely by regular blood tests if the count is only slightly reduced and there are no symptoms. Treatment of the underlying cause might be considered for those who are at risk of bleeding. For patients with very low platelet counts (<20 x 109/L), or at a high risk of bleeding, a platelet transfusion can be used to increase the numbers of platelets.

High platelet count

A high platelet count (more than 450x109/L), 'thrombocytosis', is due to overproduction of platelets by the bone marrow which can be caused by certain bone marrow disorders or might simply be a side-effect of another condition (reactive thrombocytosis).

The platelet count may be increased as a reactive thrombocytosis in association with -

Infection - in response to many infections
Inflammation - chronic conditions such as Crohns disease, or other inflammatory processes
Recent trauma - if there has been tissue damage, or after having an operation
Poor spleen function - or in patients who have had their spleen removed
Bleeding or recent blood loss - as a reactive process in response to bleeding
Iron deficiency anaemia - especially where the anaemia is due to chronic blood loss (e.g. from a stomach ulcer)
Cancer - thrombocytosis is commonly found in association with lung, breast and ovarian cancer
Drugs/medication - e.g. corticosteroids can stimulate platelet production
Rebound phenomenon - after treatment with growth factors or during recovery following chemotherapy.

The platelet count may also be increased as the consequence of a bone marrow disorder; this is sometimes called 'primary thrombocytosis'. Essential thrombocythaemia (ET) is a condition where an acquired defect in bone marrow cells results in an abnormally high number of platelets whose production is uncontrolled. A high platelet count along with a high white cell count and red cell count may also be found in a similar condition affecting the bone marrow called polycythaemia vera (PV). These conditions, which can be referred to as 'myeloproliferative neoplasms', might not cause any symptoms and are often picked up incidentally when a full blood count is performed as a routine check or for another reason. Although in some people there may be no clinical signs or symptoms, there are risks associated with having abnormally high platelet counts, including blood clots and risk of bleeding. PV is associated with mutations in a gene called JAK2. ET is associated with mutations in the JAK2, MPL or CALR genes. If PV or ET is suspected then tests to look for mutations in these genes may be carried out.

Different types of bone marrow disorders such as chronic myeloid leukaemia (CML), myelodysplasia (MDS) and other myeloproliferative syndromes can also be linked to high platelet counts (labtestsonline, 2016d).

Erythrocyte sedimentation rate - ESR

The ESR measures the time required for erythrocytes from a whole blood sample to settle to the bottom of a vertical tube. Factors influencing the ESR include red cell volume, surface area, density, aggregation, and surface charge. The sample must be examined within 2 hours of collection and it must be handled gently, no clotting of sample must take place.

The ESR is a sensitive, but nonspecific test that is frequently the earliest indicator of disease. It often rises significantly in widespread inflammatory disorders due to infection or autoimmune mechanisms. Such elevations may be prolonged in localized inflammation and malignancies.

The test is fairly inexpensive, however, it is nonspecific, as it cannot pinpoint the exact location of the inflammation. Because it is limited, ESR is usually ordered in addition to other blood tests (nurseslearning, 2016).

Results

Results from your ESR rate test will be reported in the distance in millimeters (mm) red blood cells have descended in one hour (hr).

Males	Females
0–22mm/hr	0–29mm/hr (nurseslearning, 2016)

Table 13.16 – Normal Range of ESR

Normal values: 0-20 mm/hr (gradually increase with age) (nurseslearning, 2016).

The upper threshold for a normal ESR rate value may vary somewhat from one medical practice to another.

The results of your ESR rate test are one piece of information to help your doctor check your health. Talk to your doctor about what your ESR rate results mean in light of the symptoms you're experiencing and the results of other diagnostic tests (mayoclinic, 2013c).

Increased ESR

This may indicate pregnancy, acute or chronic inflammation, tuberculosis, rheumatic fever, paraproteinemias, rheumatoid arthritis, some malignancies, or anaemia (nurseslearning, 2016).

Decreased ESR

This may indicate polycythemia, sickle cell anemia, hyperviscosity, or low plasma protein (nurseslearning, 2016).

Accuracy of test results

A number of conditions can affect the properties of blood, thereby affecting how quickly red blood cells sink in a sample of blood. So information about inflammatory disease - what your doctor intends to learn from the ESR rate test - may be obscured by the influence of other conditions. These complicating factors include:

- Anaemia,
- Pregnancy,
- High cholesterol,
- Kidney problems.

Your doctor will take into account possible complicating factors when interpreting the results of your ESR rate test (mayoclinic, 2013c).

International Normalised Ratio - INR

Basically this is used to monitor the dose of anticoagulants, such as warfarin, and check that your dose is correct (NHS, 2016a).

The INR is specifically used to measure the exact effect of warfarin in the blood. It can also measure the effects of vitamin K deficiency (warfarin works by inactivating vitamin K and hence the activity of several vitamin K-dependent clotting factors in the blood). By standardising the INR, a medical professional can adjust the dose of warfarin to give the appropriate degree of anticoagulation. The higher the INR the less likely is a clot, but the more likely a bleed. Many patients have a target INR of 2.0–3.0 as an ideal compromise reducing the chances of a clot while being safe with respect to bleeding. The target range may be lower or higher than this depending on individual circumstances (labtestsonline, 2012a).

In healthy people an INR of 1.1 or below is considered normal. An INR range of 2.0 to 3.0 is generally an effective therapeutic range for people taking warfarin for disorders such as atrial fibrillation or a blood clot in the leg or lung. In certain situations, such as having a mechanical heart valve, you might need a slightly higher INR.

When the INR is higher than the recommended range, it means that your blood clots more slowly than desired, and a lower INR means your blood clots more quickly than desired (mayoclinic, 2015b).

What your results mean

Clotting too slowly

Blood that clots too slowly can be caused by -

- Blood-thinning medications,
- Liver problems,
- Inadequate levels of proteins that cause blood to clot,
- Vitamin K deficiency,
- Other substances in your blood that hinder the work of clotting factors (mayoclinic, 2015b).

Clotting too fast

Blood that clots too quickly can be caused by -

- Supplements that contain vitamin K,
- High intake of foods that contain vitamin K, such as liver, broccoli, chickpeas, green tea, kale, turnip greens and products that contain soybeans,
- Oestrogen-containing medications, such as birth control pills and hormone replacement therapy (mayoclinic, 2015b).

Prostate specific antigen - PSA

A PSA test measures the amount of prostate specific antigen in the blood. PSA is a protein produced by the prostate, a golf ball sized gland that sits just below a man's bladder. It helps to liquefy the semen (the fluid produced when you ejaculate). A small amount of PSA also enters the bloodstream, and this can be detected by a PSA test. PSA levels in the blood may be higher than normal if you have certain conditions, such as prostate infection, inflammation, enlargement or cancer (mydr, 2011).

The prostate specific antigen test measures levels of PSA in the blood. PSA is a protein produced by the prostate gland. Conditions such as prostate cancer, benign prostate hyperplasia (BPH) and prostatitis are considered when abnormally high levels of PSA are discovered. In the past, normal levels of PSA were considered below 4.0 ng/mL. However, more recent data have shown that prostate cancer may be present even when PSA levels are below 4.0 ng/mL. In addition, data has been shown in patients with PSA above 4.0 ng/mL but with no signs of prostate cancer (fastbleep, 2016a).

A 'normal' PSA level is less than -

- 3 ng/ml for men aged 50–59,
- 4 ng/ml for men aged 60–69,

- 5 ng/ml for men aged 70 and over (medrevise, 2016).

Risk factors

The biggest risk factor for prostate cancer is age but other factors may also play a part. Risk is greater in -

- overweight or obese (NHS, 2015g),
- those with a family history of prostate cancer,
- black Caribbean men,
- black African men (gov.uk, 2015).

How should I prepare for a PSA test?

Before you have a PSA test, tell your doctor about any medicines, supplements or herbal products you are taking, as they may affect the results. One medicine in particular, finasteride (e.g. Propecia, Proscar), which is used for treating baldness and benign prostatic hypertrophy (non-cancerous enlargement of the prostate), can affect PSA results.

You should also tell your doctor if you have had any urinary problems or investigations of the urinary tract such as a prostate biopsy or cystoscopy in the few weeks before a PSA test is scheduled, as these can also affect the results.

As ejaculation can make PSA levels rise briefly, some doctors recommend avoiding sexual activity for 48 hours before a PSA test (mydr, 2011).

Pros and cons of the PSA test

Pros

- It may reassure you if the test result is normal.
- It may give you an indication of cancer before symptoms develop.
- It may find cancer at an early stage, when treatment could prevent the cancer becoming more advanced.
- PSA testing may reduce your risk of dying from prostate cancer by 21%.
- If treatment is successful, you may avoid the risks of advanced cancer.
- In cases of advanced cancer, treatment will usually extend life (NHS, 2015g).

Cons

- It can miss cancer and provide false reassurance.

- It may lead to unnecessary worry and medical tests when there is no cancer.
- It cannot tell the difference between slow-growing and fast-growing cancer.
- It may make you worry by finding slow-growing cancer that may never cause any symptoms or shorten your life.
- To save one life from prostate cancer, 27 men would have to be diagnosed with it (NHS, 2015g).

Before having the test

If you're having a PSA test, you should not have -

- an active urinary infection
- ejaculated in the last 48 hours
- exercised heavily in the last 48 hours
- had a prostate biopsy in the last six weeks

Each of these may give an inaccurate PSA reading (NHS, 2015g).

What happens after the test?

There are usually three main options after a PSA test.

A normal PSA level

If your PSA level is not raised, you are unlikely to have cancer. No immediate action is needed, although you may have further PSA tests in the future. However, the PSA test doesn't always pick up prostate cancer (NHS, 2015g).

A slightly raised PSA level

Three out of four men with a raised PSA level will not have prostate cancer. If your PSA level is slightly higher than normal, you probably don't have cancer, but you might need more PSA tests (NHS, 2015g).

A raised PSA level

One out of four men with a raised PSA level will have cancer. The higher the level of PSA, the more likely it is to be a sign of cancer. If your PSA level is definitely raised, your GP will arrange for you to see a specialist for further tests to find out if you have prostate cancer (NHS, 2015g).

Digital rectal examination

A PSA test alone cannot tell you whether you have prostate cancer. Your doctor may also perform a digital rectal examination (DRE). This is an examination of the prostate gland, during which the doctor will insert a gloved finger into your rectum.

The DRE checks for signs of prostate cancer, such as the prostate gland feeling hard. However, a gland that feels normal does not necessarily mean you don't have cancer.

Many early cancers may not be detected by a DRE, so a DRE is not recommended as a substitute for the PSA test.

Your doctor will also consider your age, any family history of prostate cancer, your ethnic background, and any previous PSA test results.

In some cases, extra PSA tests may help make the situation clearer or show any changes (NHS, 2015g).

Key PSA statistics

- About 15% of all men with a normal PSA level have prostate cancer,
- Three out of four men with a raised PSA level don't have prostate cancer,
- One out of four men with a raised PSA level will have cancer,
- Biopsies miss one in five prostate cancers (NHS, 2015g).

Biopsies and further testing

If your PSA level is raised, a biopsy, which involves taking tissue samples from the prostate gland, may be needed to check if you have cancer.

Prostate biopsies can miss some cancers. One in five cancers are missed at prostate biopsy. You may not know for sure that you don't have cancer after a clear result, and biopsies sometimes have to be repeated.

Biopsies can sometimes cause complications. The most common is bleeding followed by infection. Most men experience blood in the urine and blood in the sperm after a biopsy. Antibiotics will be given to prevent infections (NHS, 2015g).

Thyroid function test - TFT

A TFT is used to measure the circulating thyroid hormones within the blood. Hormones measured include: thyroxine (T4), triiodothyronine (T3) and thyroid-stimulating hormone (TSH). Of the three, TSH is the most sensitive. When TSH levels are elevated, primary hypothyroidism is most likely the issue. However, when low levels are discovered, hyperthyroidism is the disease suspected (fastbleep, 2016b).

TSH	T4	T3	Interpretation
High	Normal	Normal	Mild (subclinical) hypothyroidism
High	Low	Low or normal	Hypothyroidism
Low	Normal	Normal	Mild (subclinical) hyperthyroidism [85]
Low	High or normal	High or normal	Hyperthyroidism [86]
Low	Low or normal	Low or normal	Nonthyroidal illness; Rarely hypothyroidism due to pituitary disease (labtestsonline, 2012b)

Table 13.17 – A summary of test results and their meaning

Hypothyroidism

Hypothyroidism means you have too little thyroid hormone. This makes your body use energy more slowly than it should and some parts of your body may work slower than normal. Hypothyroidism is common; in fact, you can have hypothyroidism for a number of years before it is recognized and treated. It is more common in women than men and it becomes more common as you get older. Symptoms of hypothyroidism include -

- Weight gain or fluid retention,
- Depression,
- Constipation,
- Feeling cold,
- Dry skin,
- Thinning hair and brittle nails,
- Tiredness,
- Memory problems and poor concentration,
- A slow heart rate,
- Heavy /abnormal periods or infertility (not as common),
- Goitre (depending on the cause of the hypothyroidism).

[85] For patients on thyroxine replacement, this pattern of results might indicate overreplacement and a careful check for clinical signs or symptoms of such should be made

[86] For patients on thyroxine replacement, this pattern of results might indicate overreplacement and a careful check for clinical signs or symptoms of such should be made

Once again sometimes only a few of these symptoms may be apparent in cases of hypothyroidism and the symptoms can often be mild (labtestsonline, 2012b).

Hyperthyroidism

Hyperthyroidism means you have too much thyroid hormone. This makes your body use energy faster than it should and therefore some cells and tissues in your body work faster than they should do. Symptoms of hyperthyroidism are -

- Palpitations (fast or abnormal heart rate),
- Feeling anxious, nervous, irritable or emotional,
- Anxiety & depression,
- Difficulty sleeping,
- Diarrhoea,
- Feeling hot,
- Weakness & fatigue,
- Weight loss despite feeling hungry,
- Tremor,
- Hair loss,
- Light or absent periods,
- A swelling of your thyroid gland (goitre),
- Eye problems such as blurred vision and eyes that appear enlarged if you have a type of hyperthyroidism called Graves disease.

It is important to realise that most people will not have all the symptoms and in some people the symptoms may be very mild at first (labtestsonline, 2012b).

Chapter 14

Urine tests and their results

This test identifies and measures some of the by-products of normal and abnormal metabolism, cells, cell fragments, and bacteria in urine. Urine is produced by the kidneys, which filter wastes out of the blood, help regulate the amount of water in the body, and conserve proteins, electrolytes, and other compounds that the body can reuse. Anything that is not needed is excreted in the urine.

How should I collect and store a urine sample?

You should -

- collect your urine sample in a completely clean (sterile) container,
- store it in a fridge, in a sealed plastic bag, if you cant hand it in straight away.

Collecting a urine sample

Your doctor or another healthcare professional should give you a container and explain how you should collect the urine sample.

You can collect a urine sample at any time of day, unless your GP or practice nurse advises you otherwise.

The types of urine sample you might be asked for include a random specimen, first morning specimen or timed collection.

To collect a clean urine sample -

- label the container with your name, date of birth and the date,
- wash your hands,
- start to urinate, but dont collect the first part of urine that comes out,

- collect a sample of urine "mid-stream" (see below) in a sterile screw-top container,
- screw the lid of the container shut,
- wash your hands thoroughly.

If your doctor gives you any other instructions, follow these.

What is a mid-stream urine sample?

A mid-stream urine sample means that you dont collect the first or last part of urine that comes out. This reduces the risk of the sample being contaminated with bacteria from -

- your hands ,
- the skin around the urethra.

Storing a urine sample until you hand it in

If you cant hand your urine sample in within an hour, you should keep it in the fridge at around 4C (39F) for no longer than 24 hours. Put the container of urine in a sealed plastic bag first. If the urine sample isnt kept in a fridge, the bacteria in it can multiply. If this happens, it could affect the test results.

What are urine samples used for?

Your GP or another healthcare professional may ask for a urine sample to help them diagnose or rule out health conditions. Urine contains waste products that are filtered out of the body. If it contains anything unusual, this may indicate an underlying health problem.

For example, a high level of glucose (sugar) in your urine may be a sign of type 2 diabetes. Other reasons for a urine sample include checking if you -

- have a Urinary tract infections - UTI's,
- have a Sexually transmitted infections - STI's (NHS, 2014g).

Urine and electrolytes

The electrolytes - urine test measures specific chemicals called electrolytes in urine. It usually measures the levels of calcium, chloride, potassium, or sodium.

Calcium

This test measures the amount of calcium in urine. All cells need calcium in order to work. Calcium helps build strong bones and teeth. It is important for heart function, and helps with muscle contraction, nerve signaling, and blood clotting (ucsfhealth, 2009a).

How the test is performed

A 24-hour urine sample is generally needed -

- On day 1, urinate into the toilet when you get up in the morning,
- Collect all subsequent urine (in a special container) for the next 24–hours,
- On day 2, urinate into the container in the morning when you get up,
- Cap the container. Keep it in the refrigerator or a cool place during the collection period.
- If the container does not have your patient details on it, then you need to label the container with your name, the date, and the time of completion,
- Return it to your hospital/GP, or prearranged collection point (ucsfhealth, 2009a).

How to prepare for the test

Your doctor may tell you to temporarily stop taking any drugs that may affect the test results.

Drugs that may increase urine calcium measurements include antacids, anticonvulsants, carbonic anhydrase inhibitor diuretics, and loop diuretics.

Drugs that may decrease urine calcium measurements include adrenocorticosteroids, birth control pills, and thiazide diuretics.

NEVER stop taking any medicine without first talking to your doctor (ucsfhealth, 2009a).

Why the test is performed

This test is used to diagnose or monitor diseases of the parathyroid gland or kidneys, which can cause a calcium control disorder. If there is not enough calcium in your body fluids, it can lead to hyperexcited nerves and muscles. Too much calcium has the opposite effect.

The most common type of kidney stone contains calcium. This test may be used to diagnose such stones (ucsfhealth, 2009a).

Normal Values

If a person is eating a normal diet, the expected amount of calcium in the urine is 100 to 300 mg/day. If eating a diet low in calcium, the amount of calcium in the urine will be 50 to 150 mg/day (ucsfhealth, 2009a).

Note: mg/day = milligrams per day

What abnormal results mean

High levels

High levels of urine calcium may be due to -

- Hyperparathyroidism,
- Idiopathic hypercalciuria,
- Kidney failure,
- Milk-alkali syndrome,
- Renal tubular acidosis,
- Sarcoidosis,
- Use of loop diuretics,
- Vitamin D intoxication (ucsfhealth, 2009a).

High is hypercalcaemia: two big causes: hyperparathyroidism and cancer (bony metastases release calcium). Other causes are hyperthyroidism, sarcoidosis, TB and kidney transplant (medrevise, 2010).

Low levels

Low levels of urine calcium may be due to: -

- Hypoparathyroidism,
- Malabsorption disorders,
- Use of thiazide diuretics,
- Vitamin D deficiency (ucsfhealth, 2009a).

Low is hypocalcaemia: underactive parathyroid, low Vitamin D, CKD, alcoholism (medrevise, 2010).

Chloride

Chloride is a negatively charged molecule known as an electrolyte. It works with other electrolytes, such as potassium, salt (sodium), and carbon dioxide (CO2), to help keep the proper balance of body fluids and maintain the body's acid-base balance (ucsfhealth, 2009b).

How the test is performed

A 24-hour urine sample is generally needed -

- On day 1, urinate into the toilet when you get up in the morning,
- Collect all subsequent urine (in a special container) for the next 24–hours,
- On day 2, urinate into the container in the morning when you get up,
- Cap the container. Keep it in the refrigerator or a cool place during the collection period.
- If the container does not have your patient details on it, then you need to label the container with your name, the date, and the time of completion,
- Return it to your hospital/GP, or prearranged collection point (ucsfhealth, 2009b).

How to prepare for the test

The health care provider will instruct you, if necessary, to discontinue drugs that may interfere with the test.

Drugs that may decrease the level of chloride in the urine chloride include -

- Acetazolamide
- Nonsteroidal anti-inflammatory drugs

Drugs that may increase the level of chloride in the urine chloride include -

- Corticosteroids
- Diuretics

Why the test is performed

Your doctor may order this test if you have signs of a disturbance in your body's fluid level or acid-base balance. It may be used to help determine the causes of hypokalemia, and to aid in the diagnosis of renal tubular acidosis (ucsfhealth, 2009b).

Normal Values

The normal range is 20 to 250 milliequivalents per day (mEq/day). This range depends greatly on your salt intake and how hydrated you are.

Note: Normal value ranges may vary slightly among different laboratories. Talk to your doctor about the meaning of your specific test results.

What abnormal results mean

High levels

Increased urine chloride levels may be caused by -

- Adrenocortical insufficiency,
- Increased salt intake,
- Inflammation of the kidney that results in salt loss,
- Production of an unusually large amount of urine (ucsfhealth, 2009b).

Lowered levels

Decreased urine chloride levels may be due to -

- Cushing syndrome,
- Decreased salt intake,
- Fluid loss that occurs with diarrhoea, vomiting, sweating, and gastric suction,
- Salt retention (ucsfhealth, 2009b).

Creatinine

High creatinine implies the kidneys are having issues. Main causes glomerulonephritis, pyelonepritis, acute renal failure, deydration and shock. Rarely low, and not usually an issue if it is (medrevise, 2010).

Potassium

The potassium urine test measures the amount of potassium in the urine (ucsfhealth, 2009c).

How the test is performed

A 24-hour urine sample is generally needed -

- On day 1, urinate into the toilet when you get up in the morning,
- Collect all subsequent urine (in a special container) for the next 24–hours,
- On day 2, urinate into the container in the morning when you get up,
- Cap the container. Keep it in the refrigerator or a cool place during the collection period.
- If the container does not have your patient details on it, then you need to label the container with your name, the date, and the time of completion,

- Return it to your hospital/GP, or prearranged collection point (ucsfhealth, 2009c).

How to prepare for the test

Your health care provider may tell you to temporarily stop taking certain drugs that may affect test results. Drugs that can affect urine potassium measurements include -

- Certain antibiotics,
- Diuretics,
- Glucocorticoids,
- Nonsteroidal anti-inflammatories (ucsfhealth, 2009c).

Why the test is performed

Your doctor may order this test if you have signs of a condition that affects body fluids. This may include dehydration, vomiting, or diarrhoea.

It may also be done to diagnose or confirm disorders of the kidneys or adrenal glands.

Additional conditions under which the test may be performed include medullary cystic disease (ucsfhealth, 2009c).

Normal Values

The usual range for a person on a regular diet is 25 to 120 milliequivalents per liter per day. However, lower or higher urinary levels may occur depending on dietary potassium intake and the relative amount of potassium in the body.

Normal value ranges may vary slightly among different laboratories. Talk to your doctor about the meaning of your specific test results (ucsfhealth, 2009c).

What abnormal results mean

Higher levels

Higher than normal urine potassium levels may be due to -

- Acute tubular necrosis
- Cushing syndrome (rare)
- Diabetic acidosis and other forms of metabolic acidosis
- Eating disorders (anorexia, bulimia)

- Low magnesium levels
- Hyperaldosteronism (very rare)
- Vomiting (ucsfhealth, 2009c).

High is hyperkalaemia: caused by kidney disease, Addison's, injury to tissue, infection, diabetes and too much IV potassium. Also caused by some types of drugs, NSAIDS, beta blockers, ACE inhibitors and potassium sparing diuretics (medrevise, 2010).

Lower levels

Low urine potassium levels may be due to the use of glucocorticoids or nonsteroidal anti-inflammatories.

Too much or too little potassium in the diet may also affect test results (ucsfhealth, 2009c).

Low is hypokalaemia: from potassium loss (diarrhoea and vomiting, from insulin use, or from use of non potassium sparing diuretics (medrevise, 2010).

Sodium

The sodium urine test measures the amount of salt (sodium) in a urine sample.

Sodium can also be measured in a blood sample (ucsfhealth, 2009d).

How the test is performed

This test may be done using a random urine sample or a 24-hour urine collection.

If a 24-hour urine sample is needed -

- On day 1, urinate into the toilet when you get up in the morning,
- Collect all subsequent urine (in a special container) for the next 24–hours,
- On day 2, urinate into the container in the morning when you get up,
- Cap the container. Keep it in the refrigerator or a cool place during the collection period.
- If the container does not have your patient details on it, then you need to label the container with your name, the date, and the time of completion,
- Return it to your hospital/GP, or prearranged collection point (ucsfhealth, 2009d).

How to prepare for the test

Your health care provider will instruct you, if necessary, to discontinue drugs that may interfere with the test.

High levels

Drugs that can increase test measurements include -

- Certain antibiotics,
- Certain corticosteroids,
- Diuretics,
- Prostaglandins (ucsfhealth, 2009d).

Low levels

Drugs that can decrease test measurements include -

- Nonsteroidal anti-inflammatory drugs (NSAIDs) (ucsfhealth, 2009d).

Why the test is performed

The test is often used to determine your hydration status and your kidney's ability to conserve or remove sodium from the urine (ucsfhealth, 2009d).

Additional conditions under which the test may be performed -

- Acute tubular necrosis,
- Hepatorenal syndrome,
- Medullary cystic kidney disease,
- Glomerulonephritis,
- Prerenal azotemia,
- Uncontrolled high blood pressure (hypertension) (ucsfhealth, 2009d).

Normal Values

Normal values are generally 15 to 250 milliequivalents per liter per day (mEq/L/day), depending on how much fluid and salt you consume. Normal value ranges may vary slightly among different laboratories. Talk to your doctor about the meaning of your specific test results (ucsfhealth, 2009d).

What abnormal results mean

Greater than normal urine sodium levels may be caused by too much salt in the diet or certain medications.

Low levels

Lower than normal urine sodium levels may indicate -

- Aldosteronism,
- Congestive heart failure,
- Diarrhoea and fluid loss,
- Kidney failure (ucsfhealth, 2009d).

Low is hyponatraemia: from sodium loss (diarrhoea and vomiting, thiazide diuretics, excessive sweating, kidney disease or Addison's), from excess fluids (drinking too much water, heart failure, cirrhosis, nephrotic syndrome). Sometimes your body makes too much ADH, leading to extra water and thus low sodium (medrevise, 2010).

High levels

High is hypernatraemia: almost always due to dehydration. Rarely, due to increased salt intake, Cushing's syndrome, or diabetes insipidus (medrevise, 2010).

Special considerations Too little or too much sodium in the diet may affect test results (ucsfhealth, 2009d).

Urea

normal 2.5 - 7.9 mmol/L - goes high for the same reasons as creatinine (medrevise, 2010).

Albumin

Low implies liver disease, or kidney problems, inflammation, shock. High usually implies dehydration (medrevise, 2010).

Urinary tract infections - UTI's

See Urinary Tract Infections - UTI's.

Chapter 15

Sexually transmitted infections - STI's

sexually transmitted infections (STI's) sometimes called sexually transmitted diseases (STD's) - are infections you can pick up and pass on during sex. You can lower your risk by using condoms and Femidoms, having regular check-ups and limiting your exposure.

STI's can be caused by one of three things -

Bacteria - Gonorrhoea, Chlamydia, Shigella, and Syphilis - Infections caused by bacteria are usually easily cured with antibiotics.

Viruses - HIV, Genital herpes, Genital warts, Molluscum contagiosum and the liver infection Hepatitis B - Viruses are harder to treat but with time your body often gets rid of some viruses on its own. Other viruses such as HIV cannot be cured. You can be vaccinated against some viruses, eg, hepatitis A and B.

Parasites - Pubic lice, Scabies, Trichomoniasis - They can be caught without having sex - eg, from bedding and towels - but this isn't common.

Symptoms of STI's

Some STI's can cause symptoms within a few days.

Symptoms of others may not show for days, weeks or months. Sometimes you may notice no symptoms at all or mistake them for something else.

Whether you have symptoms or not, a sexual health check-up will detect any infections.

How can I stay safer?

Using a condom or Femidom cuts the chance of getting or passing on STI's - the condom or Femidom is the only type of contraception that offers any protection against them.

Condoms and Femidoms don't take away all the risk, however, as they may not cover the part of the body where the sexually transmitted infection (STI) is (such as a herpes sore or a syphilis rash). Also, some STI's are spread during types of sex where people are not likely to use condoms or Femidoms, eg, oral sex.

You can still get an STI if you have very few sexual partners - but the more sexual partners you have, the more likely you are to have sex with someone with an infection.

These reduce the risk of STI's being passed on -

- using condoms or Femidoms,
- having fewer partners,
- being checked for STI's.

STI's are passed from one person to another through unprotected sex, genital contact, or rarely oral sex.

You can be tested for STI's at a sexual health clinic, genitourinary medicine (GUM) clinic or at your GP's surgery.

These are listed in alphabetical order, not in order of severity.

Chlamydia

Chlamydia is the most common STI in the UK and is easily passed on during sex. Most people don't experience any symptoms, so they are unaware they're infected. In women, chlamydia can cause pain or a burning sensation when urinating, a vaginal discharge, pain in the lower abdomen during or after sex, and bleeding during or after sex or between periods. It can also cause heavy periods.

In men, chlamydia can cause pain or a burning sensation when urinating, a white, cloudy or watery discharge from the tip of the penis, and pain or tenderness in the testicles.

It's also possible to have a chlamydia infection in your rectum (bottom), throat or eyes.

Diagnosing chlamydia is done with a urine test or by taking a swab of the affected area. The infection is easily treated with antibiotics, but can lead to serious long-term health problems if left untreated, including infertility.

It's passed on from one person to another through unprotected sex (sex without a condom) and is particularly common in sexually active teenagers and young adults.

In 2013, more than 200,000 people tested positive for chlamydia in England. Almost 7 in every 10 people diagnosed with the condition were under 25 years old.

What causes chlamydia?

Chlamydia trachomatis is a bacteria, which is found in the semen and vaginal fluids of men and women who have the infection. Chlamydia is easily passed from one person to another through sexual contact. Anyone who is sexually active can get it and pass it on. You dont need to have lots of sexual partners (fpa, 2014a).

How is it passed on?

Chlamydia is usually passed from one person to another during sex. You can become infected with chlamydia if you come into contact with the semen or vaginal fluids of someone who already has the infection.

The bacteria can live inside the cells of the cervix, the urethra, the rectum (back passage) and sometimes the throat and eyes.

The infection is most commonly spread through -

- unprotected vaginal, anal or oral sex,
- sharing sex toys if you don't wash them or cover them with a new condom each time they're used,
- Infected semen or vaginal fluid coming into contact with the eye can cause conjunctivitis (fpa, 2014a).

Chlamydia can also be passed from a pregnant woman to her baby.

It is not yet clear if chlamydia can be spread by transferring infected semen or vaginal fluid to another person's genitals on the fingers or through rubbing vulvas (female genitals) together.

You cannot catch chlamydia from kissing, hugging, sharing baths or towels, swimming pools, toilet seats or from sharing cups, plates or cutlery (fpa, 2014a).

Symptoms of chlamydia

Most people who have chlamydia don't notice any symptoms.

If you do get symptoms, these usually appear between one and three weeks after having unprotected sex with an infected person. For some people they don't develop until many months later.

Sometimes the symptoms can disappear after a few days. Even if the symptoms disappear you may still have the infection and be able to pass it on (fpa, 2014a).

Symptoms in women

At least 70% of women with chlamydia don't notice any symptoms. If they do get symptoms, the most common include -

- pain when urinating,
- unusual vaginal discharge,
- pain in the tummy or pelvis,
- pain or bleeding during sex,
- bleeding after sex,
- bleeding between periods,
- heavier periods than usual (fpa, 2014a).

If chlamydia is left untreated, it can spread to the womb and cause a serious condition called pelvic inflammatory disease (PID). This is a major cause of ectopic pregnancy and infertility in women (fpa, 2014a).

Symptoms in men

At least half of all men with chlamydia don't notice any symptoms. If they do get symptoms, the most common include -

- pain when urinating,
- white, cloudy or watery discharge from the penis,
- burning or itching in the urethra,
- pain in the testicles (fpa, 2014a).

If chlamydia is left untreated, the infection can cause swelling in the epididymis and the testicles. This could affect your fertility (fpa, 2014a).

Chlamydia in the rectum, throat or eyes

Chlamydia can also infect -

the rectum - if you have unprotected anal sex - this can cause discomfort and discharge from your rectum,

the throat - if you have unprotected oral sex - this is uncommon and usually causes no symptoms,

the eyes - if they come into contact with infected semen or vaginal fluid - this can cause eye redness, pain and discharge (conjunctivitis) (NHS, 2015b).

How will I know if I have it?

You can only be certain you have chlamydia if you have a test so don't delay in getting a check-up.

The National Chlamydia Screening Programme in England shows that risk factors for chlamydia increase if you are under 25, have a new sexual partner, or more than one sexual partner in the last year, and have not used condoms.

You may wish to have a test if -

- you, or a partner, have or think you might have symptoms,
- you have recently had unprotected sex with a new partner,
- you, or a partner, have had unprotected sex with other partners,
- during a vaginal examination your doctor or nurse says that the cells of the cervix are inflamed or there is a discharge,
- a sexual partner tells you they have a sexually transmitted infection,
- you have another sexually transmitted infection,
- you are pregnant or planning a pregnancy (fpa, 2014a).

You could still have chlamydia even if a partner has tested negative - you cannot always rely on a partner's negative test result.

If you have chlamydia you may wish to be tested for other sexually transmitted infections as you can have more than one sexually transmitted infection at the same time (fpa, 2014a).

What is the treatment for it?

The common treatment for chlamydia is a course of antibiotics which, if you take it according to the instructions, is at least 95% effective.

- Treatment of chlamydia involves taking a course of antibiotic tablets either as a single dose or a longer course (up to two weeks).
- If there is a high chance you have the infection, treatment may be started before the results of the test are back. You will always be given treatment if your partner is found to have chlamydia.
- You may also need other treatment if complications have occurred.
- Do tell the doctor or nurse if you are pregnant, or think you might be, or you are breastfeeding. This will affect the type of antibiotic that you are given.
- There is currently no evidence that complementary therapies can cure chlamydia (fpa, 2014a).

azithromycin - single dose,

doxycycline - two capsules a day for a week (avert, 2015a).

If you are allergic to certain antibiotics, or are pregnant, the doctor may give you different antibiotics such as ofloxacin and erythromycin.

To avoid re-infection, avoid having sex during treatment (avert, 2015a).

What happens if it isn't treated?

If chlamydia is treated early it is unlikely to cause any long-term problems. Not everyone who has chlamydia has complications. However, without proper treatment the infection can spread to other parts of the body. The more times you have chlamydia the more likely you are to get complications (fpa, 2014a).

In women

Pelvic inflammatory disease (PID) - infection of the uterus, ovaries and fallopian tubes. Can be treated with antibiotics,

Cervicitis - inflammation of the cervix,

Blocked fallopian tubes (Salpingitis) - inflammation of the fallopian tubes, preventing an egg from travelling from the ovary to the womb. Can sometimes be treated with surgery,

Swollen Bartholins glands (Bartholinitis) - Chlamydia can cause the glands which produce a woman's lubricating mucus to become blocked and infected, leading to a cyst. The cyst can become infected and develop into an abscess. The abscess can be treated with antibiotics (avert, 2015a).

In men

Epididymitis - inflammation of the tubes that carry sperm to the testicles,

Urethritis - inflammation of the urine tube,

Reactive arthritis - inflammation of the joints, and in some people, the urethra and the eyes (conjunctivitis). Painkillers can control symptoms (avert, 2015a).

Can it go away without treatment?

It can, but it is unlikely. If you delay seeking treatment you risk the infection causing long-term damage and you may still be able to pass the infection on to someone else (fpa, 2014a).

Genital herpes

Genital herpes is a common infection caused by the herpes simplex virus (herpes simplex virus (HSV)), which is the same virus that causes cold sores (NHS, 2014d). There are two types, HSV-1 and HSV-2.

HSV-1 - causes cold sores around the mouth and lips,
HSV-2 - causes cold sores around the genitals and rectum - known as 'genital herpes' (avert, 2015b).

The virus enters the body through small cracks in the skin or through the moist soft lining (mucous membranes) of the mouth, vagina, rectum, urethra and under the foreskin. Following an infection by the herpes simplex virus some people will experience an outbreak of genital herpes (fpa, 2014b). Some people develop symptoms of HSV a few days after coming into contact with the virus. Small, painful blisters or sores usually develop, which may cause itching or tingling, or make it painful to urinate (NHS, 2014d).

After you've been infected, the virus remains dormant (inactive) most of the time. However, certain triggers can reactivate the virus, causing the blisters to develop again, although they're usually smaller and less painful (NHS, 2014d). In some people the virus can become active again from time to time and cause further outbreaks of genital herpes - known as recurrent outbreaks (fpa, 2014b).

It's easier to test for HSV if you have symptoms. Although there's no cure for genital herpes, the symptoms can usually be controlled using antiviral medicines.

HSV can affect any mucous membrane (moist lining), such as those found in the mouth (cold sores).

Genital herpes is a chronic (long-term) condition. The virus remains in your body and can become active again. The average rate of recurrence is four to five times in the first two years after being infected. However, over time, it tends to become active less frequently and each outbreak becomes less severe (NHS, 2014d).

How is it passed on?

Genital herpes can be passed from one person to another during sexual contact. Anyone who is sexually active can get the virus. Both men and women can have genital herpes, and pass it on.

The herpes simplex virus is most likely to be passed on just before, during or straight after an outbreak.

Genital herpes can be passed on -

- From one person to another during vaginal or anal sex, or by sharing sex toys.
- By skin to skin contact during sex. It can be passed on by close genital contact - you don't need to have penetrative sex (vaginal or anal) to pass it on.
- By skin to skin contact during sex if the virus is active on the skin outside the area protected by a condom or a latex or a polyurethane square.
- If you receive oral sex from someone who has a cold sore or is just about to get one.
- If a person with herpes on the hand or finger touches a partner's vagina, genitals or anal area.
- It is possible for a pregnant woman to pass the virus to her baby if she is having an outbreak at the time of giving birth (fpa, 2014b).

If you already have one type of herpes simplex virus it is still possible for you to get the other type although you may not notice symptoms.

You cannot get genital herpes from hugging, sharing baths or towels, from swimming pools, toilet seats or from sharing cups, plates or cutlery (fpa, 2014b).

Symptoms

Most people with the HSV don't experience any symptoms of genital herpes when first infected. As a result, many people don't know they have the condition.

Symptoms may not appear until months or sometimes years after you're exposed to the virus.

If you experience symptoms when first infected, they usually appear four to seven days after you have been exposed to the virus. The symptoms are usually more severe first time around than in cases of recurrent infections.

Primary infection

The symptoms of genital herpes for the first time include -

- Feeling generally unwell with aches, pains and flu-like symptoms such as fever, tiredness, headache, swollen glands, aches and pains in the lower back and down the legs or in the groin. This will be followed by -
  - ⋆ Stinging, tingling or itching in the genital or anal area (fpa, 2014b).
  - ⋆ small blisters that burst to leave red, open sores around your genitals, rectum, thighs and buttocks,
  - ⋆ blisters and ulcers on the cervix (lower part of the womb) in women ,

- ⋆ vaginal discharge in women (avert, 2015b).
- ⋆ Pain when passing urine caused by the urine flowing over the sores (fpa, 2014b).

These symptoms may last up to 20 days. However, the sores will eventually scab and heal without scarring (avert, 2015b).

Recurrent infections

Although the initial symptoms of genital herpes clear up, the virus remains dormant (inactive) in a nearby nerve. The virus may be reactivated from time to time, travelling back down the nerve to your skin and causing recurrent outbreaks.

Symptoms of a recurrent outbreak may include -

- you may get a flu-like illness before an outbreak,
- the blisters and sores are usually fewer, smaller, and less painful and heal more quickly (fpa, 2014b),
- a tingling, burning or itching sensation around your genitals, and sometimes down your leg, before blisters appear,
- painful red blisters that soon burst to leave sores around your genitals, rectum (back passage), thighs and buttocks,
- blisters and ulcers on the cervix in women (NHS, 2014d), (avert, 2015b).

Recurrent outbreaks are usually shorter and less severe. This is because your body has produced protective antibodies (proteins that fight infection) in reaction to the previous infection. Your body now recognises the virus and mounts a response that is able to fight HSV more effectively.

Over time, you should find any recurrent genital herpes infections become less frequent and less severe (NHS, 2014d).

How will I know if I have it?

You can only be certain you have genital herpes if you have a check-up when you've got signs or symptoms. You could have genital herpes even if your partner(s) has never had an outbreak.

It is possible to have more than one sexually transmitted infection at the same time. You may wish to have a check-up for infection if -

- you or a partner have, or think you might have, symptoms,
- you have recently had unprotected sex with a new partner,
- you or a partner have had unprotected sex with other partners,
- a sexual partner tells you they have a sexually transmitted infection,
- you have another sexually transmitted infection,
- you are pregnant or planning a pregnancy.

Having genital herpes might mean you are more at risk of becoming infected with HIV if you're having sex with an HIV positive partner or of passing it on if you are HIV positive (fpa, 2014b).

What is the treatment?

The aim of the treatment is to relieve the pain, and to prevent the virus from multiplying.

- Treatment is recommended when you have the first outbreak as this may provide some relief.
- Treatment is usually started within five days of the start of the first outbreak and while new blisters or sores are still forming. It involves taking antiviral tablets daily (sometimes up to five times a day) for five days. There are several different antiviral tablets that can be used.
- Some people find it helpful to take antiviral treatment when they get another outbreak of genital herpes. You may be given some tablets to take at home. These need to be started as soon as the outbreak begins.
- People who have repeated outbreaks (usually more than six in a year) may be given longer courses of the tablets to try to reduce the number of outbreaks. This is known as suppressive therapy. Suppressive therapy can stop outbreaks completely.
- If you are pregnant, or trying to become pregnant, tell the doctor or nurse so they can talk to you about pregnancy and Herpes simplex. If you have an outbreak of herpes in pregnancy it is still possible to have treatment,
- As genital herpes is caused by a virus and not bacteria, antibiotics will not help.
- The treatment you can buy for facial cold sores is not suitable for genital herpes (fpa, 2014b).

Is there anything I can do myself to relieve the discomfort?

There are several things you can do to ease the discomfort and speed up the healing process -

- Apply an ice pack. Put ice cubes in a plastic bag and then wrap them in a clean towel or flannel. Put them on the sores for up to an hour or so. Ice should not be put directly onto the skin.
- Put cold, wet tea bags on the sores. They are soothing and speed up healing.
- Take a cool shower to soothe the sores.
- Apply a local anaesthetic ointment such as lidocaine. This will help relieve the pain. You can buy this from the pharmacy.
- Avoid washing too often, and dab the affected area gently to dry it.
- Gently bathe the area using cottonwool and a warm salt water solution (1tsp to 1pt water).

- If urinating is painful, go to the toilet in a warm bath or shower.
- Wash your hands before touching the blisters or sores. This helps to avoid introducing bacteria which may cause an infection and delay the healing process.
- Drink extra fluids, such as water or soft drinks.
- Wear loose clothing.
- Use a mild pain-relieving drug, if you need to (fpa, 2014b).
- keeping the affected area clean using plain or salt water to prevent blisters or ulcers from becoming infected and help them heal quicker,
- applying a wrapped up ice pack to the sores to ease the pain and speed up the healing process,
- applying petroleum jelly, such as Vaseline, or a painkilling cream to any blisters or ulcers to reduce the pain when passing urine,
- drinking plenty of fluids to dilute your urine - this will make passing urine less painful,
- avoiding tight clothing because it may irritate the blisters and ulcers (avert, 2015b).

When will the signs and symptoms go away?

Outbreaks will last a different length of time in each person and will depend on your general state of health and whether this is the first or a recurrent outbreak of genital herpes. The first outbreak of herpes may last from 2–4 weeks in total.

- The flu-like symptoms usually last for about a week.
- Individual sores take around 5–10 days to heal. Once the sores start healing they are less painful.
- Pain and irritation can last up two weeks or longer (fpa, 2014b).

The signs and symptoms of a recurrent outbreak of genital herpes will usually last for a shorter time than the first outbreak (fpa, 2014b).

How can I prevent further outbreaks?

Some people find different triggers bring on an outbreak. If you notice a pattern, you may be able to do something about it by changing certain aspects of your life.

Common triggers can include -

- being ill, run down, tired or stressed,
- different times in the menstrual cycle,
- friction from sex or masturbation,
- ultraviolet light on the affected skin area (such as from sunbathing or using sun beds),
- tight clothing and nylon or lycra underwear,
- drinking alcohol or smoking (fpa, 2014b).

Recurrences eventually stop altogether within 18–24 months for many people, although it may take much longer for others (fpa, 2014b).

What happens if its not treated?

It is not essential to have treatment as genital herpes will clear up by itself. However, prompt treatment at the start of an outbreak can be a great help - it can reduce the time the outbreak lasts, help the healing process and can reduce the risk of you passing the virus on to someone else (fpa, 2014b).

In rare cases, blisters can become infected by other bacteria causing a skin infection that spreads to other parts of the body like the lips, hands or fingers (avert, 2015b).

Genital herpes and HIV

If you are experiencing recurrent outbreaks of genital herpes you should also consider getting tested for HIV as this may be a sign of a weakened immune system (avert, 2015b).

Pregnancy and genital herpes

A pregnant woman can pass genital herpes on to her baby. A healthcare professional will advise you about what to do if you develop genital herpes whilst you are pregnant, or if you have recurrent genital herpes and become pregnant (avert, 2015b).

How can I protect myself against Genital Herpes and other STI's?

The blisters and sores are highly infectious, so if you or a partner have cold sores or genital herpes -

- avoid kissing when you, or a partner, have cold sores around the mouth,
- avoid oral sex when you, or a partner, have mouth or genital sores,
- avoid any genital or anal contact when you, or a partner, have genital sores or blisters, or if you feel an outbreak starting (fpa, 2014b).

It is possible to get genital herpes and other sexually transmitted infections by having sex with someone who has the infection but has no symptoms. The following measures will help protect you from genital herpes and most other sexually transmitted infections including HIV, chlamydia and gonorrhoea. If you have a sexually transmitted infection they will also help prevent you from passing it on to a partner (fpa, 2014b).

- Use condoms (male or female) every time you have vaginal or anal sex.
- If you have oral sex, use a condom to cover the penis, or a latex or polyurethane (soft plastic) square to cover the female genitals or male or female anus.
- If you are a woman and rub your vulva against your female partner's vulva one of you should cover the genitals with a latex or polyurethane square.
- If you are not sure how to use condoms correctly see Condoms.
- Avoid sharing sex toys. If you do share them, wash them or cover them with a new condom before anyone else uses them (fpa, 2014b).

Genital warts

Genital warts are small fleshy growths, bumps or skin changes that appear on or around the genital or anal area.

Genital warts are very common. In England, they are the second most common type of sexually transmitted infection (STI) after chlamydia.

Genital warts are the result of a viral skin infection caused by the human papilloma virus (human papilloma virus (HPV)). They are usually painless and do not pose a serious threat to health.

But they can be unpleasant to look at and cause psychological distress.

There is no evidence that your fertility will be affected by genital warts.

What causes them?

Genital warts are caused by an infection of the skin of the genital and anal area with the HPV.

There are over 100 different types of HPV which can affect different parts of the body, including the hands and feet (a wart on the foot is called a verruca). Approximately 30 types of HPV can live in and around the genital and anal areas but most genital warts are caused by just two types of virus (types 6 and 11) (fpa, 2014c).

How are they passed on?

The virus that causes genital warts is easily passed from one person to another through sexual contact. Anyone who is sexually active can get the virus. Both men and women can have the virus, and pass it on.

- Genital warts can spread from one person to another during vaginal or anal sex.

- The virus can be spread by skin to skin contact so it can be passed on by close genital contact - you don't need to have penetrative sex (vaginal or anal) to pass it on.
- The virus will not pass through a condom but as condoms do not cover all of the genital area it is possible to infect genital skin that is not covered by the condom.
- The virus is most likely to be passed on when warts are present but it is still possible to pass the virus on after warts have disappeared.
- It is possible, but very rare, to develop warts in the mouth or throat, or on the lips from oral sex.
- Warts can spread from the genital area to the area around the anus without having anal sex.
- It is possible for warts on the hand to be passed to the genitals but this is very rare.
- It is possible for a pregnant woman who has genital warts at the time to pass the virus to her baby at birth, but this is rare.
- You cannot get genital warts from kissing, hugging, sharing baths or towels, from swimming pools, toilet seats or from sharing cups, plates or cutlery (fpa, 2014c).

What are the signs and symptoms of them?

Most people with HPV infection will not develop visible warts and the virus will go away on its own. This means you may not know whether you or your partner have the virus.

If warts do appear, this can happen from three weeks to many ,or even years, after coming into contact with the virus. You might notice small, fleshy growths, bumps or skin changes which may appear anywhere in or on the genital or anal area.

- In women, warts can be found on the vulva, cervix, upper thighs, in the vagina and on, or inside, the anus.
- In men, warts can be found on the penis, scrotum, urethra, the upper thighs and on, or inside, the anus.
- You might see or feel them, or your partner might notice them. Often they are so tiny, or so difficult to see, that you don't even know you have them.
- They can be flat or smooth small bumps or quite large, pink, cauliflower-like lumps.
- Warts can appear on their own or in groups.
- Genital warts are usually painless but may occasionally itch and cause some inflammation.
- They may cause bleeding from the anus or the urethra.
- If your flow of urine is distorted this may be a sign of warts in the urethra (fpa, 2014c).

How will I know if I've got it?

You can usually only be certain you have genital warts if a doctor or nurse looks at the warts and confirms you have the infection. Even if you or your partner feel sure you have genital warts, it is still advisable to have a check-up to confirm this.

You could still have genital warts even if your partner doesn't have any visible warts.

It is possible to have more than one sexually transmitted infection at the same time. You may wish to have a check-up for infection if -

- you or your partner have, or think you might have, symptoms,
- you have recently had unprotected sex with a new partner,
- you or your partner have had unprotected sex with other partners,
- a sexual partner tells you they have a sexually transmitted infection,
- you have another sexually transmitted infection,
- you are pregnant or planning a pregnancy (fpa, 2014c).

What is the treatment for it?

You will only be offered treatment if you have visible warts. The treatment will depend on what the warts look like, how many you have and where they are.

The aim of treatment is to remove visible warts. How effective the treatment is varies and depends on the size and type of warts, the treatment that is used and how good your immune system is at fighting the virus.

Some people do not need treatment or they choose not to have any. However, for most people, having treatment is likely to make the warts go away more quickly. As genital warts are caused by a virus and not bacteria, antibiotics will not get rid of warts.

Visible warts can be removed by -

- Putting cream or a liquid onto the warts (for a few days each week). This can usually be done by yourself at home. Some people ask a partner to apply the cream or liquid for them. You may have to apply this treatment for a number of weeks.
- Freezing (cryotherapy).
- Heat (electrocautery), using local anaesthetic.
- Surgery, using local anaesthetic.
- Laser treatment, using local anaesthetic.

Some creams can weaken latex condoms, diaphragms and caps. Polyurethane types can be safely used. Ask the doctor or nurse for advice.

Sometimes more than one treatment is used at the same time. These treatments may be uncomfortable, but they are not usually painful. Treatments can cause irritation and soreness for a couple of days, so the doctor may recommend you use some pain-relieving drugs.

- Avoid perfumed soap, bath oils, bubble baths, creams and lotions until treatment is completed as these may irritate the skin.
- Tell the doctor or nurse if you are pregnant, or think you might be, as this may affect the type of treatment you are given.
- Wart treatments sold at the pharmacy are not suitable for genital warts.
- There is no evidence that complementary therapies can cure genital warts (fpa, 2014c).

What happens if it isn't treated?

If left untreated genital warts may disappear, stay the same, or grow larger in size or number. Over time most warts will eventually go away without treatment. For some people this may take a long time, particularly if you have an illness that affects the way your immune system works, making it difficult to fight off infection (fpa, 2014c)

Can it go away without treatment?

It is not usually harmful to your health if the warts are not treated but you may find them uncomfortable and may not like the way they look. Treating the warts may reduce the risk of you passing them on to someone else (fpa, 2014c)

Preventing genital warts

Using condoms can help protect against the virus that causes genital warts. A vaccine is also available.

Condoms

Using condoms (male or female) every time you have vaginal or anal sex is the most effective way to avoid getting genital warts, other than being celibate.

Condoms also helps protect you from other STI's and pregnancy.

However, the protection offered by condoms is not 100%. Genital warts are the result of a viral skin infection caused by the HPV.

Because HPV is spread by skin-to-skin contact, it is possible for the skin around your genital area not covered by the condom to become infected.

But condoms remain the safest option. If you have oral sex, cover the penis with a condom. A dental dam, which is a latex or polyurethane (plastic) square, can be used to cover the anal area or female genitals.

See also Condoms.

Dental dams are usually only available at sexual health and genitourinary medicine (GUM) clinics, although your local pharmacist may be able to order some for you.

Avoid sharing sex toys. However, if you do share them, wash them or cover them with a new condom before anyone else uses them.

Following these measures will also help protect you from getting a number of other STI's, such as HIV, chlamydia and gonorrhoea.

HPV vaccines

HPV vaccines are currently not available for free outside of the The UK-wide National Health Service (NHS) vaccination schedule. In the UK, HPV vaccines are offered to all girls in school year 8 aged 12 to 13 years.

Since September 2012, the vaccine Gardasil has been used and can help protect against HPV types 6 and 11, which cause around 90% of genital warts.

It also protects against types 16 and 18, which are linked to more than 70% of cases of cervical cancer in the UK.

Before September 2012, a different vaccine called Cervarix was used to protect against HPV types 16 and 18.

HPV vaccines cannot protect against all types of HPV. If you are a woman and have received HPV vaccinations, you should still attend cervical screening (smear tests) as the vaccines do not guarantee that you will not develop cervical cancer in the future.

HPV vaccines are designed to try to help protect you from developing certain types of HPV infection. They are likely to be of most benefit before you have had sexual contact. It is not clear if there would be any benefit in receiving HPV vaccination if you -

- are a man,
- are a woman too old to have been included in the NHS vaccination schedule,
- have already had sex (NHS, 2014e).

Gonorrhoea

Gonorrhoea is a STI caused by bacteria called Neisseria gonorrhoea or gonococcus. It used to be known as 'the clap' (NHS, 2015d).

Gonorrhoea is caused by bacteria which are found mainly in the semen and vaginal fluids of men and women who have the infection (fpa, 2014d).

Gonorrhoea is easily passed between people through -

- unprotected vaginal, oral or anal sex,
- sharing vibrators or other sex toys that haven't been washed or covered with a new condom each time they're used.

The bacteria can infect the cervix, the urethra, the rectum, and less commonly the throat or eyes.

The infection can also be passed from a pregnant woman to her baby. If you're pregnant and may have gonorrhoea, it's important to get tested and treated before your baby is born. Without treatment, gonorrhoea can cause permanent blindness in a newborn baby.

Gonorrhoea isn't spread by kissing, hugging, sharing baths or towels, swimming pools, toilet seats, or sharing cups, plates and cutlery, because the bacteria can't survive outside the human body for long (NHS, 2015d).

Gonorrhoea is easily passed from one person to another through sexual contact. Anyone who is sexually active can get it and pass it on. You don't need to have lots of sexual partners (fpa, 2014d).

Gonorrhoea is resistant to many commonly used antibiotics. You need to be tested in a specialised sexual health service to ensure you receive the correct treatment.

If you have gonorrhoea we recommend that you should have routine tests for other sexually transmitted infections including chlamydia, trichomonas, syphilis and HIV (BASHH, 2014).

How common is gonorrhoea?

It is the second most common bacterial STI in the UK.

It is found most frequently in young people under the age of 25 years, in men who have sex with men and in people living in large cities (BASHH, 2014).

Signs and symptoms

You may not notice any obvious signs or symptoms if you have been infected with gonorrhoea. Signs and symptoms can show up 1–14 days after coming into contact with gonorrhoea, many months later, or not until the infection spreads to other parts of your body.

Women

- An unusual vaginal discharge which may be thin or watery, yellow or green,
- Pain, or a burning sensation, when passing urine,
- Lower abdominal pain or tenderness, this is less common,
- Rarely, bleeding between periods or heavier periods (including women who are using hormonal contraception), this is less common.

Men

- An unusual discharge from the tip of the penis the discharge may be white, yellow or green,
- Pain, or a burning sensation, when passing urine,
- inflammation (swelling) of the foreskin,
- Rarely, pain or tenderness in the testicles, this is rare.

Symptoms in men usually appear within 2–5 days of catching the infection (BASHH, 2014).

Men and women

Infection in the rectum - This does not usually have any signs and symptoms but may cause anal pain, discomfort or discharge.

Infection in the throat - This usually has no symptoms.

Infection in the eyes - This can cause pain, swelling, irritation and discharge (conjunctivitis).

Babies

Gonorrhoea can be passed from a mother to her baby during childbirth. Newborn babies normally show symptoms in their eyes during the first two weeks. The eyes become red and swollen, and have a thick, pus-like discharge.

Gonorrhoea can be treated with antibiotics when you're pregnant or when you're breastfeeding. The antibiotics won't harm your baby (NHS, 2015d).

How will I know if I have it?

You can only be certain you have gonorrhoea if you have a test. If you think you may have gonorrhoea it is important that you don't delay getting a test.

You may wish to have a test if -

- you have, or think you might have, symptoms,
- you have recently had unprotected sex with a new partner,
- you or your partner have had unprotected sex with other partners,
- during a vaginal examination your doctor or nurse says that the cells of the cervix are inflamed and/or there is an unusual discharge,
- a sexual partner tells you they have a sexually transmitted infection,
- you have another sexually transmitted infection,
- you are pregnant or planning a pregnancy (fpa, 2014d).

You could still have gonorrhoea even if your partner has tested negative - you should not rely on a partner's negative test result.

If you have had gonorrhoea and it has been treated, you will not be immune to the infection - you can get it again.

If you have gonorrhoea you may wish to be tested for other sexually transmitted infections as you can have more than one sexually transmitted infection at the same time. Having an infection such as gonorrhoea can mean you are more at risk of becoming infected with HIV or transmitting it if you are HIV positive.

Testing for it

There are many different ways to test for gonorrhoea. In many cases, a swab will be used to remove a sample for testing, although men may only be asked to provide a urine sample.

Cervical smear tests and routine blood tests do **not** detect gonorrhoea. If you are not sure whether you have been tested for gonorrhoea, just ask.

A swab looks a bit like a cotton bud, but it's smaller and rounded. It's wiped over parts of the body that may be infected to pick up samples of discharge. This only takes a few seconds and isn't painful, although it may be a little uncomfortable.

The different tests that may be used to detect gonorrhoea in men and women are described below.

Women

For women, a doctor or nurse will usually take a swab to collect a sample from the vagina or cervix during an internal examination. In some cases, a sample may also be taken from the urethra.

Sometimes you may be asked to use a swab or tampon to collect a sample from inside your vagina yourself.

Women aren't usually asked to provide a urine sample to check for gonorrhoea, because this is a less accurate test for women. (NHS, 2015d).

Men

Men will normally be asked to provide a urine sample, or a swab may be used to remove a sample of discharge from the end of the penis.

If you're asked to provide a urine sample, it's important not to urinate for about two hours beforehand, because this can wash the bacteria away and affect the results of the test (NHS, 2015d).

Infections of the rectum, throat and eyes

If there's a possibility that your rectum or throat is infected, the doctor or nurse may need to use a swab to collect a sample from these areas.

If you have symptoms of conjunctivitis, such as red, inflamed eyes with discharge, a sample of the discharge may be collected from your eye (NHS, 2015d).

How accurate are the tests?

The accuracy of a gonorrhoea test depends on the kind of test used and which part of your body the sample is collected from.

As no test is 100% accurate there is a small chance that the test will give a negative result when you do have the infection. This is known as a false negative result. This can sometimes explain why you might get a different result when you go to a different clinic to have another test or why you and your partner might get a different test result.

It is possible for some gonorrhoea tests to be positive if you haven't got gonorrhoea, but this is uncommon. If there are doubts about the result you may be offered a second test to confirm the presence of gonorrhoea (fpa, 2014d).

Getting the results

Some clinics may be able to carry out rapid tests, when the doctor can view the sample through a microscope and give you your test results straight away. Otherwise, you'll have to wait up to two weeks to get the results (NHS, 2015d).

What is the treatment?

The treatment for gonorrhoea is antibiotics. The treatment is at least 95% effective.

- Treatment involves having an antibiotic injection (usually in the buttocks or thigh)(fpa, 2014d) and a single dose of antibiotic tablet(s). It's sometimes possible to have another antibiotic tablet instead of an injection, if you prefer (NHS, 2015d).
- If there is a high chance you have the infection, treatment may be started before the results of the test are back. You will always be given treatment if your partner is found to have gonorrhoea.
- You may also need other treatment if complications have occurred.
- There is no evidence that complementary therapies can cure gonorrhoea.

You should avoid having sex until you (and your partner) have been treated and given the all-clear, to prevent re-infection or passing the infection on to anyone else (NHS, 2015d).

You should notice an improvement in the signs and symptoms quite quickly.

- Discharge or pain when you urinate should improve within 2–3 days.
- Discharge and discomfort in the rectum should improve within 2–3 days.
- Bleeding between periods or heavier periods that have been caused by gonorrhoea should have improved by your next period.
- Pelvic pain and pain in the testicles should start to improve quickly but may take up to two weeks to go away.

If you have pelvic pain or painful sex that does not improve, see your doctor or nurse. It may be necessary to have some further treatment or to investigate other possible causes of the pain (fpa, 2014d).

You will need to have a follow-up test 2–4 weeks after taking antibiotics. This is particularly important if -

- you think you may have come into contact with gonorrhoea again,
- you had unprotected sex with your partner in the week following the treatment,
- the signs and symptoms don't go away,
- you had gonorrhoea of the throat,
- your test was negative but you develop signs or symptoms of gonorrhoea.

How quickly the test can be repeated will depend on which test is being used. The clinic or general practice will advise you.

If you were treated for gonorrhoea in early pregnancy you may be advised to have another test later in the pregnancy.

You can always go back to the doctor, nurse or clinic if you have any questions or need any advice on how to protect yourself from infection in the future (fpa, 2014d).

What happens if it isn't treated?

If gonorrhoea is treated early it is unlikely to cause any long term problems. Not everyone who has gonorrhoea has complications. However, without effective treatment the infection can spread to other parts of the body. The more times you have gonorrhoea the more likely you are to get complications.

- In women, gonorrhoea can spread to other reproductive organs causing PID. This can lead to long-term pelvic pain, blocked fallopian tubes, infertility and ectopic pregnancy.
- In men, gonorrhoea can lead to a painful infection in the testicles and possibly reduced fertility.
- Less commonly, gonorrhoea can cause inflammation of the joints and tendons, and skin lesions (fpa, 2014d).

Can it go away without treatment?

It can but it is unlikely. The infection may be there for many months before it goes away and without treatment you cannot be sure when or if it will go away. If you delay seeking treatment you risk the infection causing long-term damage and you may pass the infection on to someone else (fpa, 2014d).

Hepatitis

Hepatitis is an inflammation of the liver. There are three main types: A, B and C.

Hepatitis can be acute or chronic. Acute hepatitis happens after initial infection and is short term. It can lead to chronic hepatitis which is long term.

Some types of hepatitis - such as hepatitis A - only cause acute infection.

Others can be long term (chronic) and cause lasting damage to the liver. Very serious cases can lead to liver failure or cancer.

Some types of hepatitis can be vaccinated against and treated (tht, 2015a).

Viral causes of hepatitis

There are seven viruses that are known to cause hepatitis. These are designated by the letters A to G. However, the cause of some hepatitis is still unknown, leading scientists to believe there are other viruses that have yet to be discovered.

The three most common viral forms of hepatitis are -

- Hepatitis A,
- Hepatitis B,
- Hepatitis C,

The other forms of hepatitis - D, E, F and G - are very rare (tht, 2015a).

Hepatitis A

Hepatitis A is caused by a virus that infects the liver. It is easy to pass on during sex or get from contaminated food and water. Nearly everyone makes a full recovery (tht, 2015b).

Symptoms

Hepatitis A symptoms can be so mild you may not realise you have it, but up to six weeks after infection it can cause -

- mild flu-like symptoms,
- diarrhoea,
- nausea,
- extreme tiredness,
- itchy skin,
- stomach pain,
- jaundice (tht, 2015b)

Symptoms can last several weeks, taking months to get back to normal.

Transmission

Someone with hepatitis A is most infectious two weeks before jaundice appears.

The virus lives in faeces and minute traces of it carry the infection on the hands or on food prepared by an infected person. Water can also be contaminated, especially abroad.

The virus needs to get into the mouth to infect someone. This can happen during sex when tiny amounts of faeces get on fingers and into mouths through -

- rimming
- fingering
- anal sex without condoms
- handling used condoms and sex toys that have been in someone else's anus (tht, 2015b).

Protection

You can protect yourself by getting vaccinated - it's especially important that you do it if you -

- have close contact with someone who has the infection
- are a gay man
- inject drugs
- travel to parts of the world where the infection is common (tht, 2015b).

You might be able to get vaccinated for free by your GP or a sexual health clinic. The vaccine protects you for 10 years or longer.

A vaccine exists that protects against both hepatitis A and B.

If you have hepatitis A

Tell people you live with or have recently had sex with to ask their doctor about having an urgent vaccination.

Avoid sex and preparing food for others until told you are told you are no longer infectious.

- avoiding sex that involves contact with faeces,
- using condoms for anal sex,
- washing hands after touching someone's anus or handling used condoms and sex toys,
- using a latex barrier (like a condom cut into a square) for rimming and latex gloves for fisting (tht, 2015b).

If you are not vaccinated and are exposed to hep A, there is a post-exposure prophylaxis called human normal immunoglobulins (HNIGS). This can be given within two weeks after exposure and it can protect you for up to three to six months.

Treatment

Most cases are diagnosed by GP's (family doctors) rather than sexual health clinics and no special treatment is needed.

If you recently had sex with someone or share your house with others, they should see a doctor straight away about getting vaccinated to stop them getting infected.

Avoid sex and preparing food for others until told you are no longer infectious.

A blood test will confirm whether you have picked up the virus.

The usual treatment for hepatitis A is to simply rest.

You may need some time off work while you recover from the flu-like symptoms. Once you have had hepatitis A you're immune and cannot get it again, but you can get other types of hepatitis (tht, 2015b).

What else can I do to stay healthy?

- avoid alcohol until your liver recovers,
- avoid paracetamol,
- recreational drugs should be avoided to allow your liver to get better (tht, 2015b).

Hepatitis B

Hepatitis B is an infection of the liver caused by the hepatitis B virus. It is very infectious (100 times more infectious than HIV) and very easily transmitted through unprotected sex or by sharing needles to inject drugs.

Most people who contract hepatitis B do not have symptoms. If symptoms do occur they can appear one to six months after coming into contact with the virus. The infection can persist for many years and silently cause severe liver damage, including cirrhosis, liver failure and liver cancer.

In most people a full course of vaccination prevents infection. However, in a small number of people it may not be effective.

The following people should consider having the hepatitis B vaccination -

- Men who have sex with men,
- Anyone who has ever injected drugs,
- Anyone who has been paid for sex,
- Anyone who has paid for sex,
- Anyone who has had 9 or more sexual partners within the last 12 months,
- Anyone who has a sexual partner with Hepatitis B infection,
- Anyone who has been sexually assaulted recently (umbrellahealth, 2016a).

How do you get it?

Hepatitis B infection can be passed on -

- through unprotected anal, vaginal or oral sex (sex without a condom)

- as a result of blood-to-blood contact -
  - ⋆ via sharing of injecting equipment, such as needles, spoons and filters
  - ⋆ through the use of non-sterile needles for tattooing, piercing or acupuncture
- through transmission from mother to baby during pregnancy, when giving birth or during breastfeeding. All pregnant women in the UK are tested for hepatitis B.
- if you work closely with blood and bodily fluids

The virus can be passed on in these body fluids -

- blood,
- semen,
- pre-cum,
- vaginal secretions (tht, 2015c).

It is passed on through -

- oral, vaginal or anal sex without a condom,
- rimming,
- sharing sex toys,
- sharing injecting drug equipment such as needles and syringes which can carry infected blood,
- a pregnant woman with the virus can give it to her baby during childbirth (tht, 2015c).

It can be found in saliva but there are no proven cases of it being passed on through kissing. Infections from bites are rare. You can pass on hepatitis B from two weeks before developing jaundice (tht, 2015c).

Avoid sharing -

- razors,
- toothbrushes,
- nail scissors,
- hair clippers, and
- tweezers (tht, 2015c),
- towels (umbrellahealth, 2016a).

Traces of blood on any of these can pass on hepatitis B. This includes dried blood as the virus can survive for at least a week outside of the body (tht, 2015c).

Symptoms

Many people with hepatitis B do not even realise that they are infected and most people who are infected have no symptoms for many years.

Many people who get hepatitis B notice no symptoms or they are so mild that they may not realise they have it. But weeks or months after infection it can cause -

- loss of appetite,
- vomiting (umbrellahealth, 2016a).
- mild flu-like illness,
- diarrhoea,
- nausea,
- extreme tiredness,
- itchy skin,
- stomach pain,
- jaundice (tht, 2015c).

Symptoms can last several weeks, taking months to get back to normal.

Most people make a full recovery but up to one in 20 become 'carriers' with chronic (long-term) infection. They usually feel fine but stay infectious to others, with a small risk of going on to develop liver disease.

Around one in 100 people gets a more serious illness which can be fatal if not treated immediately (tht, 2015c).

Diagnosis

Hepatitis B is diagnosed by a blood test (umbrellahealth, 2016a).

How can I protect myself and others?

Vaccination

In most people a full course of hepatitis B vaccination prevents infection. However, in a small number of people it may not be effective.

Vaccination is done through a course of injections into the upper arm. It is essential to complete the full course.

- You will have blood taken before the first vaccination is given to ensure that you do not already have hepatitis B,
- After you have received the injection, we recommend waiting 10 minutes in the clinic in case of any reaction to the vaccine,
- A booster vaccination is recommended five years after completing the course if you remain at risk of infection.

Possible side effects of the vaccination include -

- localised pain in the arm,
- flu-like symptoms for up to 72 hours.

Who should be vaccinated?

The following people should consider having the hepatitis B vaccination -

- have close contact with someone with the infection (tht, 2015c).
- Men who have sex with men,
- Anyone who has ever injected drugs,
- Anyone who has been paid for sex,
- Anyone who has paid for sex,
- Anyone who has had 9 or more sexual partners within the last 12 months,
- Anyone who has a sexual partner with Hepatitis B infection,
- Anyone who has been sexually assaulted recently (NHS, 2015a).
- inject drugs,
- travel to parts of the world where the infection is common (tht, 2015c).

There is a vaccine which can protect you against both hepatitis A and B.

You might be able to get vaccinated for free by your GP or some sexual health clinics.

You may need a booster injection of the vaccination after five years.

If you have hepatitis B tell people you live with or recently had sex with to urgently ask their doctor about vaccination. Avoid sex until told you are no longer infectious (tht, 2015c).

Although not as effective as being vaccinated, the following can also cut the risk -

- condoms for penetrative sex
- a latex barrier (eg, a condom cut into a square) for rimming (tht, 2015c).

If you are a carrier you may want to tell a partner and explain that you are infectious. They can then decide if they want to take precautions (eg, get vaccinated) or are happy to take any risk.

That way they cannot accuse you of infecting them without them knowing the risk was there.

If you are not vaccinated against hepatitis B and are exposed to the virus, there is a treatment which may stop you being infected. Hepatitis B immunoglobulin (HBIG) is an injection of antibodies. It is best to take it within 48 hours of exposure - you will be vaccinated at the same time (tht, 2015c).

What can I do if I think I have it?

Most cases are diagnosed by GP's (family doctors), not sexual health clinics, and treatment isn't needed for most people. If you had sex with someone recently or you share your house with others, they can be vaccinated to stop them getting the infection - they should see a doctor straight away.

Avoid sex until you're told are no longer infectious or until your partners have been vaccinated.

A blood test will confirm whether you have the virus (tht, 2015c).

Treatment

In most cases no treatment is needed for acute hepatitis B. It may take a while to recover and you may want to take some time off work.

If you have chronic hepatitis B you may need treatment at some point to try to slow down the replication of the virus. However, treatment cannot usually cure chronic hepatitis B. A small number of carriers go on to get liver disease (and a small number of those get liver cancer), and may need a liver transplant.

If your body clears hepatitis B, you're immune and cannot get it again - but you can get other types of hepatitis (tht, 2015c).

What else can I do to stay healthy?

- Avoid alcohol until your liver recovers,
- Hepatitis B can make you more vulnerable to infection, so smoking is best avoided due to the health problems it causes,
- recreational drugs should be avoided to allow your liver to get better,
- eat a healthy balanced diet (tht, 2015c).

Hepatitis C

Hepatitis C is the most serious type of hepatitis. It's caused by a virus that attacks the liver and is easily spread by sharing drug injecting equipment. It can also be spread through sex.

Without treatment most people with hepatitis C can't clear it, and they stay infectious to others.

There is no vaccine against hepatitis C. Some treatment can be difficult to take - although newer treatments have fewer side effects. The virus can cause liver disease that can be fatal (tht, 2015d).

Symptoms

Most people who get this infection don't notice any symptoms when they are first infected. It can take years before you feel ill, with symptoms often not easily identified as being due to hepatitis C (tht, 2015d).

The symptoms can include -

- mild flu-like symptoms,
- diarrhoea,
- nausea,
- extreme tiredness,
- itchy skin,
- stomach pain,

- jaundice,
- mental confusion and depression - these are specific to hepatitis C (tht, 2015d).

Transmission

The hepatitis C virus is found in blood and is passed on when infected blood gets into another person's bloodstream. It is seen as unlikely (but not impossible) that it can be passed on in semen.

Most people get the virus from sharing drug injecting equipment such as needles, syringes, spoons, filters and swabs. Sharing things like straws and bank notes for snorting drugs might pass the virus on.

In the UK piercing and tattooing should be safe but unsterilised equipment abroad can spread the virus.

An infected person risks infecting others if they share anything that might have blood on it, eg, toothbrushes or razors.

A pregnant woman with the virus can give it to her baby during pregnancy or childbirth.

Blood transfusions in the UK are safe because blood is screened (tht, 2015d).

Hepatitis C and sex

Hepatitis C is rarely passed on during sex between a man and a woman. There's also no significant spread of hepatitis C among HIV negative gay men. But the infection has spread sexually among gay men with HIV and is much more common among them.

The virus spreads through unprotected anal sex and fisting. It is also carried from one rectum to another during group sex, on objects such as sex toys, fingers, enema equipment, condoms, latex gloves or in contaminated lubricant (tht, 2015d).

How can I protect myself and others?

There is no vaccination against hepatitis C.

The risk of infection is reduced by not sharing injecting drug equipment (eg, needles, syringes, swabs, spoons, filters) or things that may have blood on them such as toothbrushes and razors. Also avoid sharing straws or rolled up banknotes if snorting drugs with others.

The risk of contact with blood during sex can be reduced by using condoms for anal and vaginal sex and latex gloves for fisting.

Take precautions to stop the virus spreading from person to person during group sex. Do this by covering anything which goes from one partner to another with a fresh condom or fresh latex glove for each new person it enters. Clean objects with warm water and anti-bacterial soap before using on a new partner.

Enema equipment and pots of lubricant should not be shared.

If you have hepatitis C you shouldnt give blood. In some extremely rare cases the organs of people with hep C have been donated to others with the same condition.

If you are a 'carrier' you may want to tell a partner and explain that you are infectious. They can then decide if they are happy to take any risks and want to take precautions. That way they cannot accuse you of infecting them without them knowing the risk was there (tht, 2015d).

What can I do if I think I have hepatitis C?

A doctor or sexual health clinic can test you to see if you have hepatitis C. If you do, treatment is available and you can discuss how to avoid infecting your sexual partners or people you live with.

It can take three to six months before the blood test for hepatitis C will be able to detect signs of infection in your blood (tht, 2015d).

Is there a vaccination against hepatitis C?

No, there is no vaccination against hepatitis C, however you can be vaccinated against hepatitis A and B.

If you already have hepatitis C, it is recommended to have the vaccination against hepatitis A and B to protect your liver form further damage (tht, 2015d).

Treatment

If tests show you have had the virus for longer than six months you are a 'carrier' with chronic (long-term) infection.

Drug treatment is available and has recently improved, with a better success rate and fewer side effects.

Treatment can last for 12 weeks to 12 months and involves tablets and/or injections. Avoiding alcohol and recreational drugs is advised.

If you are cured of hepatitis C you are not immune, you can get it again. You can also still get other types of hepatitis - having hepatitis C and another type is more serious (tht, 2015d).

Why should I get treated?

Hepatitis C can be fatal.

Untreated hepatitis C can lead to scarring of the liver known as 'cirrhosis'. A small number of people with cirrhosis will go on to get liver failure, the only treatment for which is a liver transplant. A small proportion of people with cirrhosis develop liver cancer (tht, 2015d).

What else can I do to stay healthy?

- avoid alcohol,
- liver disease can make you more vulnerable to infection - smoking is best avoided as it can increase the seriousness of liver damage,
- recreational drugs should be avoided to allow your liver to get better,
- eat a healthy balanced diet (tht, 2015d).

HIV

HIV is a virus that attacks the immune system, and weakens your ability to fight infections and disease. It's most commonly caught by having sex without a condom.

It can also be passed on by sharing infected needles and other injecting equipment, and from an HIV-positive mother to her child during pregnancy, birth and breastfeeding.

HIV stands for human immunodeficiency virus. The virus attacks the immune system, and weakens your ability to fight infections and disease (NHS, 2014f).

Once someone is infected with HIV the virus will remain in their body for the rest of their life. There is currently no cure for HIV and no vaccine to prevent people from becoming infected. However, treatment can help most people with HIV to live much longer and feel well.

HIV can be transmitted in a number of ways. This information is mostly about sexual transmission. It tells you about HIV, what you can do if you are worried that you might have the infection and advice on how to protect yourself.

If someone is tested and found to be infected with HIV, they are said to be HIV positive.

What causes it?

HIV is a virus. When someone becomes infected with HIV the virus weakens and damages their body's defence system (the immune system) so that it cannot fight off infections.

Someone who has HIV is diagnosed as having Acquired Immune Deficiency Syndrome (AIDS) only when their immune system cannot cope and they develop one or more particular illnesses.

Most people with HIV, who are taking treatment, will not go on to develop AIDS. The term AIDS is not used very often now. Late stage or advanced HIV infection is used instead (fpa, 2014e).

AIDS is the final stage of HIV infection, when your body can no longer fight life-threatening infections. With early diagnosis and effective treatment, most people with HIV will not go on to develop AIDS (NHS, 2014f).

How is it passed on?

HIV can be passed from one person to another through sexual contact, and in a number of other ways. Both men and women can have HIV, and can transmit the virus. You don't need to have lots of sexual partners to become HIV positive (fpa, 2014e).

HIV is a fragile virus and does not survive outside the body for long.

HIV cannot be transmitted through sweat or urine.

The most common way of getting HIV in the UK is by anal or vaginal sex without a condom. According to statistics from Public Health England, 95% of those diagnosed with HIV in the UK in 2013 acquired HIV as a result of sexual contact (NHS, 2014f).

HIV can be transmitted through heterosexual (straight) or homosexual (gay, lesbian) sex. In women who only ever have sex with women the risk of HIV being passed on is very low.

Most people with HIV will look and feel healthy, so you cannot tell who has the virus and you can transmit HIV without knowing you are HIV positive. If someone is taking anti-HIV drugs they can pass on HIV but the risk of this happening is significantly reduced.

HIV is transmitted from one person to another when the blood, semen, pre-ejaculate (precum), vaginal and anal fluids or breast milk of an infected person enters the body of an uninfected person by -

- having unprotected (without a condom) vaginal or anal sex,
- sharing sex toys,
- using a needle or injecting equipment which has already been used by someone who is infected with HIV (fpa, 2014e).

A woman with HIV can transmit the virus to her baby before or during birth, or by breastfeeding. This risk can be reduced by testing and treatment during pregnancy, planning the delivery and avoiding breastfeeding.

The risk of HIV transmission as a result of unprotected oral sex is low but it can happen. You are more at risk if -

- you are performing oral sex,
- your throat or mouth is inflamed or you have cuts, sores, abrasions or any unhealed piercing in your mouth,
- your partner ejaculates in your mouth,
- you have just brushed or flossed your teeth,
- you are giving oral sex to a woman who is having her period (fpa, 2014e).

For example, it's estimated that you only have a 1 in 5,000 chance of getting HIV if you give unprotected oral sex to someone with the infection (NHS, 2014f).

You cannot become HIV positive from hugging, saliva, kissing, sneezes, coughs, sharing baths or towels, from swimming pools, toilet seats or from sharing cups, plates or cutlery.

You cannot get HIV from any animals or insects, including mosquitoes. HIV is not passed on through biting (fpa, 2014e).

Other ways of getting HIV include -

- sharing needles, syringes and other injecting equipment,
- from mother to baby before or during birth or by breastfeeding,
- sharing sex toys with someone infected with HIV,
- healthcare workers accidentally pricking themselves with an infected needle (this risk is extremely low),
- blood transfusion (now very rare in the UK, but still a problem in developing countries) (NHS, 2014f).

HIV is not passed on easily from one person to another. The virus does not spread through the air like cold and flu viruses.

HIV lives in the blood and in some body fluids. To get HIV, one of these fluids from someone with HIV has to get into your blood.

The body fluids that contain enough HIV to infect someone are -

- semen,
- vaginal fluids, including menstrual blood,
- breast milk,
- blood,
- lining inside the anus,
- Other body fluids, like saliva, sweat or urine, do not contain enough of the virus to infect another person (NHS, 2014f).

The main ways the virus enters the bloodstream are -

- by injecting into the bloodstream (with a contaminated needle or injecting equipment),
- through the thin lining on or inside the anus and genitals,
- through the thin lining of the mouth and eyes,
- via cuts and sores in the skin (NHS, 2014f).

HIV is not passed on through -

- kissing,
- spitting,
- being bitten,
- contact with unbroken, healthy skin,
- being sneezed on,
- sharing baths, towels or cutlery,
- using the same toilets or swimming pools,
- mouth-to-mouth resuscitation,
- contact with animals or insects such as mosquitoes (NHS, 2014f).

How HIV infects the body

HIV infects cells of the immune system, the body's defence system, causing progressive damage and eventually making it unable to fight off infections.

The virus enters cells in the immune system called CD4 cells + ve lymphocyte cells, which protect the body against various bacteria, viruses and other germs.

It uses the CD4 cells to make thousands of copies of itself. These copies then leave the CD4 cells, killing them in the process.

This process continues until eventually the number of CD4 cells, also called your CD4 count[87], drops so low that your immune system stops working. This can take about 10 years, during which time you will feel and appear well (NHS, 2014f).

Who is most at risk?

People who are at higher risk of becoming infected with HIV include -

- men who have had unprotected sex with men,
- women who have had sex without a condom with men who have sex with men,
- people who have had sex without a condom with a person who has lived or travelled in Africa,
- people who inject drugs,
- people who have had sex without a condom with somebody who has injected drugs,

[87] CD4 count is a measure of immune function. By measuring someone's CD4 levels you can see how HIV has affected their immune system, showing the progression of the virus

- people who have caught another sexually transmitted infection,
- people who have received a blood transfusion while in Africa, eastern Europe, the countries of the former Soviet Union, Asia or central and southern America (NHS, 2014f).

What are the signs and symptoms?

Many people who are living with HIV have no obvious signs and symptoms at all. Recent evidence shows that between 70% to 90% of people who become infected with HIV experience flu-like symptoms within a few weeks after infection.

The most common symptoms are a fever, a rash and a severe sore throat all occurring at the same time. These symptoms in an otherwise healthy person may indicate recent HIV infection (NHS, 2014f).

Most people who are infected with HIV experience a short, flu-like illness that occurs two to six weeks after infection. After this, HIV often causes no symptoms for several years.

The flu-like illness that often occurs a few weeks after HIV infection is also known as seroconversion illness. It's estimated that up to 80% of people who are infected with HIV experience this illness.

The most common symptoms are -

- fever (raised temperature),
- sore throat,
- body rash.

Other symptoms can include -

- tiredness,
- joint pain,
- muscle pain,
- swollen glands (nodes).

The symptoms usually last one to two weeks but can be longer. They are a sign that your immune system is putting up a fight against the virus.

However, these symptoms are most commonly caused by conditions other than HIV, and do not mean you have the virus.

If you have several of these symptoms, and you think you have been at risk of HIV infection within the past few weeks, you should get an HIV test.

After the initial symptoms disappear, HIV will often not cause any further symptoms for many years. During this time, known as asymptomatic HIV infection, the virus continues to be active and causes progressive damage to your immune system. This process can take about 10 years, during which you will feel and appear well.

Once the immune system becomes severely damaged symptoms can include -

- weight loss,
- chronic diarrhoea,
- night sweats,
- skin problems,
- recurrent infections,
- serious life-threatening illnesses.

Earlier diagnosis and treatment of HIV can prevent these problems (NHS, 2014f).

How will I know if I have it?

You can only be certain you are HIV positive if you have a test.

If you or a partner think you might have become HIV positive it is important that you don't delay seeking advice and getting a test. Even if you don't have symptoms an HIV test should be considered if -

- you have recently had unprotected sex (without a condom) with a new partner,
- a sexual partner tells you they are HIV positive,
- you have shared needles or injecting equipment or had a tattoo or piercing without a sterile needle,
- you, or your partner, have had unprotected sex (without a condom) with other partners,
- you, or your partner, have another sexually transmitted infection,
- you are pregnant or planning a pregnancy (fpa, 2014e).

What is an HIV test?

An HIV test checks your blood for antibodies and antigens to HIV. When HIV enters your body, your immune system tries to fight off the infection by producing antibodies to the virus.

Cervical screening tests, routine blood tests and swabs do not detect HIV. If you are not sure whether you have been tested for HIV, just ask (fpa, 2014e).

What does the test involve?

An HIV test usually involves taking a sample of blood and sending it to a laboratory to be tested. It is now possible to test for HIV using a saliva sample or a blood-spot (pin-prick to your finger).

An HIV test should only be done with your consent. You should understand what is involved in the test and how it might affect you. If you are tested by a doctor, nurse or health adviser, they should discuss with you -

- the benefits of testing,
- how the test result (negative or positive) might affect you and aspects of your life,
- how and when the HIV test can be done,
- where the information about the test result will be recorded,
- how the result will be given to you.

They may also give you a leaflet to explain some of the things you have discussed. Don't be frightened to ask questions about anything you are not sure about.

If you are taking a test at home, ensure you read the information provided with the test in full and, if you have any questions, ring the telephone number included or call the Sexual Health Information Line.

Before you decide to have a test you may wish to talk to someone about the implications that this could have on all aspects of your life and about who might have access to the HIV test result. A doctor, nurse, health adviser or an HIV organisation can help you with this (fpa, 2014e).

How soon will I know the result of the test?

This will vary depending on where you had the test done. The doctor, nurse or health adviser will talk to you about when the result will be available.

At most services the result should be available within a week. Some clinics offer same day testing. Not all clinics provide this service and an appointment is usually required.

There are also a small number of clinics that offer rapid testing. This is when you have an HIV test and are given the result in a short space of time (often within 20 minutes). If the result is positive another test will be done to check that the result is correct (fpa, 2014e).

How accurate are the tests?

No tests are 100% accurate, but HIV tests should pick up almost all HIV infections if they are done at the right time. All positive HIV tests are repeated to confirm the result (fpa, 2014e).

What is the treatment for it?

Once HIV is diagnosed, you will be given a number of tests to monitor the stage of the infection and to show if or when treatment should be started.

People with HIV may be supported and treated by their own doctor or by a specialist at an HIV clinic or a GUM clinic. Services may work together to provide specialist care and support.

At the moment there is no cure for HIV or late stage HIV infection, but there are drugs, known as antiretroviral treatment (ART) or combination therapy, that reduce the level of HIV in the blood and prevent or delay the development of late stage HIV infection. Most people with HIV benefit from these treatments and live longer and have better health than if they had not taken them.

There are also treatments available that can help prevent or treat many of the illnesses that people with HIV are more likely to get. Your doctor or specialist can give you full information about treatment options, side effects and long-term effects of treatment. HIV organisations can also provide this information.

Treatment can be given to prevent a pregnant woman from transmitting the virus to her baby during pregnancy (fpa, 2014e).

Emergency HIV drugs

If you think you have been exposed to the virus within the last 72 hours (three days), anti-HIV medication may stop you becoming infected.

For it to be effective, the medication, called post-exposure prophylaxis (PEP), must be started within 72 hours of coming into contact with the virus. It is only recommended following higher risk exposure, particularly where the sexual partner is known to be positive.

The quicker PEP is started the better, ideally within hours of coming into contact with HIV. The longer the wait, the less chance of it being effective.

PEP has been misleadingly popularised as a "morning-after pill" for HIV - a reference to the emergency pill women can take to prevent getting pregnant after having unprotected sex.

But the description is not accurate. PEP is a month-long treatment, which may have serious side effects and is not guaranteed to work. The treatment involves taking the same drugs prescribed to people who have tested positive for HIV.

You should be able to get PEP from -

- sexual health clinics, or GUM clinics,
- hospitals - usually accident and emergency (A&E) departments.

If you already have HIV, try your HIV clinic if the PEP is for someone you've had sex with (NHS, 2014f).

However PEP can stop HIV infection after the virus has entered the body -

- PEP is an emergency measure to be used as a last resort, eg, if a condom breaks or you have a 'slip up' from your usual safer sex routine.
- PEP is a combination of powerful drugs and can be hard to get hold of, so it is no substitute for condoms, but it's important to know about in case one day you or someone you've had sex with needs it.
- PEP is not guaranteed to always work but has a high success rate.
- It is free of charge but can only be prescribed by doctors and if certain criteria are met (tht, 2015e).

What is PEP?

PEP is a month-long course of HIV drugs that someone takes very soon after sex which had a risk of HIV transmission. The drugs are the same ones taken by people with HIV. The sooner PEP is started, the more likely it is to work; within 24 hours is best, but no later than 72 hours (three days). After 72 hours PEP is unlikely to work (tht, 2015e).

How long do I need to take PEP for?

For PEP to work the drugs must be taken for four weeks. If someone stops taking it before 28 days it is unlikely that it will work (tht, 2015e).

If PEP is available, do I still need to use condoms?

Yes. PEP is not a 'morning after' pill to stop HIV as it is not taken just once but must be taken every day for 28 days. It is not a replacement for condoms. PEP drugs are powerful, have side effects and getting PEP is often not easy. Condoms on the other hand are cheap, available everywhere, have no side effects and only need to be used during sex (not for a month after sex like PEP) (tht, 2015e).

Taking PEP

For PEP to have the best chance of working it must be taken exactly as instructed by a doctor and for 28 days. Skipping doses or not taking the pills for the full month makes it likely that PEP will not work.

If a dose is missed take the next dose as soon as you remember - don't take double the dose (tht, 2015e).

Are there any side effects?

It is common for people taking PEP to get side effects. These will stop once the course of drugs has been completed - but for some people they can make sticking with PEP difficult. Headaches, tiredness, feeling sick and diarrhoea are common side effects.

If you are finding the treatment difficult, speak to the clinic that gave it to you; they can give you medication to help with side effects. Because of side effects some people need to take time off work or study while they are on PEP (tht, 2015e).

Is there anything I should avoid doing while taking PEP?

When taking PEP you will be advised not to have any further unprotected sex during the 28 days of treatment as this will make it more likely that PEP will not work.

As recreational drugs can have dangerous interactions with HIV medication, it's advisable not to use them while taking PEP (tht, 2015e).

What should I do after my course of PEP has finished?

To be sure that no infection has taken place, three months after the course of PEP drugs has been completed you will be asked to have another HIV test. If you decide not to take PEP an HIV test is recommended anyway, along with a check up for sexually transmitted infections (tht, 2015e).

If you test positive

If you are diagnosed with HIV, you will have regular blood tests to monitor the progress of the HIV infection before starting treatment.

This involves monitoring the amount of virus in your blood (viral blood test or viral load[88]) and the effect HIV is having on your immune system. This is determined by measuring your levels of CD4+ve lymphocyte cells in your blood. These cells are important for fighting infection.

[88]Viral load measures how active HIV is in your body. The higher the viral load the more infectious you would be. Effective HIV medication can keep people's CD4 count high and their viral load so low it is undetectable. However people with HIV's CD4 count and viral load can go up and down depending on their medication, whether they have another STI and their general health

Treatment is usually recommended to begin when your CD4 cell count falls towards 350 or below, whether or not you have any symptoms. In some people with other medical conditions, treatment may be started at higher CD4 cell counts. When to start treatment should be discussed with your doctor.

The aim of the treatment is to reduce the level of HIV in the blood, allow the immune system to repair itself and prevent any HIV-related illnesses.

If you are on HIV treatment, the level of the virus in your blood is generally very low and it is unlikely that you will pass HIV on to someone else (NHS, 2014f).

HIV Staging

HIV infection without symptoms Once seroconversion is over, most people feel fine and don't experience any symptoms. This is often called the asymptomatic stage and it can last for several years.

But just because you feel well at this stage doesn't mean HIV isn't doing anything. The virus is still active, infecting new cells, making copies of itself and damaging your immune system's ability to fight illness.

HIV infection with symptoms The longer you live with HIV without treatment, the greater your risk of developing symptoms. These can be caused by opportunistic infections that take advantage of your weakened immune system, certain cancers or the direct effects of HIV on the body.

When someone gets ill in one of these ways, they are said to have symptomatic HIV.

The longer someone lives with HIV without treatment, the greater their risk of developing symptoms.

Late-stage HIV infection If HIV has a chance to cause a lot of damage to your immune system, you may become ill from certain very serious infections and cancers. At this stage you may be given a diagnosis of AIDS.

But many people have had an illness which has led to them being diagnosed with AIDS, and then completely recovered and lived for many years, even decades, in very good health.

AIDS is not considered a disease, but a syndrome - a collection of different signs and symptoms, all caused by the same virus, HIV. You cannot 'catch AIDS' and there is no 'AIDS test'. An AIDS diagnosis is usually based on the presence of certain illnesses.

Many people never experience late-stage HIV infection. It depends on a range of factors, including how well you respond to treatment and on lifestyle factors that influence your health, such as diet, exercise and smoking (tht, 2015e).

New treatment guidelines

If you don't start treatment, damage to your immune system will happen in the three stages described above.

Without treatment, your immune system will become weaker and you will start becoming ill, and may eventually develop late-stage HIV or AIDS.

Patients used to be advised to start treatment when their CD4 count dropped to 350 or lower. But recently the British HIV Association (BHIVA) treatment guidelines have been changed to say that anyone with HIV who is ready to commit to treatment should start regardless of their CD4 count. This reflects the findings of the START study.

START found that people who waited to start treatment until their CD4 count dropped to 350 had a much higher chance of developing AIDS-related illnesses such as cancers.

Starting treatment also reduces the chances that you will pass on HIV (tht, 2015e).

What happens if it isn't treated?

Once you have become infected with HIV you will remain infected with the virus for the rest of your life, and will be able to tranmit the virus to someone else. There is currently no way of curing the virus or removing it from the body.

Every individual will react differently to HIV. If the HIV isn't monitored carefully and treatment given when necessary, it will cause long-term damage, and this will develop into late stage HIV infection (which can lead to death) (fpa, 2014e).

Can it go away without treatment?

No!

Molluscum contagiosum

Molluscum contagiosum (MC) is a viral infection that affects the skin. It most commonly affects children, although it can occur at any age.

Usually, the only symptom of MC is a number of small, firm, raised papules (spots) that develop on the skin. They are not painful, but can be itchy.

Although the spots can look unpleasant, MC is generally a harmless condition that will normally resolve in a few months without any specific treatment (NHS, 2014i).

What causes MC?

MC is caused by a virus known as the MCV.

This virus can be spread through -

close direct contact - such as touching the skin of an infected person,
touching contaminated objects - such as towels, flannels, toys and clothes,
sexual contact - this includes close skin contact, including genital contact during sex.

If you become infected by the virus and spots appear on your skin, the virus can also spread to other areas.

It is not known exactly how long someone with MC is contagious for, but it is thought the contagious period may last up until the last spot has completely healed (NHS, 2014i).

Who is affected?

MC can affect anyone at any age, but the condition is most common in young children - particularly those aged between one and five.

It is also more common in people with a weakened immune system - either due to a condition such as HIV or a treatment such as chemotherapy.

MC can affect a person on more than one occasion, but this is uncommon (NHS, 2014i).

Symptoms

The main symptom of MC is the development of a number of small spots on the skin.

The spots are usually firm and dome-shaped, with a small dimple in the middle. They are usually less than 5mm (0.5cm) across, but can sometimes be bigger.

They are typically pink or red, although they may have a tiny white or yellow head in the centre. If this head ruptures (splits), a thick yellowy-white substance will be released, which is highly infectious.

It's important not to squeeze the spots, as this will increase the risk of the infection spreading to other parts of the body.

The spots associated with MC are usually painless, although they can sometimes be itchy and some people develop areas of red, dry and cracked skin around them.

Most people will have between 20 and 30 spots, although people with a weakened immune system often have more. The spots may develop in small clusters and can be spread across different parts of the body.

Common parts of the body affected by MC include the -

- face,
- neck,
- trunk (torso),
- limbs (NHS, 2014i).

In sexually active adults, the spots usually appear on the groin area, spreading upwards over the pubic and abdominal (tummy) areas, genitals and inner thighs.

The spots are usually firm, raised and painless. You may notice that some of the spots have a tiny grey head in the centre and look pearly. This head may rupture (split), causing a thick yellowy-white substance to escape. This substance is highly infectious so you should avoid handling or squeezing the spots, or shaving the skin in that area, as this can spread the infection to other parts of the body.

The spots do not usually leave scars, but you may notice that each one leaves a tiny patch of lighter skin or a small pitted mark (umbrellahealth, 2016b).

How the condition progresses

In many cases, the individual spots will start to crust over and heal within two months. Some people may experience mild swelling and redness around each spot as it begins to heal.

The spots do not usually leave scars, but they may leave a small area of lighter skin or a tiny pitted mark.

As the virus that causes MC can spread to other parts of the body, new spots may develop as the old ones are healing. This can result in an episode of MC lasting for quite a long time.

Most cases clear up within around 6–18 months, but the condition can, occasionally, persist for several years (NHS, 2014i).

When to seek medical advice

Visit your GP if you think you or your child may have MC. Your GP will examine your skin (or your child's) and ask about any other symptoms.

The spots of MC are usually easy to recognise, so your GP should be able to diagnose the condition without the need for further tests.

Your GP can advise you about whether any treatment is appropriate, and what steps you can take to reduce the risk of the infection spreading to other people (NHS, 2014i).

Diagnosis

The spots caused by molluscum contagiosum (MC) are usually easy to recognise.

Your GP should be able to diagnose the condition without carrying out further tests (NHS, 2014i).

Confirming a diagnosis

If your GP thinks that the infection may be caused by something other than MC, they may want to carry out some tests.

For example, they may take a sample from one of the spots to test it for the molluscum contagiosum virus (MCV). This is known as a skin biopsy.

If you have spots on your genitals, your GP may refer you to a GUM clinic to be tested for STI's.

If you prefer, you can go to an STI clinic directly. Consultation is confidential and free (NHS, 2014i).

Referral to a specialist

Your GP may refer you to a specialist if -

- you have HIV and your symptoms are severe,
- you have a weakened immune system for another reason - such as receiving chemotherapy,
- you have spots on your eyelids or near your eye, and/or your eye is red or painful (NHS, 2014i).

Treatment

Treatment for molluscum contagiosum (MC) is not routinely recommended because most cases clear up in around 6 to 18 months without the need for treatment.

If left alone, MC doesn't tend to result in scarring or cause any symptoms other than spots.

Many of the treatments available for MC can be painful and may be upsetting for young children, and some may increase the chances of permanent scarring.

Treatment is usually only recommended for adults and older children who have spots that are particularly unsightly and are affecting their quality of life.

Treatment is also recommended for people with weakened immune systems, as the condition can take several years to clear in these cases (NHS, 2014i).

Topical treatments

There are a number of topical treatments (creams, lotions and ointments) that can be used to treat MC, although there's not enough evidence to know if any particular treatment is more effective than the others (NHS, 2014i).

Potassium hydroxide

Potassium hydroxide is a medication available in liquid form that can improve MC by breaking down the skin cells infected by the virus, allowing the immune system to tackle it.

The liquid is applied twice a day on each spot. The spots should eventually become inflamed, before healing and disappearing within the next few weeks.

You should stop using the medication once the spots have started to become inflamed, or after 14 days if the medication doesn't seem to be working.

Side effects of potassium hydroxide can include redness and a slight burning or itching sensation, which usually only lasts for a few minutes after the medication is applied (NHS, 2014i).

Podophyllotoxin

Podophyllotoxin comes in liquid form and poisons the cells of the spots. A special application stick is used to draw up the correct dosage of liquid, which is then dripped onto each spot. You may experience some mild irritation.

The treatment will need to be applied for a few days, followed by a few days without treatment. This is referred to as a treatment cycle (NHS, 2014i).

Imiquimod

Imiquimod is a cream that can be used to treat larger spots or large clusters of spots. It works by stimulating your immune system into attacking the spots. You apply the cream to the spots, then wash it off after 6-10 hours. This should be done three times a week.

It may take several weeks of treatment before you notice an improvement. Common side effects of imiquimod include -

- hard and flaky skin,
- redness and swelling of the skin,
- a burning or itching sensation after applying the cream,
- headache.

These side effects are usually mild and should pass within two weeks of stopping treatment (NHS, 2014i).

Benzoyl peroxide

Benzoyl peroxide is usually available in cream or gel form. It's applied to the spots once or twice a day, after washing and drying the affected area. Use benzoyl peroxide sparingly, because too much can harm your skin.

Benzoyl peroxide makes your skin more sensitive to sunlight, so either avoid excessive exposure to sunlight and ultra-violet (UV) light, or wear sun cream. Avoid getting the medication on hair and clothes, as it can bleach them. Wash your hands thoroughly after you finish applying the medication.

Common side effects of benzoyl peroxide include -

- dry and red skin,
- a burning, itching or stinging sensation,
- some peeling of the skin,

These side effects are usually mild and should resolve after the treatment has finished (NHS, 2014i).

Tretinoin

Tretinoin is available as a liquid that is applied once or twice a day to individual spots. As with benzoyl peroxide, tretinoin can make your skin sensitive to sunlight and UV light.

Tretinoin is not suitable for use during pregnancy because it can cause birth defects. It's important to use a reliable method of contraception while taking tretinoin if you are a sexually active woman.

The most common side effects of tretinoin are mild irritation and stinging of the skin. It may take several months before you notice an improvement in your symptoms (NHS, 2014i).

Other treatments

There are a number of minor procedures that can help remove or destroy MC spots.

They can be painful, so are not generally suitable for children, and they must always be carried out by a suitably qualified healthcare professional (NHS, 2014i).

Cryotherapy

Cryotherapy involves freezing the spots with liquid nitrogen to remove them. Each spot is frozen for 5-10 seconds, so that a layer of ice forms over the spot and surrounding skin.

You may need several sessions of cryotherapy before each spot clears completely. You will need to wait two to three weeks between each treatment session (NHS, 2014i).

Diathermy

Diathermy uses heat to remove the spots. The area being treated is numbed with a local anaesthetic and a heated electrical device is used to burn off the spots (NHS, 2014i).

Curettage

Curettage removes spots by scraping them off with a thin, metal, spoon-like instrument called a curette. As with diathermy, you may have a local anaesthetic before having this type of treatment (NHS, 2014i).

Pulsed-dye lasers

Pulsed-dye laser treatment is a relatively new type of treatment for MC. It uses a powerful beam of light to destroy the cells that make up each spot. You may experience some skin discolouration and discomfort in the treated areas, but this should improve within a few weeks. The procedure may need to be repeated several times to clear all of your spots.

Pulsed-dye laser treatment uses expensive equipment and its availability on the NHS is limited. Therefore, you will probably have to pay privately for the treatment, which can be expensive (NHS, 2014i).

Don't squeeze the spots

Squeezing or scratching molluscum contagiosum spots is not recommended because it can cause pain and bleeding and can increase the chances of scarring. It also increases the risk of spreading the infection (NHS, 2014i).

Complications

Although molluscum contagiosum (MC) usually clears up on its own eventually without the need for treatment, it rarely causes any other problems.

However, complications can occasionally occur. Some of the main complications associated with MC are outlined below (NHS, 2014i).

Bacterial infection

In some cases, the spots of MC can become infected with bacteria. This is known as a secondary bacterial infection and it's thought to be more likely if you have atopic eczema (a skin condition caused by an allergy) or a weakened immune system.

Signs of a secondary bacterial infection can include redness, swelling and pain in the skin and underlying tissue.

See your GP if you think your or your childs spots have become infected. They will usually prescribe antibiotics to treat the infection (NHS, 2014i).

Scarring

After MC has healed and cleared, small patches of paler skin or tiny indented scars may be left behind. This is more likely to happen if the spots became infected or if you have had treatment for them.

Scarring is most common in areas of skin where there is more fatty tissue, such as your thighs (NHS, 2014i).

Eye problems

In rare cases, if you or your child has MC around the eyes, a secondary eye infection may develop, such as conjunctivitis or keratitis.

Conjunctivitis affects the thin layer of skin inside the eyelids called the conjunctiva. It causes your eyes to become red, swollen and watery. You may also have a sticky coating on your eyelids and eyelashes.

Keratitis is similar to conjunctivitis, but it affects your cornea (the transparent layer of cells that cover the surface of your eye). If you have keratitis, your eyes may be painful and sensitive to light, and you may have blurred vision.

See your GP if you or your child have any problems with your eyes. If necessary, they will refer you to a specialist in diagnosing and treating eye conditions, called an ophthalmologist, who may prescribe eye drops to reduce your symptoms and treat the infection (NHS, 2014i).

Pubic lice

Pubic lice (*Phthirus pubis*) are tiny parasitic insects that live on coarse human body hair, such as pubic hair. They are yellow-grey and about 2mm long. They have a crab-like appearance, so they are often known as 'crabs'. The eggs appear as brownish dots fixed to coarse body hair. As well as being found in pubic hair, the lice are also sometimes found in -

- underarm and leg hair,
- hair on the chest, abdomen and back,
- facial hair, such as beards and moustaches,
- eyelashes and eyebrows (very occasionally),
- Unlike head lice, pubic lice don't live in scalp hair (NHS, 2016c).
- Pubic lice can live off the body. However, because pubic lice depend on human blood for survival, they will rarely leave the body unless there is close body contact with another person. Pubic lice move by crawling from hair to hair - they cannot fly or jump,
- Occasionally public lice may be spread by contact with clothing, bedding and towels that have been used by someone with public lice (fpa, 2014g).

Pubic lice are spread through close bodily contact, most commonly sexual contact.

What are the signs and symptoms?

Some people will not have any symptoms, or may not notice the lice or eggs, so you may not know whether you or your partner have pubic lice.

It can take several weeks after coming into contact with pubic lice before signs and symptoms appear. Signs and symptoms are the same for both men and women. You might notice -

- itching in the affected areas,
- black powdery droppings from the lice in your underwear,
- brown eggs on pubic or other body hair,
- irritation and inflammation in the affected area, sometimes caused by scratching,
- sky-blue spots (which disappear within a few days) or very tiny specks of blood on the skin, such as on your thighs or lower abdomen (caused by lice bites) (fpa, 2014g).

Itching is the most common symptom of pubic lice and is an allergic reaction to their saliva. The itching is usually worse at night, when the lice are most active (NHS, 2016c).

You might see the lice, eggs or droppings, or your partner might notice them. Some people see pubic lice move, but they are tiny and difficult to see, and they keep still in the light.

Sometimes pubic lice will be noticed during a routine genital or medical examination even if a doctor or nurse isn't looking for them (fpa, 2014g).

What do pubic lice look like?

Adult pubic lice are very small (2mm long) and aren't easy to see. They're a yellow-grey or dusky red colour and have six legs.

Pubic lice are sometimes known as crabs because they have two large front legs that look like the claws of a crab. These are used to hold onto the base of hairs.

The lice lay their eggs (nits) in sacs that are stuck firmly to hairs and are a pale brownish colour. When the eggs hatch, the empty egg sacs are white.

Although pubic lice and lice eggs are small and difficult to see, they may be visible in coarse hair anywhere on your body (apart from hair on your head) (fpa, 2014g).

What is the treatment for it?

- Treatment for pubic lice is simple and involves using a special cream, lotion or shampoo. The doctor, nurse or pharmacist will advise you on what treatment to use and how to use it.

- You apply the cream, lotion or shampoo to the affected area and sometimes the whole body. Lotions tend to be more effective than shampoos. Some treatments can be rinsed off after 10–15 minutes; others are left on for longer.
- To be effective, treatment needs to be repeated after 3–7 days.
- You do not need to shave off pubic or other body hair.
- You should wash your clothing, bedding and towels in a washing machine on a very hot cycle (50řC or higher) to kill the lice and avoid re-infection.
- You can also buy treatments for pubic lice from pharmacies - these are useful for anyone who is sure they have pubic lice and wants to self-treat. The pharmacist will be able to advise if you have any questions, or are unsure how to use the treatment.
- If you decide to treat yourself, you may still want to consider having a sexual health check to make sure you don't have a sexually transmitted infection.
- Do tell the doctor, nurse or pharmacist if you are, or think you might be, pregnant or if you are breastfeeding. This will affect the type of treatment you are given.
- There is currently no evidence that complementary therapies can cure pubic lice.
- Your sexual partner(s) should be treated at the same time even if they don't have any signs and symptoms (fpa, 2014g).

Side-effects

Insecticides used to treat pubic lice may cause skin irritation, such as itchiness, redness, stinging or burning. If you have skin irritation, wash the insecticide off the affected area.

Some aqueous and alcohol-based medications may discolour permed, coloured or bleached hair. Check the patient information leaflet (NHS, 2016c).

Follow-up treatment

The first treatment application will probably kill the lice, but the eggs may not have been destroyed. This means more lice could hatch and the cycle will start again.

Reapplying the treatment after three or seven days will ensure that any lice are killed before they're old enough to lay more eggs.

Check for lice a week after your second treatment, or return to your GP, practice nurse, or sexual health clinic so they can check for you.

Finding empty eggshells (dead nits) doesn't necessarily mean you're still infested as they can remain stuck to the hairs even after treatment (NHS, 2016c).

Treating an eyelash infestation

Eyelash infestations are rare. If your eyelashes are infested, seek specialist advice from your doctor. They'll be able to recommend the correct treatment for you.

You can't use the same insecticide lotion or cream that's used on your body because it will irritate your eyes. Make sure you follow the treatment instructions carefully (NHS, 2016c).

Washing clothing, towels and bedding

Wash clothing, towels and bedding in a washing machine. This should be on a hot cycle (50C or higher) to ensure the lice are killed and to prevent reinfection (NHS, 2016c).

Complications of pubic lice

Sometimes, a pubic lice infestation can lead to minor complications, such as skin or eye problems.

Scratching can irritate your skin, or it could lead to an infection such as impetigo (a bacterial skin infection) or furunculosis (boils on the skin).

Eye infections, such as conjunctivitis, and eye inflammation, such as blepharitis, can sometimes develop if your eyelashes have been infested with pubic lice.

Seek medical advice if you have severe skin irritation or sore eyes (NHS, 2016c).

Can it go away without treatment

No. And if you delay seeking treatment you risk passing the condition on to someone else (fpa, 2014g).

Scabies

Scabies is a contagious skin condition caused by tiny mites that burrow into the skin.

The main symptom of scabies is intense itching that's worse at night. It also causes a skin rash on areas where the mites have burrowed.

The intense itching associated with scabies is thought to be caused by the immune system reacting to the mites and their saliva, eggs and faeces (NHS, 2015h).

What causes it?

Scabies mites are called 'Sarcoptes scabiei'. They feed using their mouths and front legs to burrow into the outer layer of skin (epidermis), where they lay eggs.

After three to four days, the baby mites (larvae) hatch and move to the surface of the skin, where they mature into adults.

Scabies like warm places, such as skin folds, between the fingers, under fingernails, or around the buttock or breast creases. They can also hide under watch straps, bracelets or rings (NHS, 2015h).

The mites which cause scabies can be found in the genital area, on the hands, between the fingers, on the wrists and elbows, underneath the arms, on the abdomen, on the breasts, around the nipples in women, on the feet and ankles, and around the buttocks.

The mites can live for up to 72 hours off the body, so it is possible for scabies to be spread by clothing, bedding and towels (fpa, 2014g).

How is it passed on?

Scabies is usually spread through prolonged periods of skin-to-skin contact with an infected person, or through sexual contact.

It's also possible - but rare - for scabies to be passed on by sharing clothing, towels and bedding with someone who's infected.

It can take up to eight weeks for the symptoms of scabies to appear after the initial infection. This is known as the incubation period (NHS, 2015h).

Scabies mites can't fly or jump, which means they can only move from one human body to another if two people have direct and prolonged physical contact.

For example, scabies mites can be transmitted by -

- holding hands with an infected person for a prolonged period of time,
- having sex with an infected person,
- sharing clothing, towels and bedding with an infected person (although this is rare).

It's unlikely that scabies will be transmitted through brief physical contact, such as shaking hands or hugging.

Scabies mites can survive outside the human body for 24 to 36 hours, making infection by coming into contact with contaminated clothes, towels or bed linen a possibility. However, it's rare for someone to be infected in this way.

Scabies infestations can spread quickly because people are usually unaware they have the condition until two to three weeks after the initial infection.

There's an increased risk of catching scabies in confined environments, such as schools and nursing homes, where people are in close proximity to one another (NHS, 2015h).

What are the signs and symptoms?

Some people will not have any visible signs or symptoms at all, or may not be aware of them.

It can take up to six weeks after coming into contact with scabies before signs and symptoms appear. Signs and symptoms are the same for both men and women. You might notice -

- Intense itching in the affected areas which may only be noticed at night, or which becomes worse in bed at night or after a hot bath or shower.
- An itchy red rash or tiny spots. Sometimes the diagnosis can be difficult because the rash can look like other itchy conditions, such as eczema.
- Inflammation or raw, broken skin in the affected areas - usually caused by scratching.

Scabies mites are very tiny and impossible to see with the naked eye. Fine silvery lines are sometimes visible in the skin where mites have burrowed.

Sometimes scabies will be noticed during a routine genital or medical examination even if a doctor or nurse isn't looking for it (fpa, 2014g).

What is the treatment for it?

- Treatment is simple and involves using a special cream or lotion. The doctor, nurse or pharmacist will advise you on what treatment to use and how to use it.
- You apply the cream or lotion usually to the whole body from the neck downwards. This ideally should be done overnight. The treatment should be rinsed off after 12 hours.
- You should wash clothing, bedding and towels in a washing machine on a very hot cycle (50řC higher) to kill the mites and avoid re-infection.

- You can also buy treatments for scabies from pharmacies. These are useful for anyone who is sure they have scabies and wants to self-treat. The pharmacist will be able to advise if you have any questions, or are unsure how to use the treatment.
- If you decide to treat yourself, you may still want to consider having a sexual health check, to make sure you dont have a sexually transmitted infection.
- Do tell the doctor, nurse or pharmacist if you are, or think you might be, pregnant or if you are breastfeeding. This will affect the type of treatment you are given.
- Close contacts in your household should be treated at the same time, as well as your sexual partner, even if they do not have any signs or symptoms.
- There is no evidence that complementary therapies can cure scabies (fpa, 2014g).

What happens if it isn't treated?

No. And if you delay seeking treatment you risk passing the condition on to someone else (fpa, 2014g).

Can it go away without treatment?

No.

Shigella

Shigella is a bacteria that causes severe stomach upset. Infection can be treated with a course of antibiotics. It is passed on through infected faeces - this can be through contaminated food or sexually (tht, 2015f).

Symptoms

Although some people experience no symptoms, shigella may cause diarrhoea and stomach cramps.

In more serious cases diarrhoea can be severe and may contain blood or mucus (this is also known as 'dysentery').

You might also have a fever and experience nausea or vomiting as well as stomach cramps.

Symptoms usually start a day or two after becoming infected and last up to a week (tht, 2015f).

What should I do if I think I might have shigella?

Seek medical advice by visiting your GP or a sexual health clinic. Tell them that you may have picked up a stomach infection from sex, possibly shigella. That way they will know which tests to give you.

Anyone with bad diarrhoea should -

Get tested - If you do test positive for shigella, wait at least 48 hours after symptoms stop before going back to work. If your work involves handling food or contact with patients, you should not go back to work until tests have ruled out shigella. If you test positive for shigella you cannot go back to work until a health professional says so (tht, 2015f).

Wash hands frequently! - You may be infectious for up to a month, so wash hands with soap and warm water after using the toilet and before touching food. Don't prepare food for others while you're ill or until a week after symptoms stop. Wash the clothes, bedding and towels of an infected person on the highest setting of the washing machine (tht, 2015f).

Avoid -

- Sex, until a week after symptoms stop.
- Sharing towels. Use separate towels at home. Frequently clean taps, door handles, the toilet flush and seat with hot soapy water.
- Jacuzzis/hot tubs/spas. You might contaminate and infect others (tht, 2015f).

Transmission

Shigella is caused by bacteria found in faeces. Only a tiny amount needs to get into your mouth to pass it on (eg, via your fingers).

It's often caused by contaminated food but it can also be passed on sexually.

Sex that may involve contact with faeces is a risk eg, anal sex, fisting, handling a condom or sex toy used for anal sex, oral sex, touching someone's backside or rimming.

Someone with shigella can be infectious for up to a month (tht, 2015f).

Treatment

The infection can be cured with antibiotics, although not everyone will need them. Drinking fluids will stop you losing too much water.

How to lower the risk during sex

- Wash your hands during or after sex, especially if you're rimming, touching someone's backside or handling used condoms or sex toys. Even better, have a shower.
- Wear condoms for anal sex. Latex gloves offer protection if fingering or fisting. For barrier protection when rimming, cut a condom up into a square. Dont share sex toys or douching equipment.
- Skin on the buttocks, around the backside or groin may carry the bacteria, so avoid licking these areas. Showering after sex is even better than washing (tht, 2015f).

Syphilis

Syphilis is a bacterial infection that is usually caught by having sex with someone who is infected.

The bacteria that cause syphilis are called 'Treponema pallidum'. They can enter your body if you have close contact with an infected sore, normally during vaginal, anal or oral sex, or by sharing sex toys with someone who is infected.

It may also be possible to catch syphilis if you are an injecting drug user and you share a needle with somebody who is infected.

Pregnant women can pass the condition on to their unborn baby. If untreated, syphilis can cause serious health problems for the mother and her baby, or cause miscarriage or stillbirth. This is why all pregnant women are offered a blood test to check if they have syphilis as part of routine antenatal screening.

It is extremely rare for syphilis to be spread through blood transfusions, as all blood transfusions in the UK are tested for syphilis.

Syphilis also cannot be spread by using the same toilet, clothing, cutlery or bathroom as an infected person, as the bacteria cannot survive for long outside the human body (fpa, 2014h).

How common is it?

The number of diagnoses of syphilis has risen substantially in the UK in the past decade. There have been several local outbreaks across England, the largest of which was in London between 2001 and 2004. Rates are highest among men who have sex with men.

However, syphilis is still one of the less common sexually transmitted infections in the UK. Between 2011 and 2012, there were 2,978 cases of syphilis diagnosed in the UK (NHS, 2014l).

Statistics for 2014 showed that of all the STI's, syphilis had seen the sharpest rise - with a 33% increase in diagnoses (brook, 2015d).

What causes it?

Syphilis is caused by bacteria known as Treponema pallidum. This is easily passed from one person to another through sexual contact. Anyone who is sexually active can get it. Both men and women can have syphilis, and pass it on (fpa, 2014h).

How is it passed on?

You can pass syphilis on without knowing you have the infection because symptoms can be mild and you may not notice or recognise them.

- Syphilis can be passed from one person to another during sex and by direct skin contact with someone who has syphilis sores or a syphilis rash. It can be passed on before symptoms are noticeable, or after theyve disappeared.
- The infection can spread if you have vaginal, anal or oral sex, or share sex toys. Using a condom correctly will reduce your chance of getting or passing on syphilis.
- Syphilis can also be transmitted by blood transfusion. However, in the UK all blood donors are screened to detect this before the blood is used.
- It is also possible for a pregnant woman to pass the infection to her unborn baby. This is known as congenital syphilis.

You cannot catch syphilis from kissing, hugging, sharing baths or towels, swimming pools, toilet seats or from sharing cups, plates or cutlery (fpa, 2014h).

Unless someone with syphilis is treated, they can pass syphilis on for up to two years after the infection (brook, 2015d).

What are the signs and symptoms?

The signs and symptoms are the same in both men and women. They can be difficult to recognise and you might not notice them.

Syphilis can develop in stages -

- the first stage is called primary syphilis
- the second stage is called secondary syphilis
- the latent stage is called latent syphilis
- the third stage is called tertiary syphilis.

If you do get symptoms, you might notice the following -

First stage syphilis

- One or more sores (called a chancre pronounced shanker) usually painless will appear where the bacteria entered the body. On average, this will be 23 weeks after coming into contact with syphilis but it can be sooner or later.
- These sores can appear anywhere on the body. In women, they are found mainly on the vulva (the lips around the opening to the vagina), the clitoris, cervix (entrance to the uterus womb), and around the opening of the urethra (tube where urine comes out) and the anus.
- In men, they appear mainly around the opening of the urethra, on the penis and foreskin, and around the anus.
- Less commonly, in men and women, sores may appear in the mouth, and on the lips, tonsils, fingers or buttocks.
- The sores of first stage syphilis are very infectious and may take 26 weeks to heal. By this time, the bacteria will have spread to other parts of the body and it will then be known as second stage syphilis.

Second stage syphilis

If the infection remains untreated the second stage usually occurs some weeks after any sores have appeared and healed. Syphilis is still infectious at this stage and can be passed on to someone else.

The symptoms include -

- A painless rash that is not normally itchy. It can spread all over the body, or appear in patches, but it is often seen on the palms of the hands and soles of the feet.
- Flat, warty-looking growths on the vulva in women and around the anus in both men and women (often mistaken for genital warts).
- A flu-like illness, tiredness and loss of appetite, with swollen glands (this can last for weeks or months).
- White patches on the tongue or roof of the mouth.
- Patchy hair loss.

Latent syphilis

When syphilis remains untreated, without any signs or symptoms of infection, it is known as latent (or hidden) syphilis. Diagnosis is made by a positive blood test (fpa, 2014h).

Latent syphilis can still be passed on during the first year of this stage of the condition, usually through sexual or close physical contact. However, after a couple of years, you cannot pass the infection to others, even though you remain infected.

The latent stage can continue for many years (even decades) after you first become infected.

Latent syphilis is rare in the UK. However, without treatment, there is a risk that latent syphilis will move on to the third, most dangerous stage - third stage syphilis (NHS, 2014l).

Third stage syphilis, or Tertiary syphilis

Untreated syphilis may, after many years, start to cause serious damage to the heart, brain, bones and nervous system.

The symptoms of tertiary syphilis can begin years or even decades after initial infection. Around a third of people who are not treated for syphilis develop serious symptoms at this stage.

The symptoms of tertiary syphilis will depend on what part of the body the infection spreads to. For example, it may affect the brain, nerves, eyes, heart, bones, skin or blood vessels, potentially causing any of the following symptoms -

- stroke
- dementia
- loss of co-ordination
- numbness
- paralysis
- blindness
- deafness
- heart disease
- skin rashes

At this stage, syphilis can be dangerous enough to cause death (fpa, 2014h).

Tertiary syphilis also has effects on the skeleton, specifically the skull. I have seen skulls from Anglo-Saxon people who have died of tertiary syphilis and had the skull surface eroded away leaving patches of roughened bone as compared to the rest of the skull.

How will I know if I have it?

You can only be certain you have syphilis if you have a test. If you think you might have syphilis it is important that you dont delay getting a test. Even if you dont have symptoms you may wish to be tested, particularly if -

- you, or a partner, think you might have symptoms
- you have recently had unprotected sex with a new partner
- you, or a partner, have had unprotected sex with other partners
- a sexual partner tells you they have a sexually transmitted infection
- you have another sexually transmitted infection
- you are pregnant or planning a pregnancy.

Don't delay seeking advice clinics don't mind doing sexual health check-ups (fpa, 2014h).

Testing for syphilis

Examination - Before doing any tests, the doctor or nurse will start by examining you, to look for the signs of syphilis. This may include an internal examination of the vagina and possibly of the anus. They may also look in your mouth and throat and for skin rashes.

Swab test - If you have a chancre (the sore that appears in stage one) then the nurse or doctor may take a swab. The swab looks like a small cotton bud and is used to collect a sample of the fluid from the chancre. Taking the swab should not be painful. This will then be send to a lab for testing and results are generally available in 7 to 10 days.

Blood test - Syphilis can also be confirmed by taking a blood test. When the bodys immune system reacts to syphilis, it produces antibodies (infection-fighting proteins) and the blood test looks for those antibodies.

You will nearly always be advised to repeat the blood test after three months. This is because a positive result may detect antibodies from a previous episode that was successfully treated (and therefore you may actually be free from syphilis) and when you do in fact have syphilis, you can get a negative result at first because the antibodies may not be detectable for the first three months after infection.

The blood test cannot inform you how long you have had the infection.

Syphilis testing is free and you can get this at some Brook services, GUM or sexual health clinics or at some GP surgeries. Cervical smear tests and routine blood tests will not detect syphilis.

It is possible to buy syphilis self-tests to do at home but the accuracy of these tests can vary. Some are very accurate if you carefully follow the instructions but others are less reliable. Get advice from your nearest Brook clinic, GUM or sexual health clinic, GP or pharmacy if youre unsure.

If youve had unprotected sex, dont wait and hope for the best, have a test as soon as you can. Its the only way you can be sure that you have syphilis or not and left untreated, it can cause serious damage to your body (brook, 2015d).

What is the treatment for it?

First and second stage syphilis is treated using a single antibiotic injection into your buttock, or a course of injections or by taking antibiotic tablets or capsules. Penicillin is the most common treatment for syphilis, but there are several different antibiotics that can be used. Let the doctor or nurse know if you are allergic to penicillin (fpa, 2014h).

You will be prescribed another antibiotic in tablet form if you are allergic to penicillin.

Later stages of the disease need to be treated with three penicillin injections, which are given at weekly intervals. Treatment usually lasts around two weeks, but can take longer in some cases (NHS, 2014l).

- Treatment usually lasts around 10–14 days but sometimes longer. If complications have occurred you may also need other treatment.
- If there is a high chance of you having the infection, treatment may be started before the results of the test are back. You will usually be given treatment if any sexual partner has syphilis.
- You cannot buy any treatments without a prescription.
- There is no evidence that complementary therapies can cure syphilis.
- Treatment can safely be given in pregnancy (fpa, 2014h).

Side effects of antibiotics

Some of the antibiotics used to treat syphilis can interfere with methods of contraception that contain the hormones oestrogen and progestogen, such as the combined pill or contraceptive patch.

Tell your doctor or nurse if you are using these methods of contraception so they can advise you on additional contraceptive methods to prevent you getting pregnant.

Refrain from any kind of sexual activity or close physical contact with another person until your treatment is complete and your sexual partner has been tested and treated (NHS, 2014l).

Jarisch-Herxheimer reaction A small number of people experience a reaction to the antibiotics, which is known as the 'Jarisch-Herxheimer reaction'. It is thought that the reaction is triggered by the toxins released when a large number of bacteria are killed after antibiotic treatment.

The Jarisch-Herxheimer reaction causes flu-like symptoms such as fever, headaches and muscle and joint pain. These normally only last 24 hours, are nothing to worry about, and cause no serious problems.

The symptoms can be treated with paracetamol, but contact your GP or the genitourinary medicine (GUM) clinic if the symptoms are severe or do not settle down (NHS, 2014l).

Follow-up test

Once the course of antibiotics has finished, you will be asked to return to the GUM clinic so a follow-up blood test can be carried out to check that the infection has gone (NHS, 2014l). You may be advised to return for another test after three months to ensure you are clear of syphilis (brook, 2015d).

You can still catch syphilis again, even after you have been successfully treated for it (NHS, 2014l).

Tertiary syphilis

Treatment of tertiary syphilis requires longer courses of antibiotics and may need intravenous treatment (administered directly into the vein). While treatment can stop the infection, it cannot repair any damage that has already been caused by the tertiary syphilis (NHS, 2014l).

What happens if it isn't treated?

Without proper treatment the infection can spread to other parts of the body causing serious, long-term complications.

Left untreated, syphilis may start to cause very serious damage to the heart, brain, eyes, other internal organs, bones and nervous system. This damage could lead to death (fpa, 2014h).

Can it go away without treatment?

No. If you delay seeking treatment you risk the infection causing long-term damage and you might pass the infection on to someone else (fpa, 2014h).

Trichomoniasis

What causes it?

Trichomonas vaginalis is a tiny parasite which causes an infection.

In women the infection can be found in the vagina and the urethra (tube where urine comes out).

In men it can be found in the urethra.

The infection is easily passed from one person to another through sexual contact. Anyone who is sexually active can get it and pass it on. You dont need to have lots of sexual partners (fpa, 2014j).

How is it passed on?

Trichomonas is usually passed from one person to another during sex. The infection can be spread through unprotected vaginal sex and possibly through sharing sex toys if you dont wash them or cover them with a new condom each time they are used.

We dont know if the infection can be spread between women by rubbing vulvas (female genitals) together or by transferring discharge from one vagina to another on the fingers.

It is possible for a pregnant woman to pass the infection to her baby at birth.

You cannot catch trichomonas from oral or anal sex, or from kissing, hugging, sharing cups, plates or cutlery, toilet seats or towels (fpa, 2014j).

What are the signs and symptoms?

Up to half of infected men and women will not have any signs or symptoms at all. Signs and symptoms usually show up within a month of coming into contact with trichomonas. You might notice -

Women

- Soreness, inflammation and itching in and around the vagina.
- Itchy inner thighs.
- Discomfort when having sex.
- A change in vaginal discharge there may be a small amount or a lot, and it may be thick or thin, or frothy and yellow.
- You may also notice a fishy-smelling smell that may be unpleasant.
- Pain when passing urine (fpa, 2014j).

Men

- A discharge from the penis, which may be thin and whitish.
- Pain, or a burning sensation, when passing urine.
- Inflammation of the foreskin (this is uncommon) (fpa, 2014j).

How will I know if I have it?

You can only be certain you have trichomonas if you have a test.

A test for trichomonas is usually offered to -

- women who have signs and symptoms of trichomonas
- men who have signs and symptoms which have not been caused by other infections such as chlamydia and gonorrhoea

- men and women whose sexual partner has trichomonas
- women whose cervical screening test suggests that they may have trichomonas.

You may also wish to discuss with a doctor or a nurse whether you need to have a test if -

- you have recently had unprotected sex with a new partner
- you or a partner have had unprotected sex with other partners
- during a vaginal examination your doctor or nurse notices an unusual discharge or the cervix is red and inflamed
- a sexual partner tells you they have a sexually transmitted infection
- you have another sexually transmitted infection
- you are pregnant or planning a pregnancy.

You could still have trichomonas even if a partner has tested negative - you should not rely on a partners negative result.

If you have trichomonas you may wish to be tested for other sexually transmitted infections as you can have more than one sexually transmitted infection at the same time. Having an infection such as trichomonas can mean that you are more at risk of becoming infected with HIV or transmitting it if you are HIV positive (fpa, 2014j).

What is the treatment for it?

- The treatment involves taking a course of metronidazole tablets for between five to seven days. If you take it according to the instructions it is at least 95% effective.
- You will be advised not to drink alcohol during the treatment and for 48 hours afterwards. This is because antibiotics used to treat trichomonas react with alcohol and can make you feel very unwell (brook, 2015e).
- If there is a high chance you have the infection, treatment may be started before the results of the test are back. You will always be given treatment for trichomonas if your partner is found to have trichomonas.
- Do tell the doctor or nurse if you are pregnant, think you might be, or are breastfeeding, as this can affect the treatment you are given. Not all women are given treatment during pregnancy. The doctor or nurse will discuss the options with you.
- There is no evidence that complementary therapies can cure trichomonas (fpa, 2014j).

What happens if it isn't treated?

If trichomonas isnt treated you may be at more risk of becoming infected with HIV or transmitting it if you are HIV positive. Trichomonas may also cause problems with a pregnancy. Trichomonas is not thought to affect your fertility (fpa, 2014j).

Can it go away without treatment?

Trichomonas is unlikely to go away without treatment, however, for some people, trichomonas may cure itself. If you delay seeking treatment you risk passing the infection on to someone else (fpa, 2014j).

How to avoid sexually transmitted infections - STI's?

In general, sexually transmitted infections are highly preventable. The only method guaranteed to prevent STI's is to avoid any kind of sexual contact, but this is not practical for most people. There are things you can do to limit the risk of exposure to infections while still enjoying an active sex life.

The best way to avoid most STI's is to use a condom when you have sex. There are some other things you can do to reduce the chances of catching an STI. These include -

- limiting the number of people you have sex with,
- talking honestly with potential partners about your sexual history,
- getting tested, along with your partner, before having sex,
- avoiding sex when under the influence of alcohol or drugs. People who are drunk or using drugs often fail to have safe sex,
- when appropriate, getting vaccinated against the human papillomavirus (HPV) and hepatitis B (HBV)

The only time unprotected sex is completely safe from infection with chlamydia, gonorrhoea, HIV or syphilis is if you and your partner have sex only with each other, and if it's been at least six months since each of you tested negative for these STI's (Trust, 2016).

Otherwise you should take the following precautions.

Use condoms when you have sex

Use condoms every time you have sex. If you use a lubricant, make sure it's water-based (lubricants which are not water-based might damage the condom). You should wear a condom throughout sex.

Condoms are not 100% guaranteed to prevent disease or pregnancy, but they are extremely effective if used properly, so learn how to do this.

- Checking the expiry date on the condom,
- Make sure the condom's packaging has not been punctured,
- Follow the instructions to make sure you put the condom on correctly,
- Always leave room at the tip of the condom,
- Unroll the condom onto the penis. Don't try to unroll it before putting it on,
- Use a condom-safe lubricant during intercourse (look for water-based lubricants to avoid damaging the condom),
- Hold the base of the condom when withdrawing after sex, so that it doesnt slip off,
- Dispose of the condom properly,
- Never remove a condom and put it on again,
- Never reuse a condom. Use a new condom each time you have sex (Trust, 2016).

Use condoms or dental dams during oral sex

A dental dam is a rectangular piece of latex that can be used to cover the genitals or anus during oral sex.

Using a condom or dental dam during oral sex stops the mouth from coming into direct contact with the genitals or anus. This can prevent the spread of STI's which can be passed via the mouth (Trust, 2016).

Avoid sexual contact if you think you or your partner(s) have an STI

Always avoid sex with anyone who has genital sores, a rash, discharge or other potential symptoms of an STI.

To prevent giving an STI to someone else if you suspect you may have one -

- stop having sex until you see a doctor and are treated,
- follow your doctor's instructions for treatment,
- use condoms whenever you have sex, especially with new partners,
- don't resume having sex unless your doctor has given you the all-clear,
- return to your doctor to get rechecked if advised,
- be sure your partner or partners are also treated (Trust, 2016).

Avoid other types of contact

Condoms and other barriers, including dental dams, are very good at preventing the exchange of infected bodily fluids. They can also help to minimise skin-to-skin contact. This reduces the transmission of diseases that spread from skin to skin. However, they doesnt prevent transmission entirely. STI's that spread through skin-to-skin contact include -

- syphilis,
- herpes,
- genital warts.

Avoid sharing towels or underclothing.

You can also catch scabies and public lice through skin-to-skin contact or sharing towels, bedding and clothing (Trust, 2016).

Summary

Though STI's are common, there are ways to reduce your risk and make sex safer. If you are unsure about the right method for you, talk to your partner, or your GP. Being honest about your sexual practices with your medical advisors can help them to help you reduce the risk of catching an STI. Safer sex is for everyone, because everyone who is sexually active is potentially at risk (Trust, 2016).

Condoms

How do condoms work?

A condom covers the penis or sex toy and acts as a barrier between it and the mouth, vagina, penis or anus.

Condoms protect against pregnancy by stopping the sperm contained in semen coming into contact with a vagina. As condoms stop sexual fluids being transferred between partners they are also the only method of contraception that protects against most STI's.

When condoms are used correctly they are 98% effective at protecting against pregnancy. This means that two women out of every 100 who use condoms as contraception will become pregnant within a year. They are the only method of contraception that protects against both pregnancy and sexually transmitted infections (STI's).

Some people like to use condoms with another method of contraception (e.g. the pill, implant, injection), so they can enjoy sex without having to worry about pregnancy and STI's (brook, 2015b).

How do I get condoms?

You can get condoms free from -

- Brook services,
- Young people's clinics,
- Contraception and sexual health clinics,
- Some GP's,
- Some genitourinary medicine (GUM) clinics.

Or buy your condoms, even if you're under 16, from -

- Pharmacies,
- Petrol stations,
- Machines in public toilets, bars and clubs,
- Most supermarkets,
- Mail order or online.

If you feel embarrassed to get condoms - dont be. There is no need to feel embarrassed about asking for condoms, as it's nothing to be ashamed of. Deciding to use condoms shows that you have respect for your body and are responsible enough to look after your sexual health.

If you go to a service to get condoms, you will usually have a private consultation where they will ask you a few questions and they may show you how to use condoms by giving a demonstration on a plastic penis.

You and a friend or partner can also go to a clinic together and keep each other company. This might make it a bit easier for you (brook, 2015b).

How do you use condoms?

If you follow the instructions on the pack it will make it much less likely that you will have any problems.

- Check the expiry date and make sure there are no rips or holes in the pack,
- Check that the condoms have the BSI kite mark or CE mark on the pack,
- Before opening, feel for the rib of the condom inside the packaging. Push this to the side so that when you tear it open you dont tear the condom as well
- Unroll the condom a bit to check it is the right way round. Check which way to roll it down BEFORE it touches the penis,
- Pinch the tip of the condom between your thumb and forefinger to get rid of any air,
- Make sure the condom is put on the penis as soon as it is erect (hard), before it goes near anyone's mouth, vagina or anus, to help protect against unplanned pregnancy and STI's,
- Use your other hand to roll the condom down the penis all the way to the base,

- If you are having anal sex, you should use additional water-based lubricant which you can apply directly to the anus or on the outside of the condom,
- Check the condom is in place during sex,
- After ejaculation, hold the condom on at the base until the penis is withdrawn from your partners mouth, vagina or anus, and then take it off, wrap it in tissue and throw it in the bin (not down the toilet),
- Always use a brand new condom if you have any sexual contact again they can only be used once.

Never use two condoms together as this increases the chances of them splitting or tearing.

Some condoms have spermicide on them and these are being phased out because research has shown that a spermicide called nonoxynol 9 doesnt protect against some STI's (and may even increase the risk). Avoid using spermicide lubricated condoms if you can, or using spermicide as an additional lubricant (brook, 2015b).

Look after your condoms

Keeping condoms in your pocket or at the bottom of your bag for a long time might damage them. If the wrappers look damaged throw them away and get new ones. Always check the expiry date - out of date condoms are less effective (brook, 2015b).

How are condoms tested to make sure they will work?

Condoms go through several different tests to check -

- they are free from holes,
- the strength and stretch of the latex,
- the air pressure needed to burst one,
- the safety of the packaging (fpa, 2016).

Where should I keep condoms?

Always keep packets of condoms and individual condoms where they cannot be damaged by strong heat, sharp objects, light or damp (fpa, 2016).

Male condoms

A woman can get pregnant if a man's sperm reaches one of her eggs (ova). Contraception tries to stop this happening by keeping the egg and sperm apart or by stopping egg production. One method of contraception is the condom.

There are two types of condoms: male condoms, which are worn on the penis, and female condoms, which are worn inside the vagina. This page is about male condoms, where you can get them and how they work.

Male condoms are made from very thin latex (rubber), polyisoprene or polyurethane, and are designed to stop a man's semen from coming into contact with his sexual partner.

When condoms are used correctly during vaginal sex, they help to protect against pregnancy and sexually transmitted infections (STI's).

When used correctly during anal and oral sex, they help to protect against STI's. Condoms are the only contraception that protect against pregnancy **and** STI's (NHS, 2015e).

- If used correctly every time you have sex, male condoms are 98% effective. This means that two out of 100 women using male condoms as contraception will become pregnant in one year (NHS, 2015e).
- If male condoms are not always used according to instructions, about 18 in 100 women will get pregnant in a year (fpa, 2016).
- You can get free condoms from contraception clinics, sexual health clinics and some GP surgeries.
- Oil-based products, such as moisturiser, lotion and Vaseline, can make latex and polyisoprene condoms less effective, but they are safe to use with condoms made from polyurethane.
- Water-based lubricant, available in pharmacies and sexual health clinics, is safe to use with all condoms.
- It's possible for a condom to slip off during sex. If this happens, you may need emergency contraception, and to get checked for STI's.
- Condoms need to be stored in places that aren't too hot or cold, and away from sharp or rough surfaces that could tear them or wear them away.
- Putting on a condom can be an enjoyable part of sex, and doesn't have to feel like an interruption.
- If you're sensitive to latex, you can use polyurethane or polyisoprene condoms instead.
- A condom must not be used more than once. Use a new one each time you have sex.
- Condoms have a use-by date on the packaging. Don't use out-of-date condoms.
- Always buy condoms that have the BSI kite mark and the CE mark on the packet. This means that they've been tested to high safety standards. Condoms that don't have the BSI kite mark and CE mark won't meet these standards, so don't use them (NHS, 2015e).

Can anyone use condoms?

Yes, male and female condoms are suitable for most people.

Some men and women are sensitive to the latex in male condoms. If this is a problem you can use male polyurethane condoms or female condoms.

Men who do not always keep their erection during sex may find it difficult to use a male condom (fpa, 2016).

How a condom works

Condoms are a barrier method of contraception. They stop sperm from reaching an egg by creating a physical barrier between them. Condoms can also protect against STI's if used correctly during vaginal, anal and oral sex.

It's important that the man's penis does not make contact with the woman's vagina before a condom has been put on. This is because semen can come out of the penis before a man has fully ejaculated (come). If this happens, or if semen leaks into the vagina while using a condom, seek advice about emergency contraception from your GP or contraception clinic. You should also consider having an STI test (NHS, 2015e).

How to use a condom

- Take the condom out of the packet, taking care not to tear it with jewellery or fingernails do not open the packet with your teeth.
- Place the condom over the tip of the erect penis.
- If there's a teat on the end of the condom, use your thumb and forefinger to squeeze the air out of it.
- Gently roll the condom down to the base of the penis.
- If the condom won't roll down, you're probably holding it the wrong way round if this happens, throw the condom away because it may have sperm on it, and try again with a new one.
- After sex, withdraw the penis while it's still erect hold the condom onto the base of the penis while you do this.
- Remove the condom from the penis, being careful not to spill any semen.
- Throw the condom away in a bin, not down the toilet.
- Make sure the man's penis does not touch his partner's genital area again.
- If you have sex again, use a new condom (NHS, 2015e).

Condoms with spermicide

Some male condoms come with spermicide on them. Spermicide is a chemical that kills sperm. These condoms are slowly being phased out, as research has found that a spermicide called nonoxynol 9 does not protect against STI's such as chlamydia and HIV, and may even increase the risk of infection. It is best to avoid using spermicide-lubricated condoms, or spermicide as an additional lubricant (NHS, 2015e).

When should I use lubricants with a condom?

Most male condoms come ready lubricated to make them easier to use. Some people also like to use additional lubrication. Any lubricant can be used with male polyurethane condoms.

However, if you are using a male latex or polyisoprene condom you should never use oil-based products - such as body oils, creams, lotions or petroleum jelly - as a lubricant. This is because they can cause damage and make the condom more likely to split.

Some ointments can also damage latex or polyisoprene. If you are using medication in the genital area - for example, creams, pessaries, or suppositories - ask your doctor, nurse or pharmacist if it will affect latex or polyisoprene condoms.

You can check the condom packaging to find out whether a condom is made from latex, polyurethane or polyisoprene.

Some condoms don't have any lubricant on them so that you can choose not to use lubricant, or to use a lubricant of your own choice (fpa, 2016).

Who can use condoms?

Most people can safely use condoms. There are many different varieties and brands of male condom, and it's up to you and your partner which type of condom you use. However, condoms may not be the most suitable method of contraception for everyone.

- Some men and women are sensitive to the chemicals in latex condoms. If this is a problem, polyurethane or polyisoprene condoms have a lower risk of causing an allergic reaction.
- Men who have difficulty keeping an erection may not be able to use male condoms, as the penis must be erect to prevent semen leaking from the condom, or the condom slipping off (NHS, 2015e).

Are there different types of condoms?

There are many different types of male condom to choose from, including regular, larger, trim, stimulating and fun.

Regular condoms

These are made from latex or polyurethane. They are an average length and width to suit most men and are straight sided with a round or teated end. Adult penis sizes do vary, but not by much. However, you may feel more comfortable with a larger or smaller condom (fpa, 2016).

Larger condoms

These are condoms designed to fit a larger penis. They vary in shape and some are flared to improve comfort and to make them easier to put on (fpa, 2016).

Smaller condoms

Often known as trim condoms, small condoms are designed for a thinner or shorter penis (fpa, 2016).

Made-to-measure condoms

Custom-made condoms are available for those who cannot find a condom that is the right size or comfortable (fpa, 2016).

Ejaculation delayers

Most ejaculation delayer condoms contain benzocaine. Benzocaine is a low strength local anaesthetic, similar to that used in throat lozenges. It is put in the condom lubricant or teat and works by temporarily numbing the nerve endings of the penis (fpa, 2016).

Heightened stimulation condoms

Some contain a special lubricant that creates a warm or tingling sensation for both partners. Others contain extra lubricant to increase sensation. All brands now have at least one style of condom that is textured - ribbed, dotted, and/or studded - which aims to increase sensation during sex (fpa, 2016).

Fun condoms

Coloured, flavoured, glow-in-the-dark and novelty condoms are all aimed at making sex more fun. Check the packaging to make sure that they can be used to protect against pregnancy and sexually transmitted infections (fpa, 2016).

Strong condoms

These condoms are slightly thicker and sometimes have additional lubricant. They are usually made of latex. Strong condoms are not less likely to break (fpa, 2016).

Thin condoms

These condoms are thinner than a regular condom, providing greater sensitivity for both partners (fpa, 2016).

Vegan condoms

Many latex condoms contain a milk protein called casein. Vegan condoms are free from all animal products (fpa, 2016).

Advantages and disadvantages of condoms

It is important to consider which form of contraception is right for you and your partner. Take care to use condoms correctly, and consider using other forms of contraception for extra protection (NHS, 2015e).

Advantages

- When used correctly and consistently, condoms are a reliable method of preventing pregnancy.
- They help to protect both partners from STI's, including Chlamydia, Gonorrhoea and HIV.
- You only need to use them when you have sex - they do not need advance preparation and are suitable for unplanned sex.
- In most cases, there are no medical side effects from using condoms.
- Male condoms are easy to get hold of and come in a variety of shapes, sizes and flavours (NHS, 2015e).

Disadvantages

- Some couples find that using condoms interrupts sex - to get around this, try to make using a condom part of foreplay.
- Condoms are very strong, but may split or tear if not used properly.
- Some people may be allergic to latex, plastic or spermicides - you can get condoms that are less likely to cause an allergic reaction.
- When using a male condom, the man has to pull out after he has ejaculated and before the penis goes soft, holding the condom firmly in place.
- If male condoms aren't used properly, they can slip off or split. If this happens, practise putting them on so that you get used to using them properly (NHS, 2015e).

Can anything make condoms less effective?

Sperm can sometimes get into the vagina during sex, even when using a condom. This may happen if -

- the penis touches the area around the vagina before a condom is put on,
- the condom splits or comes off,
- the condom gets damaged by sharp fingernails or jewellery,
- you use oil-based lubricants, such as lotion, baby oil or petroleum jelly, with latex or polyisoprene condoms - this damages the condom,
- you are using medication for conditions like thrush, such as creams, pessaries or suppositories - this can damage latex and polyisoprene condoms and stop them working properly.

If you think that sperm has entered the vagina, talk to your GP or staff at a contraception clinic about emergency contraception and the risk of STI's.

As well as condoms, you can use other forms of contraception, such as the contraceptive pill, for extra protection against pregnancy. However, other forms of contraception will not protect you against STI's. You will still be at risk of STI's if the condom breaks (NHS, 2015e).

Using lubricant

Condoms come ready lubricated to make them easier to use, but you may also like to use additional lubricant, or lube. This is particularly advised for anal sex, to reduce the chance of the condom splitting.

Any kind of lubricant can be used with condoms that are not made of latex. However, if you are using latex or polyisoprene condoms, do not use oil-based lubricants, such as -

- body oil or lotion,
- petroleum jelly or creams (such as Vaseline).

This is because they can damage the condom and make it more likely to split (NHS, 2015e).

If a condom splits or comes off?

If the condom splits or comes off, you can use emergency contraception to help prevent pregnancy. This is for emergencies only and shouldn't be used as a regular form of contraception.

Depending on the type of pill, you need to take the emergency contraceptive pill up to 72 hours or up to 120 hours (five days) after unprotected sex. The intrauterine device (IUD) can be used as emergency contraception up to five days after sex.

If you have been at risk of pregnancy, you have also been at risk of STI's. You should have a check-up at -

- a GP surgery,
- a contraception clinic,
- a sexual health clinic or genitourinary medicine (GUM) clinic,
- a young person's clinic (NHS, 2015e).

Risks

For most people, there are no serious risks associated with using condoms, although some people are allergic to latex condoms. You can get condoms that are less likely to cause an allergic reaction (NHS, 2015e).

Where to get condoms

Everyone can get condoms for free, even if they are under 16. They are available from -

- contraception clinics,
- sexual health or GUM (genitourinary medicine) clinics,
- some GP surgeries,
- some young people's services.

You can also buy condoms from -

- pharmacies,
- supermarkets,
- websites,
- mail-order catalogues,
- vending machines in some public toilets,
- some petrol stations.

If you buy condoms online, make sure that you buy them from a pharmacist or other legitimate retailer. Always choose condoms that carry the BSI kite mark and the European CE mark as a sign of quality assurance. This means they have been tested to the required safety standards.

Contraception services are free and confidential, including for people under the age of 16.

If you're under 16 and want contraception, the doctor, nurse or pharmacist won't tell your parents (or carer) as long as they believe you fully understand the information you're given, and your decisions.

Doctors and nurses work under strict guidelines when dealing with young people under 16. They'll encourage you to consider telling your parents but they won't make you. The only time that a professional might want to tell someone else is if they believe you're at risk of harm, such as abuse. The risk would need to be serious, and they would usually discuss this with you first (NHS, 2015e).

Female condoms

A woman can get pregnant if a mans sperm reaches one of her eggs (ova). Contraception tries to stop this happening by keeping the egg and sperm apart or by stopping egg production. One method of contraception is the female condom.

Female condoms are made from thin, soft plastic called polyurethane (some male condoms are made from this too). Female condoms are worn inside the vagina to prevent semen getting to the womb.

When used correctly during vaginal sex, they help to protect against pregnancy and sexually transmitted infections (STI's). Condoms are the only contraception that protect against pregnancy **and** STI's. Currently, there is only one brand of female condom available in the UK, called "Femidom" (NHS, 2015c).

- If used correctly and consistently, female condoms are 95% effective.This means that five out of 100 women using female condoms as contraception will become pregnant in a year (NHS, 2015c).
- If female condoms are not always used according to instructions, about 21 in 100 women will get pregnant in a year (fpa, 2016).
- You can put the condom in any time before sex, but always before the penis touches the vagina or genital area. You can put the condom in when you are lying down, squatting or with one leg on a chair. Find the position that suits you best.
- Be careful how you take the condom out of the packet - sharp fingernails and jewellery can tear the condom (fpa, 2016).
- Using female condoms protects against both pregnancy and STI's.
- A female condom needs to be placed inside the vagina before there is any contact between the vagina and the penis.

- Female condoms need to be stored in places that aren't too hot or too cold, and away from sharp or rough surfaces that could tear them or wear them away.
- Always buy condoms that have the CE mark on the packet. This means they've been tested to European safety standards. Condoms that don't have the CE mark won't meet these standards, so don't use them.
- A female condom can get pushed too far into the vagina, but it's easy to remove it yourself.
- Female condoms may not be suitable for women who are not comfortable touching their genital area.
- Do not use a female condom more than once. If you have sex again, use a new female condom (NHS, 2015c).

Can anyone use condoms?

Yes, male and female condoms are suitable for most people.

Some men and women are sensitive to the latex in male condoms. If this is a problem you can use male polyurethane condoms or female condoms.

Female condoms may not be suitable for women who do not feel comfortable touching their genital area (fpa, 2016).

How do they work?

The female condom is worn inside the vagina to stop sperm getting to the womb.

It is important to use condoms correctly, and to make sure the penis doesn't make contact with the vagina before a condom has been put in. This is because semen can come out of the penis before a man has fully ejaculated (come). A female condom can be put in up to eight hours before sex (NHS, 2015c).

How to use a female condom

- Take the female condom out of the packet, taking care not to tear the condom - do not open the packet with your teeth (NHS, 2015c).
- Hold the closed end of the condom and squeeze the inner ring between your thumb and middle finger. Keeping your index finger on the inner ring helps you to insert the condom into the vagina.
- With your other hand, separate the labia (folds of skin) around your vagina. Put the squeezed ring into the vagina and push it up as far as you can.

- Now put your index or middle finger, or both, inside the open end of the condom, until you can feel the inner ring. Push the inner ring as far back into the vagina as it will go. It will then be lying just above your pubic bone. (You can feel your pubic bone by inserting your index or middle finger into your vagina and curving it forward slightly.)
- Make sure that the outer ring lies close against the area outside your vagina (vulva).
- It is a good idea to guide the penis into the condom to make sure it does not enter the vagina outside the condom. Holding the outer ring in place, outside the vagina, also helps to stop the entire condom being accidentally pushed right into the vagina (fpa, 2016).
- Make sure the penis enters into the female condom, not between the condom and the side of the vagina (NHS, 2015c).
- As the female condom is loose-fitting, it will move during sex. But you will still be protected as long as the penis stays inside the condom.
- To remove the condom, simply twist the outer ring to keep the semen inside. Then pull the condom out gently. Wrap the condom and put it in a bin. Do not put it down the toilet.
- Make sure the penis does not touch the genital area again, and if you have sex again, use a new condom (fpa, 2016).

Who can use female condoms

Most people can safely use condoms. However, they may not be the most suitable method of contraception for women who do not feel comfortable touching their genital area (NHS, 2015c).

Advantages and disadvantages of female condoms

It is important to consider which form of contraception is right for you and your partner. Take care to use condoms correctly, and consider using other forms of contraception for extra protection.

Advantages

- By preventing the exchange of bodily fluids (semen and vaginal fluid), female condoms help to protect against many STI's, including HIV.
- When used correctly and consistently, condoms are a reliable method of preventing pregnancy.
- You only need to use them when you have sex - they do not need advance preparation and are suitable for unplanned sex.
- In most cases, there are no medical side effects from using condoms.
- Female condoms can be inserted up to eight hours before sex, and mean that women share the responsibility for using condoms with their partner.

Disadvantages

- Some couples find that putting a condom in can interrupt sex - to get around this, try making using a condom part of foreplay or insert the female condom in advance.
- Condoms are very strong, but may split or tear if not used properly.
- Female condoms are not as widely available as male condoms and are more expensive to buy (NHS, 2015c).

Can anything make condoms less effective?

Sperm can sometimes get into the vagina during sex, even when using a condom. This may happen if -

- the penis touches the area around the vagina before a condom is put in,
- the female condom gets pushed too far into the vagina,
- the man's penis enters the vagina outside the female condom by mistake,
- the condom gets damaged by sharp fingernails or jewellery.

Although female condoms (when used correctly) offer reliable protection against pregnancy, using an additional method of contraception will protect you against pregnancy if the female condom fails. If a female condom slips or fails, you can use emergency contraception to help to prevent pregnancy. This is for emergencies only, and shouldn't be used as a regular form of contraception.

If you've been at risk of unintended pregnancy, you're also at risk of catching an STI, so have a check-up at -

- a GP surgery,
- a local sexual health clinic or genitourinary medicine (GUM) clinic (Find sexual health services near you),
- a young persons' service (call the sexual health line on 0300 123 7123 for details).

Using lubricant

Condoms come ready lubricated, to make them easier to use, but you may also like to use additional lubricant. This is particularly advised when using male condoms for anal sex to reduce the chance of the condom splitting.

Any kind of lubricant can be used with female polyurethane condoms. If you are using male latex condoms, do not use oil-based lubricants, such as body oil, petroleum jelly or creams (like Vaseline), as they can damage the latex and make the condom more likely to split (NHS, 2015c).

Risks

There are no serious risks associated with using female condoms (NHS, 2015c).

Where to get female condoms

Everyone can get condoms for free, even if they are under 16. They are available from the following places in your local area -

- contraception (or family planning) clinics,
- sexual health or GUM (genitourinary medicine) clinics,
- some GP surgeries,
- Brook Advisory Centres (for under-25s only).

Some places might only offer male condoms - you can ask the staff whether they provide free female condoms.

You can also buy male and female condoms from -

- pharmacies,
- supermarkets,
- websites,
- mail-order catalogues,
- vending machines in some public toilets,
- some petrol stations.

If you buy condoms online, make sure you buy them from a pharmacist or other legitimate retailer. Always choose condoms that carry the European CE mark or British BSI Kitemark as a sign of quality assurance.

Contraception services are free and confidential, including for people under the age of 16.

If you're under 16 and want contraception, the doctor, nurse or pharmacists won't tell your parents (or carer) as long as they believe you fully understand the information you're given, and your decisions.

Doctors and nurses work under strict guidelines when dealing with young people under 16. They'll encourage you to consider telling your parents, but they won't make you. The only time that a professional might want to tell someone else is if they believe you're at risk of harm, such as abuse. The risk would need to be serious, and they would usually discuss this with you first (NHS, 2015c).

Tips for using condoms

Only use condoms with a BSI kite mark or CE mark

Always choose condoms that carry the BSI kite mark or European CE mark, as they are recognised safety standards. Don't use novelty condoms, unless they carry the BSI kite mark or CE mark (NHS, 2016b).

Condom before contact

Always put on the condom before there's any contact between the penis and the vagina, mouth or anus.

New sex, new condom

Use a new condom every time you have sex.

The 30-minute condom rule

If you're having a long sex session, change condoms after 30 minutes. Friction can weaken the condom, making it more likely to break or fail.

One condom at a time

Never use two condoms together, whether that's two male condoms or a female and a male condom. They will rub against each other, and this friction can weaken them and make them more likely to break or fail.

Keep condoms cool

Heat can damage condoms, so store them somewhere cool and dry.

Condoms don't last forever

Check the expiry date on the packaging, as condoms don't last forever and may be past the point at which they work.

Safer sex on holiday

Buy condoms before going on holiday to avoid problems with language and trying to find somewhere to buy them.

Don't use lotion or oils with condoms

Don't use body lotions, moisturiser, massage oil, body oil, lipstick or any other oil-based product (such as petroleum jelly, or Vaseline) with latex, polyisoprene or lambskin condoms. This is because they can weaken the condom, making it less effective.

Use plenty of water-based lubricant, such as K-Y Jelly (available from pharmacies), especially for anal sex.

Oral sex and condoms

Using a condom (apart from lambskin condoms) during oral sex can help protect against sexually transmitted infections (STI's), including HIV and syphilis, and those that affect the mouth or throat, such as herpes, gonorrhoea and chlamydia. You could try using flavoured condoms for variety.

Don't put condoms down the toilet

Wrap used condoms in a tissue or piece of paper and put them in a dustbin. Don't flush used condoms down the toilet.

Buying condoms online

If you buy condoms online, don't buy from auction sites such as eBay. Make sure that any condoms you buy have the BSI kite mark or CE mark and haven't gone past the use-by date on the packaging.

If you don't want to get pregnant

To protect against unintended pregnancy, use another form of contraceptive as well, such as the longer-acting methods (the implant, injection, IUS, IUD) or the contraceptive pill, contraceptive patch or vaginal ring (NHS, 2016b).

Chapter 16

Other infections that can be caused by an STI

Bacterial vaginosis - BV

Bacterial vaginosis (BV) is a common yet poorly understood condition, in which the balance of bacteria inside the vagina becomes disrupted.

BV doesn't usually cause any vaginal soreness or itching, but often causes unusual vaginal discharge. If you have the condition, your discharge may -

- develop a strong fishy smell, particularly after sexual intercourse,
- become white or grey,
- become thin and watery

BV isn't serious for the vast majority of women, although it may be a concern if symptoms of BV develop in pregnancy and you have a history of pregnancy-related complications.

Around half of women with bacterial vaginosis have no symptoms (NHS, 2015a).

BV can occur in women who are not sexually active but is more common in those that are (brook, 2015a).

Causes

BV occurs when there's a change in the natural balance of bacteria in your vagina.

Your vagina should contain bacteria called lactobacilli, which produce lactic acid. This makes the vagina slightly acidic, which prevents other bacteria from growing there.

Women with BV tend to have a temporary shortage of lactobacilli, which means their vagina isn't as acidic as it should be. This allows other types of bacteria to grow.

It's still unclear what causes this change, although your risk is increased if you -

- are sexually active, particularly if you have a new sexual partner or multiple sexual partners,
- use an intrauterine device (IUD) a contraceptive device that fits inside the womb,
- smoke.

For reasons that are unclear, BV is more common in black women than in other ethnic groups (NHS, 2015a).

There are also a number of other factors that can increase your risk of developing BV, including -

- using scented soaps or bubble baths,
- having an intrauterine device (IUD) fitted,
- perform vaginal douching,
- using vaginal deodorant (NHS, 2015a).

Is BV an STI?

BV isn't generally considered a STI. However, there's conflicting evidence on the subject.

Evidence that suggests BV may be an STI includes -

- rates of BV are higher in women who have multiple sexual partners,
- rates of BV are lower in women who use a condom during sex.

There's also evidence that women with BV can pass the condition to women they have sex with, although how this happens is still unclear.

However, there's also evidence to suggest BV may not be an STI, as -

- there's no equivalent of BV in men,
- treating male partners with antibiotics doesn't prevent the recurrence of BV,
- rates of BV can vary significantly in different ethnic groups, which can't be explained by sexual activity alone,
- BV can sometimes occur in women who aren't sexually active.

Many experts think sexual activity plays a role in BV, but other factors are probably also responsible for the condition (NHS, 2015a).

Can I pass it on to my partner?

There's no evidence that the bacteria causing BV affects male sexual partners.

However, some evidence suggests that women with BV may be able to pass the condition on to female sexual partners (NHS, 2015a).

Diagnosing it

See your GP or visit a sexual health or genitourinary medicine (GUM) clinic as soon as possible if you have any abnormal discharge from your vagina.

It's important to determine whether you have BV or a similar condition, such as trichomoniasis or gonorrhoea. These can both also cause abnormal vaginal discharge.

Tests for BV are sometimes offered to women during pregnancy or before certain procedures.

Examination

Your GP or healthcare professional may diagnose BV from a description of your symptoms and by examining your vagina. In particular, they'll look for -

- a thin, greyish discharge,
- an unpleasant smell.

In some cases, this may be enough to confirm your diagnosis. However, you may need further tests if you're sexually active and may have a STI instead.

Tests

A sample of cells may be taken from the wall of your vagina using a plastic loop or swab. A swab looks a bit like a cotton bud, but is smaller, soft and rounded.

The swab or loop picks up samples of discharge and cells. It only takes a few seconds and isn't usually painful, although it may be slightly uncomfortable for a moment.

The samples are examined to check for signs of BV. In some centres, the result may be available immediately, but it can take up to a week to get the results if the sample is sent to a laboratory.

The level of acidity (pH) of your vagina may also be measured. A swab will be taken from inside your vagina and wiped over a piece of specially treated paper. The paper changes colour depending on the pH level. A pH level higher than 4.5 is an indication that you may have BV (NHS, 2015a).

How accurate are the tests?

Tests for bacterial vaginosis are usually accurate. The doctor or nurse will discuss your test results with you (fpa, 2014i).

Treating it

BV can be treated successfully with antibiotics.

There's currently no evidence that probiotics, such as those found in some yoghurts, are able to treat or prevent BV.

Antibiotics

Metronidazole is the most common and preferred antibiotic treatment for BV. It's available in three forms. These are -

- tablets to be taken twice a day for five to seven days,
- a single larger-dose tablet you take only once,
- a gel you apply to your vagina once a day for five days (NHS, 2015a)
- There is currently no evidence that complementary therapies can cure BV (fpa, 2014i).

In most cases, metronidazole tablets taken over five to seven days are recommended, as they're considered to be the most effective treatment. These can be taken if you have symptoms of BV while you're pregnant.

If you're breastfeeding, metronidazole gel is usually recommended, as the tablets can affect your breast milk.

Occasionally, an alternative antibiotic may be recommended instead of metronidazole, such as clindamycin cream applied to the inside of the vagina once a day for seven days. This cream may be prescribed if you've had a reaction to metronidazole in the past, for example.

Whichever course of antibiotics you're prescribed, it's important to finish it, even if you start to feel better. This helps to reduce the risk of symptoms persisting or recurring (NHS, 2015a).

You may be given a cream or gel instead that you use in the vagina for around a week. Be aware that some of these creams can weaken the latex in condoms, diaphragms and caps but ask the doctor or nurse who gives you the cream for more advice (brook, 2015a).

Side-effects

Metronidazole can cause nausea, vomiting and a slight metallic taste in your mouth. It's best to take it after eating food. Contact your doctor if you start vomiting when you take the drug. They may recommend trying an alternative form of treatment.

Don't drink alcohol while taking metronidazole and for at least 48 hours after finishing the course of antibiotics. Drinking alcohol while taking this medicine can cause more severe side effects.

Further treatment

For some women, the first course of treatment doesn't treat BV effectively.

If your initial treatment has been unsuccessful, your doctor will need to check you took the medicine correctly. If you did, you may be prescribed one of the different options described above.

If you have an intrauterine device (IUD) that may be contributing to your BV, your doctor may recommend having it removed and using an alternative form of contraception.

Vaginal pH correction treatments

Vaginal pH correction treatments are a relatively new way of treating BV. These usually involve applying a gel to the inside of your vagina that changes the acid balance, making it a less hospitable environment for harmful bacteria. Most vaginal pH correction treatments are available over the counter from pharmacists.

However, it's not clear how effective these treatments are for treating BV. Some studies have suggested they may help, whereas others suggest they're either ineffective or less effective than antibiotics.

Referral to a specialist

If you have repeated episodes of BV in a short space of time, your GP may refer you to a genitourinary medicine (GUM) specialist for further investigation and treatment.

If you're pregnant, you may be referred to your midwife or obstetrician (a specialist in pregnancies), who can discuss treatment options with you.

Things to avoid during treatment

While you're being treated for BV, there are some things you should avoid to reduce the chances of treatment being unsuccessful.

For example, you should avoid cleaning the inside of your vagina (douching) or using antiseptics, scented soaps and bubble baths (NHS, 2015a).

Complications

For the vast majority of women, BV is easily treated and doesn't cause any further problems. However, if the condition isn't treated, there's a small risk you may develop complications.

Pregnancy complications

There's some evidence to suggest untreated BV symptoms during pregnancy can increase your risk of pregnancy-related complications, particularly if you've had these problems in the past.

Pregnancy-related complications that have been associated with BV include -

premature birth - where the baby is born before the 37th week of pregnancy,
miscarriage - the loss of pregnancy during the first 23 weeks,
the amniotic sac breaking open too early the amniotic sac is the bag of fluid where an unborn baby develops,
chorioamnionitis - an infection of the chorion and amnion membranes (the membranes that make up the amniotic sac) and the amniotic fluid (the fluid that surrounds the foetus),
postpartum endometritis - infection and inflammation of the womb lining after giving birth, particularly after having a caesarean section (NHS, 2015a).

See your GP or visit a sexual health or genitourinary medicine (GUM) clinic as soon as possible if you're pregnant and have symptoms of BV. While your risk of developing these complications is small, treatment may reduce the risk.

If BV hasn't caused symptoms, there's no evidence to suggest it increases the risk of complications in pregnancy. Treatment might not be recommended if BV is detected while you're pregnant but don't have any symptoms.

Sexually transmitted infections

There's evidence that having BV can make you more at risk of catching STI's, such as chlamydia. This is possibly because the change in bacteria levels inside your vagina reduces your protection against infection.

Pelvic inflammatory disease

Although a link isn't entirely clear, some evidence suggests that BV may increase your risk of developing pelvic inflammatory disease (PID). PID causes infection and swelling of the upper female genital tract, including the womb, fallopian tubes and ovaries.

Symptoms of PID include -

- pain around the pelvis or lower abdomen,
- discomfort or pain during sex felt deep inside the pelvis,
- bleeding between periods and after sex (NHS, 2015a).

If diagnosed at an early stage, PID can usually be treated successfully with a course of antibiotics. However, an estimated one in five women with the condition become infertile because of severe scarring on the fallopian tubes.

It's important to see your GP if you experience any symptoms of PID. Delaying treatment or having repeated episodes of PID can increase your risk of infertility.

In-vitro fertilisation

Women who have BV and are using in-vitro fertilisation (IVF) may have a lower success rate and an increased risk of early miscarriage.

If you're having IVF and have symptoms of BV, see your GP or speak to your infertility specialist.

Recurrent BV

It's relatively common for BV to recur after treatment with antibiotics. It's estimated that more than half the women treated for BV develop the condition again within three months.

If your BV returns, see your GP or sexual health or GUM clinic to discuss further treatment options (NHS, 2015a).

What happens if it isnt treated?

For many women bacterial vaginosis goes away by itself (fpa, 2014i).

Proctitis

Proctitis is soreness and swelling (inflammation) of the rectum. It is not a STI but can be caused by STI's.

Proctitis can occur in men and women, and is more common in people who have anal sex.

Signs & symptoms

Proctitis symptoms may be temporary or longer-term and may include -

- Pain during a bowel movement,
- Soreness in your anal area,
- Feeling like you haven't completely emptied your bowels,
- Spasms or cramping during bowel movements (brook, 2015c).

Causes of it?

There are many causes of proctitis but sexually transmitted infections such as Gonorrhoea, Syphilis, Genital herpes, Genital warts and Chlamydia are the most common.

Other causes may include -

- Chrones disease and ulcerative colitis,
- Foreign objects inserted into the rectum,
- Trauma to the rectum,
- A side effect of taking antibiotics (brook, 2015c).

Diagnosis

Proctitis diagnosis will depend on what is suspected to have caused it. If it isn't thought to be linked to a sexually transmitted infection, you may require further tests with a specialist. This may include a procedure that involves inserting a camera into the rectum in order to examine the surface of your rectum. As part of this, the doctor may take a small piece of tissue from your rectum or a sample of discharge for testing (brook, 2015c).

Treatment

Because proctitis is generally caused by sexually transmitted infections, treatment will focus on dealing with the STI.

Although not all cases of proctitis are caused by an STI, it is possible to pass it on during sex so it is recommended that you don't have sex until it has cleared up.

It is important that you tell your current and any recent sexual partners if you are being treated for an STI, so that they go for treatment too. In the UK it is recommended you tell any sexual partners you have had over the last six months.

Some clinics may also offer to contact your partner using what's called a 'contact slip'. This is to warn them they may have been exposed and to recommend they get tested and it doesn't mention your name (brook, 2015c).

Thrush

Thrush is usually caused by the yeast fungus candida albicans. This yeast lives harmlessly on the skin and in the mouth, gut and vagina. Normally it is kept under control. Occasionally, however, conditions change and signs and symptoms can develop. This is commonly known as thrush, thrush infection or candida, and sometimes as monilia. There is a separate section on Vaginal Thrush (fpa, 2014i).

Causes

Many people have a small amount of this fungus in their bodies. However, it does not usually cause problems because it is kept under control by the bodys immune system and other harmless bacteria (so-called "good bacteria").

Thrush can develop when the good bacteria in your body (which keeps candida under control) is destroyed. For example, if you are taking antibiotics to treat an infection, the antibiotics will not distinguish between good and bad bacteria, and will fight off both types.

Also, if you are run down and your immune system is weak, the candida fungus that causes thrush may multiply (NHS, 2014n).

Personal hygiene

Candida tends to grow in warm and moist conditions. Therefore, you may develop thrush if you do not dry your penis carefully after washing.

Using perfumed soaps and shower gels can irritate your penis, making thrush more likely to develop. Candida also thrives on skin that is already damaged (NHS, 2014n).

Symptoms

- Irritation, burning or itching under the foreskin or on the tip of the penis,
- Redness, or red patches, under the foreskin or on the tip of the penis,
- A thin or thicker discharge, like cottage cheese, under the foreskin which sometimes smells yeasty,
- Difficulty in pulling back the foreskin (fpa, 2014i).

As a skin infection

Most candidal skin infections develop in areas of the body where folds of skin come together, such as the -

- armpits,
- groin,
- areas between your fingers,
- skin between your genitals and anus (NHS, 2014n).

People who are obese are also at risk of developing a skin infection between their rolls of skin.

The infection usually begins as a red and painful itchy rash. Small red spots can also develop on the rash. Affected skin may then scale over, producing a white-yellow curd-like substance. If the skin between your fingers is affected, it becomes thick, soft and white (NHS, 2014n).

How will I know if I have thrush?

If you think that you may have thrush you can speak to your doctor, nurse or pharmacist. Thrush is not a sexually transmitted infection but it is important that you don't delay seeking advice if you think you may have been at risk of a sexually transmitted infection (fpa, 2014i).

Diagnosis

Visit your GP if you have the symptoms of thrush (either on your penis or skin) and you do not have a history of the condition.

If you have a previous history of thrush that has been diagnosed, you do not usually need another diagnosis unless it fails to respond to treatment.

Thrush can be diagnosed at -

- your GP surgery,
- your local sexual health or GUM clinic,
- some contraception clinics and young people's services (NHS, 2014n).

Thrush is diagnosed by a physical examination of the head of your penis or the affected area of skin.

It's important to get thrush diagnosed in case the symptoms are caused by a different condition, such as a STI or a bacterial skin infection (NHS, 2014n).

A doctor or nurse may -

- look at the penis and genital area
- use a swab to collect a sample of cells from the genital area including under the foreskin (fpa, 2014i).

A swab looks a bit like a cotton bud, but is smaller, soft and rounded. The swab is wiped over the parts of the body that could be affected and easily picks up samples of discharge and cells. It only takes a few seconds and is not usually painful, though it may be uncomfortable for a moment.

Samples taken during the examination are looked at under a microscope to check for thrush. Sometimes the result is available immediately. If the sample is sent to a laboratory for testing, the result is usually available within a week.

Routine blood tests do not detect infections such as thrush (fpa, 2014i).

Further testing

Further testing is usually only required if -

- your symptoms are severe,
- your symptoms persist, despite treatment,
- you have recurring episodes of thrush (NHS, 2014n).

How accurate are the tests?

Tests for thrush are less accurate in men, so diagnosis in men is often made by looking at the penis and genital area (fpa, 2014i).

Treatment

Treatment is simple for both men and women and is only necessary if you have signs and symptoms of thrush.

You may be given some antifungal cream, pills or a combination. The doctor or nurse will advise you how to use the treatment. The cream is applied to the genital area.

You can also buy some antifungal treatments from a pharmacy these are useful if you are sure you have thrush and want to treat yourself. The pharmacist will be able to advise if you have any questions, or are unsure how to use the treatment.

It is very important to take the treatment as instructed and finish any course of treatment even if the symptoms go away earlier.

Some antifungal products can weaken latex condoms. Polyurethane types can be safely used. Ask the doctor, nurse or pharmacist for advice (fpa, 2014i).

The recommended treatment for thrush in men depends on which area of the body is affected.

For thrush that doesn't affect the penis, a type of anti-fungal cream called topical imidazole is usually recommended.

Fluconazole is the first-choice treatment for thrush that affects the penis. It's also used as an alternative anti-fungal medication if your symptoms do not improve within 14 days of using a topical imidazole (NHS, 2014n).

Topical imidazole

Topical imidazoles work by breaking down the membranes (walls) of the fungi cells. Examples of topical imidazoles include -

- clotrimazole,
- econazole,
- ketoconazole,
- miconazole (NHS, 2014n).

Most of these are available from your pharmacist without a prescription. Your pharmacist can advise which treatment is most suitable for you.

The most common side effect of a topical imidazole is a mild burning sensation when you apply the cream.

In a few people, some topical imidazoles have caused more severe burning and a serious skin irritation. If this happens, stop using the cream and contact your GP for advice.

If your skin feels itchy, your GP may prescribe a corticosteroid cream as an additional treatment. Corticosteroids reduce levels of inflammation within the affected tissue. This should help to resolve the symptoms of itchiness (NHS, 2014n).

Fluconazole

Fluconazole is usually taken as a tablet and is often available over the counter without a prescription.

Fluconazole works by destroying some of the enzymes (a type of protein that triggers useful chemical reactions inside the body) that fungi cells need to survive and reproduce.

The most common side effects of fluconazole are -

- nausea,
- abdominal (stomach) pain,
- diarrhoea,
- flatulence (NHS, 2014n).

Contact your GP for advice if your symptoms do not improve after 14 days of taking fluconazole. You may need to be referred to a dermatologist for specialist treatment. A dermatologist is a doctor who specialises in treating skin conditions (NHS, 2014n).

Avoid having sex

If you have thrush, avoid sex until the infection has cleared up, as your infection can be spread or made worse during sex.

If you do have sex, use a condom to avoid infecting your partner.

Some heterosexual men get a mild form of balanitis (inflammation of the head of the penis) after having sex. This is probably caused by an allergy to the candida fungus in your partners vagina. However, it will usually clear up if your partner gets treatment.

Gay men may also get thrush by having unprotected sex. The infection will usually clear up with treatment. Avoid sex until the infection has cleared up, and always use a condom (NHS, 2014n).

Good hygiene

If you have thrush, practising good personal hygiene can help clear up the infection. Wash the affected area carefully using warm water. Showers are a better option than baths. Avoid using perfumed soaps or shower gels on your genitals, because they can cause irritation.

After washing, make sure you dry the affected area carefully, as the candida fungus thrives in damp conditions. Wearing loose-fitting cotton underwear can help keep your skin and penis dry and cool, which helps prevent the candida fungus building up on your skin and under your foreskin (NHS, 2014n).

How effective is the treatment?

Antifungal creams or pills are usually effective if you use them according to instructions. Symptoms should disappear within a few days.

If the first treatment doesn't work, the doctor or nurse may suggest another test or a combination of treatments (fpa, 2014i).

Avoid

Men should also try to avoid medicated and highly perfumed soap, bubble bath, genital sprays and deodorants, and any other irritants such as disinfectants and antiseptics.

If you are prescribed an antibiotic for another condition, remind your doctor that you tend to get thrush and ask for some treatment for thrush at the same time (fpa, 2014i).

I get thrush regularly, is there anything that can help?

Some people may only get one episode of thrush - others may get repeat episodes. If you have four or more episodes of thrush in a year, this is known as recurrent thrush. If this happens, it is important to get medical advice and not to treat yourself. If you get recurrent thrush the doctor or nurse -

- will want to check that other conditions, such as diabetes, are not the cause of the thrush,
- may suggest that you take antifungal treatment on a regular basis,
- may check that the thrush is not being caused by a different kind of yeast,
- will help you try and identify any thrush triggers (fpa, 2014i).
- If you have had thrush in the past and you recognise your symptoms, over-the-counter treatments from your pharmacist can help clear up the infection.
- If you keep getting thrush, or it does not clear up with treatment, visit your GP so they can investigate and recommend appropriate treatment.
- If you are a heterosexual man and have thrush, it is likely that your partner may also have the condition. This is because the candida fungus often lives inside the vagina. It is therefore a good idea for both of you to get treatment to prevent the infection being passed back and forth between you (NHS, 2014n).

What happens if it isn't treated?

For many men thrush goes away by itself (fpa, 2014i).

Will my partner need treatment?

There is no need for your partner to have any treatment unless they have signs and symptoms (fpa, 2014i).

Complications

If you have a weakened immune system, there is a risk that the candida fungus will spread into your blood.

This is known as invasive candidiasis.

Invasive candidiasis

The infection can then spread quickly throughout your body, affecting many of your organs. Known risk factors for invasive candidiasis include -

having HIV
having type 1 or type 2 diabetes
taking immunosuppressants - a type of medication used to stop the body rejecting newly-donated organs,
undergoing high-dose chemotherapy or radiotherapy
having a central venous catheter (CVC) - a tube directly implanted into your chest and used to administer medication; they are often used to avoid repeated painful injections during a long-term course of medication,
having dialysis - a type of treatment where a machine is used to replicate the functions of the kidney, and is commonly used to treat kidney failure (NHS, 2014n).

Symptoms of invasive candidiasis can be wide-ranging, depending on what part of the body is affected by infection. However, initial symptoms can include -

- a high temperature (fever) of or above 38C (101.4F),
- shivering,
- nausea,
- headache (NHS, 2014n).

Get medical help immediately if you have thrush and any of the risk factors listed above, or you develop any of the above symptoms over a short period of time.

Invasive candidiasis is a medical emergency that requires immediate admission to an intensive care unit (ICU). In an ICU, functions of the body can be supported while the underlying infection is treated with anti-fungal medications.

If you are thought to be particularly vulnerable to invasive candidiasis - for example, you have diabetes and are on dialysis, your GP may recommend that you are admitted to hospital as a precaution if you develop a thrush infection (NHS, 2014n).

Urethritis

Urethritis is inflammation of the urethra and it is usually caused by an infection.

The term non-gonococcal urethritis (NGU) is used when the condition is not caused by gonorrhoea - a STI.

NGU is sometimes referred to as non-specific urethritis (NSU) when no cause can be found (NHS, 2014j).

Symptoms of non-gonococcal urethritis

NGU can cause different symptoms in men and women. In some cases, NGU does not cause any symptoms at all.

Symptoms of NGU in men

The symptoms of NGU in men can include -

- a white or cloudy discharge from the tip of the penis, usually more noticeable first thing in the morning. Sometimes this discharge is seen only when massaged out of the penis (fpa, 2014f).
- a burning or painful sensation when you urinate,
- the tip of your penis feeling irritated, itchy and sore,
- a frequent need to urinate (NHS, 2014j).

Depending on the cause of NGU, symptoms may begin a few weeks or several months after an infection.

If NGU has a non-infectious cause, such as irritation to the urethra, symptoms may begin after a couple of days. Symptoms that start a day or two after sex are usually not caused by an STI, but testing for STI's is still recommended. (NHS, 2014j).

If signs and symptoms do occur they usually show up within 2–4 weeks of contact with an infection, but they can sometimes appear within a day or two (depending on the cause of the inflammation). In mild cases, symptoms may not show up for several months (fpa, 2014f).

If a current or recent sexual partner informs you that you may have been exposed to a STI that can cause NGU, but you don't have any symptoms, don't assume that you do not have NGU. If this happens, it is always recommended that you get tested at your local GUM or sexual health clinic.

You should still seek treatment if the symptoms of NGU disappear on their own, as there is still a risk you could pass the infection on to someone else (NHS, 2014j).

Symptoms of NGU in women

NGU tends to cause no noticeable symptoms in women unless the infection spreads to other parts of the female reproductive system, such as the womb or fallopian tubes (which connect the ovaries to the womb).

If the infection does spread, a woman may develop PID. PID is a serious health condition that can cause persistent pain. Repeated episodes of PID are associated with an increased risk of infertility (NHS, 2014j).

Some women with PID don't have symptoms. If there are symptoms, they include -

- pain around the pelvis or lower part of your abdomen,
- discomfort or pain during sexual intercourse that is felt deep inside the pelvis,
- bleeding between periods and after sex,
- pain when you urinate,
- heavy or painful periods,
- unusual vaginal discharge - especially if it is yellow or green (NHS, 2014j).

A few women with PID become very ill with -

- severe lower abdominal pain,
- a fever (high temperature) of 38C (100.4F) or above,
- nausea and vomiting (NHS, 2014j).

Causes

NSU is most commonly caused by an infection, although there are many cases where no cause is found.

Although STI's can cause NGU, it does not result from a gonorrhoea infection. Urethritis caused by gonorrhoea is called gonococcal urethritis (NHS, 2014j).

Chlamydia

In men, Chlamydia is thought to be responsible for up to 43 out of 100 cases of NGU. In women, about 4 in 10 cases of NGU may be caused by Chlamydia.

Chlamydia is caused by Chlamydia trachomatis bacteria. It is an STI and is spread during unprotected sex (i.e. sex without a condom), including anal and oral sex. See also Chlamydia.

Other infections

A number of other infections can cause NGU.

These include other bacteria that usually live harmlessly in the throat, mouth or rectum. They can cause NGU if they get into the urethra, and this can occur during oral or anal sex.

Infections that can cause NGU include -

Trichomonas vaginalis - which is an STI caused by a tiny parasite,
a urinary tract infection
the herpes simplex virus - which can also cause cold sores and genital herpes,
an adenovirus - which usually causes a sore throat or an eye infection (NHS, 2014j).

- Tiny organisms called mycoplasma genitalium and ureaplasma urealyticum can live in the body without causing symptoms but sometimes they multiply quickly, leading to inflammation of the urethra. Being ill or stressed could cause this to happen. It is thought these organisms may be transmitted sexually.
- Some bacteria that live in the rectum and the mouth and throat can be passed on during sex and cause inflammation.
- Bacteria that cause infection in the urinary tract (kidneys, bladder and urethra) or the prostate gland can lead to inflammation of the urethra.
- A vaginal infection in your partner, such as thrush or bacterial vaginosis, may trigger non-specific urethritis in you (fpa, 2014f).

Non-infectious causes

It is possible for NGU to have a non-infectious cause. This is when something else leads to the urethra becoming inflamed.

Non-infectious causes of NGU include -

- damage to the urethra caused by vigorous sex or masturbation, or by frequently squeezing the urethra - some men may do this if they are worried they have an infection.
- damage to the urethra caused by inserting an object into it, such as a catheter - this can be done during an operation in hospital (NHS, 2014j).
- Antibacterial liquids - Applying liquids such as tea tree oil, antiseptic or disinfectant or using medicated or highly perfumed shower gels can cause inflammation.
- Sensitivity or irritation - Rarely, inflammation can occur if your skin is very sensitive to chemicals, such as those in latex (in condoms, for example), spermicide or soap (fpa, 2014f).

Sexually transmitted infections - STI's

Urethritis can be caused by an STI, and is therefore more common among people who are at risk of STI's. This includes people who -

- are sexually active,
- have had unprotected sex,
- have recently had a new sexual partner.

Diagnosis

NGU is usually diagnosed after tests have been carried out at a specialist clinic.

If you think you have NGU, you should visit your local GUM clinic or sexual health clinic. These clinics have access to specialist diagnostic equipment that your GP may not have.

Tests

Two tests can diagnose NGU - a swab test and a urine test. Either test can be used, although both may be carried out to ensure the diagnosis is correct.

It is recommended that you are also tested for gonorrhoea and chlamydia at the same time as NGU. These are two STI's that often cause urethritis.

You may also be offered tests for other STI's, including HIV. It is up to you whether to have these or not, but a test for all infections is recommended. You can discuss this with healthcare professionals at the clinic if you wish.

Swab test

A swab test involves taking a small sample of fluid from your urethra, and then examining the sample under a microscope to look for evidence of inflammation or bacteria known to cause NGU.

The sample is taken using a swab, which is like a small cotton bud with a plastic loop at the end. The swab is not painful, but can feel a little uncomfortable for a few seconds.

Urine test

You will be asked to provide a urine sample, which will be tested for bacteria known to cause NGU, such as Chlamydia.

You will be asked not to urinate for around two hours before providing a urine sample, because this can help make the test results more reliable (NHS, 2014j).

Results

Clinics that have microscope facilities will be able to give you some results the same day. Other clinics may need to send the samples to a laboratory for testing - in which case, the test results may not be available for a week or two.

Healthcare professionals at the clinic will tell you how and when you will get your test results, and they will also arrange your treatment (NHS, 2014j).

How accurate are the tests?

The accuracy of looking for signs of inflammation under the microscope depends on the skill of the person doing the test and how long ago you last passed urine. Most men are advised not to urinate for at least two hours beforehand so that the test is as accurate as possible.

You may be tested for various causes of non-specific urethritis, and these tests have different levels of accuracy.

If you have signs and symptoms but the test doesn't confirm non-specific urethritis, you may be asked not to pass urine overnight and come back to be tested again (fpa, 2014f).

Treatment

NGU is usually treated with a short course of antibiotics to kill the bacteria that caused the infection.

The healthcare professionals at the GUM clinic or sexual health clinic will arrange your treatment.

If your urethritis is caused by gonorrhoea, this may be treated differently (NHS, 2014j).

- If the test shows that inflammation is present, or if there is a high chance that you have an infection, you will be given treatment even if the cause is not yet known.
- There are several different antibiotics that can be used, either as a single dose or a longer course (up to two weeks).
- Some men may get non-specific urethritis more than once, and for a few men it may become persistent (keep coming back). If this happens, you may be given a second course, or a combination, of antibiotics.

- You may also need other treatment if complications have occurred (see below, What happens if non-specific urethritis isn't treated?) or the cause of the inflammation becomes known.
- There is no evidence that complementary therapies can cure non-specific urethritis (fpa, 2014f).

Antibiotics

Treatment with antibiotics may be started before you receive your test results.

If your test results do not identify an infection, or your NGU is related to inflammation caused by an object, cream or soap, antibiotics are also used frequently.

Most people with NGU are prescribed antibiotic tablets or capsules. This may be -

azithromycin - which is taken just once as a single dose
doxycycline - which is taken twice a day for seven days

You will usually not need to return to the clinic as long as you have -

- taken your treatment,
- made sure that any recent partners have been treated,
- not had any sex until a week after everyone has been treated (NHS, 2014j).

It may sometimes take two or three weeks for your symptoms to disappear completely.

You should not have sex, including vaginal, anal and oral sex, until -

- you have finished your course of doxycycline, or it has been seven days since you took azithromycin,
- you have no symptoms,
- your partner or partners have also been treated (NHS, 2014j).

Side effects

Antibiotics may cause some side effects, such as -

- feeling sick,
- vomiting,
- diarrhoea,

Antibiotics used to treat NGU may interact with the combined contraceptive pill and the contraceptive patch. If you use these methods of contraception, your GP or nurse can advise you about which additional contraception is suitable (NHS, 2014j).

NGU and sexually transmitted infections (STI's)

While not all cases of NGU are caused by a STI, it is possible to pass on NGU during sex. Therefore, you should treat all cases of NGU as an STI and ensure that all recent partners have been treated.

You also shouldn't have any kind of sex until you are certain the condition has cleared up.

NGU does not tend to cause any noticeable symptoms in women, but can still affect a woman's long-term health. The bacteria associated with NGU can trigger the development of PID, which is more serous.

Therefore, you should always tell your current partner and any recent sexual partners if you are diagnosed with NGU. They will also need to be tested and treated for the condition (NHS, 2014j).

Informing partners

It is important that your current sexual partner is tested and treated. Any sexual partners you have had since being exposed to the STI will also need to be informed, so they can be tested and treated.

It is suggested that you inform any person you have had sex with in the last three months, but this timeframe can vary. The healthcare professionals at the GUM clinic can advise you.

Some people can feel angry, upset or embarrassed about discussing STI's with their current partner or previous partners. However, don't be afraid to discuss your concerns with the healthcare professionals at the GUM or sexual health clinic. They can advise you about who to contact and the best way to contact them.

With your permission, the clinic can arrange for a "contact slip" to be given to your former partner or partners. The slip explains that they may have been exposed to an STI and advises them to have a check-up. The slip does not have your name on it, and your details will remain totally confidential.

Nobody can force you to tell any of your partners about your STI, but it is strongly recommended that you do. Left untested and untreated, STI's such as Chlamydia can have serious effects on a person's health, particularly for women.

Complications of untreated Chlamydia include -

- infection of the testicles in men,
- infection of the cervix (neck of the womb) in women,
- PID - which can increase the risk of infertility and ectopic pregnancy (NHS, 2014j).

Treatment failure

If the symptoms of NGU do not get better two weeks after you start to take antibiotics, you should return to the GUM clinic or sexual health clinic.

You will be asked if you took the medication correctly and whether anyone who may have NGU that has not been treated could have passed the infection back to you.

You may need further tests to confirm your diagnosis and to check for any STI's.

In some cases you may be given a new prescription for some different antibiotics to treat the NGU (NHS, 2014j).

Complications

NGU can have serious complications, although these are rare.

Persistent urethritis

The most common complication of NGU is persistent or recurrent urethritis. This is when you still have urethritis 1 to 3 months after being treated for NGU. This affects 1 or 2 men in every 10 who are treated for NGU, and can affect women too.

If you still have symptoms two weeks after starting a course of antibiotics, you should return to the GUM clinic or sexual health clinic (NHS, 2014j).

Reactive arthritis

Reactive arthritis is an uncommon complication of NGU, estimated to affect less than 1 in 100 people with the condition.

Reactive arthritis is caused by the immune system attacking healthy tissue for an unknown reason, rather than the bacteria responsible for NGU.

This can cause -

- joint pain,
- conjunctivitis (inflammation of the eyes),
- recurring urethritis (NHS, 2014j).

Epididymo-orchitis

Epididymo-orchitis is a possible complication of NGU in men. It is a combination of epididymitis and orchitis -

- epididymitis is inflammation of the epididymis - a long coiled tube in the testicles that helps store and transport sperm,
- orchitis is inflammation of the testicles.

Epididymo-orchitis affects fewer than 1 in 100 men with NGU (NHS, 2014j).

Pelvic inflammatory disease (PID)

In women, PID can be a result of NSU if left untreated. PID is a serious condition that can increase the risk of infertility and ectopic pregnancy (NHS, 2014j).

When will the signs and symptoms go away?

Most men notice an improvement in the symptoms quite quickly, with the discharge and pain on passing urine usually improving within a week (fpa, 2014f).

What happens if it isn't treated?

If non-specific urethritis is detected and treated early there are no complications. If left untreated, some causes of non-specific urethritis can have long term consequences, although these are uncommon. They can include -

- Painful infection in the testicles.
- Possible reduced fertility.
- Inflammation of the joints. This is known as reactive arthritis. Sometimes reactive arthritis is accompanied by inflammation of the eyes as well as the urethra - if this happens it is known as Reiters Syndrome (fpa, 2014f).

NSU caused by Chlamydia can lead to PID in your female sexual partner(s). This can lead to long term pelvic pain, blocked fallopian tubes, infertility and ectopic pregnancy (when the pregnancy develops outside the uterus).

It is not known whether some other causes of NSU (for example, mycoplasma genitalium) can lead to PID but it is thought that it may be possible (fpa, 2014f).

Can it go away without treatment?

This will depend very much on the cause. If you delay seeking treatment you risk an infection causing long-term damage and you may pass the infection on to someone else (fpa, 2014f).

Vaginal Thrush

Vaginal thrush is a common yeast infection that affects most women at some point.

It may be unpleasant and uncomfortable, but can usually be treated with medication available from pharmacies or on prescription from your GP.

However, for some women, vaginal thrush can be difficult to treat and keeps coming back (NHS, 2016d).

Causes

Vaginal thrush is caused by yeasts from a group of fungi called Candida.

Many women have Candida in their vagina without it causing any problems, but thrush can develop if the natural balance of micro-organisms in the vagina is disrupted and Candida multiplies.

You're more likely to get thrush if you -

- are in your twenties and thirties - thrush is less common in girls who haven't started their periods and women who have been through the menopause
- are pregnant
- take antibiotics
- have poorly controlled diabetes
- have a weakened immune system for example, because of a condition such as HIV or a treatment such as chemotherapy

Vaginal thrush isn't classed as an STI, but it can be triggered by sex - particularly if you have trouble relaxing and your vagina is dry - and can occasionally be passed on to sexual partners (NHS, 2016d).

Symptoms

Typical symptoms of vaginal thrush include -

- itching and soreness around the entrance of the vagina,
- vaginal discharge - this is usually odourless and may be thick and white or thin and watery,
- pain during sex,
- a stinging sensation when urinating (NHS, 2016d).

Sometimes the skin around the vagina can be red, swollen or cracked. Occasionally there may also be sores on the skin, although this is more often a sign of genital herpes.

What to do if you have vaginal thrush

If you've had thrush before and think you have it again, you can normally treat it with medicines bought from a local pharmacy.

It's a good idea to get medical advice from your GP or a sexual health clinic if -

- you have thrush for the first time,
- you're under the age of 16 or over 60,
- you're pregnant or breastfeeding,
- you have unusual symptoms, such as coloured or smelly discharge, or sores on the skin around your vagina,
- you have abnormal vaginal bleeding or pain in your lower tummy,
- you've had two episodes of thrush within the last six months,
- you've reacted badly to antifungal treatment in the past, or it didn't work,
- you or your partner have previously had a STI and you think it might have returned,
- your symptoms don't improve after 7–14 days of treatment (NHS, 2016d).

Thrush isn't usually anything to worry about in these cases, but your doctor may want to take a swab from your vagina to confirm the diagnosis and/or carry out tests to check for any underlying cause.

They can also advise you about the most suitable treatment and give you a prescription, if necessary (NHS, 2016d).

Treatment

Vaginal thrush is treated with medications you can buy over the counter from a pharmacy, or get on prescription from your GP.

If you've had thrush before and think you have it again, you can normally treat it with medication bought from a local pharmacy. Otherwise, you should see your GP for advice (NHS, 2016d).

Thrush medications

Thrush is treated with antifungal medicines that are available as pessaries, intravaginal creams or capsules.

All these medications are equally effective, but you may find that one is more convenient to use than another (NHS, 2016d).

Pessaries and intravaginal creams

A pessary is a pill that you insert into your vagina using a special applicator. Intravaginal creams are applied inside your vagina.

The main types used to treat thrush are -

clotrimazole - available over the counter from pharmacies
econazole, miconazole and fenticonazole - available on prescription

Over-the-counter pessaries are usually used daily for one to six days. Intravaginal cream is normally used once. Possible side effects include a mild burning sensation, slight redness or itching.

These treatments can also damage latex condoms and diaphragms, so you may want to avoid having sex, or use another form of contraception during treatment and for up to five days afterwards (NHS, 2016d).

Capsules

If you would prefer not to use pessaries or intravaginal cream, antifungal capsules are available.

The main types used to treat thrush are -

fluconazole - available over the counter from pharmacies
itraconazole - available on prescription

Over-the-counter thrush capsules usually come as a single dose.

Possible side-effects can include feeling sick, an upset stomach, diarrhoea and headaches (NHS, 2016d).

Skin creams

If the skin around the entrance to your vagina is also sore or itchy, you may find it helpful to use an antifungal skin cream in addition to one of the treatments above.

Creams containing clotrimazole can be bought over the counter from pharmacies.

They're available in packs that also include antifungal pessaries, intravaginal cream or capsules.

They're normally applied to the skin two or three times a day for at least two weeks.

Possible side effects include irritation, a stinging sensation or itching.

Alternatively, you could try using an ordinary emollient (moisturiser) near your vagina. This can help relieve your symptoms and causes fewer side effects than antifungal cream.

Emollients and antifungal skin cream can weaken latex condoms and diaphragms, so you may want to avoid having sex, or use another form of contraception during treatment and for up to five days afterwards (NHS, 2016d).

Sex and sexual partners

Vaginal thrush isn't classed as a STI, so sexual partners don't need to be informed, tested or treated if they don't have any symptoms.

However, there's a very small risk of passing the condition on during sex, so you may want to avoid having sex until it's cleared up.

Some treatments can also weaken latex condoms and diaphragms (see above), so you may want to avoid having sex or use another form of contraception during treatment and for a few days afterwards (NHS, 2016d).

If thrush keeps coming back

Speak to your GP if you experience frequent bouts of thrush.

They might run some tests to confirm the diagnosis and check for any possible underlying cause, such as diabetes.

They may also give you a prescription you can use whenever the symptoms return, or suggest trying a longer course of treatment lasting up to six months (NHS, 2016d).

If you're pregnant or breastfeeding

Visit your GP if you have thrush and you're pregnant or breastfeeding.

Your GP will probably suggest using pessaries or an intravaginal cream. Capsules aren't recommended because they could harm your baby.

If you're pregnant, take care when using an applicator to insert a pessary or intravaginal cream, as there's a small risk of injuring your cervix (neck of the womb).

Antifungal skin cream or emollients can normally be used safely if you're pregnant or breastfeeding and the area around the entrance to your vagina is sore or itchy (NHS, 2016d).

Alternative treatments

Some women with thrush try complementary therapies, such as bathing with diluted tea tree oil gel, eating probiotic yoghurts or supplements, or applying probiotic yoghurt to the genital area.

However, there's little evidence to suggest that tea tree oil is helpful, and it can sometimes irritate the skin.

Probiotics are unlikely to have any side effects, but there's also little evidence to suggest they can help (NHS, 2016d).

Prevention

If you get thrush frequently, you can -

- use water and an emollient soap substitute to clean the skin around your vagina, but avoid cleaning this area more than once a day,
- apply a greasier emollient to the skin around your vagina several times a day to protect it (but be aware that these moisturisers can weaken condoms),
- avoid potential irritants in perfumed soaps, shower gels, vaginal deodorants, wipes and douches,
- avoid wearing tight-fitting underwear or tights - some women find that special silk underwear designed for people with eczema and thrush is helpful
- ensure your blood sugar level is kept under control, if you have diabetes (NHS, 2016d).

Some women eat probiotic yoghurt or supplements to prevent vaginal thrush, but there's little evidence to suggest this works.

Vaginitis

Vaginitis means soreness and swelling (inflammation) of the vagina. It is not a sexually transmitted infection but sex or foreplay can trigger it and so can some STI's.

Symptoms

Not every woman with vaginitis will experience all or any of these symptoms but symptoms of vaginitis can include -

- A discharge that is not normal for you,
- Irritation or itching,
- Light bleeding or spotting,

- Pain when you wee,
- Pain during sex,
- A strong, unpleasant smell after sex may also be a sign (brook, 2015f).

Causes

Vaginitis may be caused by STI's such as -

- Trichomoniasis - caused by a tiny parasite,
- Chlamydia - caused by bacteria,
- Genital herpes - caused by the herpes simplex virus (brook, 2015f).

It may also be caused by -

- Thrush - a fungal infection that commonly affects the vagina,
- Bacterial vaginosis - BV - a bacterial infection of the vagina,
- Chemicals in shower gels, soap, fabric softener or from spermicide
- Washing inside your vagina (douching) (brook, 2015f).

Diagnosis

Vaginitis can generally be diagnosed by describing your symptoms to your GP or a health professional. You should get advice if you haven't had a vaginal infection before or if your symptoms are different to previous times. You should also get advice if you have a new sexual partner (brook, 2015f).

Treatment

Because vaginitis is often a side-effect of other conditions, treatment depends on what is causing it. For example, bacterial infections are usually treated with antibiotics and fungal infections such as thrush are usually treated with antifungal medicines.

There are a few things you can do yourself, such as -

- Keeping your genital area clean and dry. Avoid hot baths and perfumed soaps and dry yourself thoroughly,
- Avoid washing inside your vagina (sometimes called douching) as this can remove the healthy bacteria your vagina needs to stay free from infection,
- Avoid using any feminine hygiene products (sprays, deodorants and powders),
- Use pads rather than tampons if you're on your period during the infection,
- Wear loose-fitting cotton underwear,
- If you tend to experience vaginitis after sex, trying using a lubricant (brook, 2015f).

Chapter 17

Discussion

This chapter is arranged just in alphabetical order, and not in order of importance.

Accessing your health records

The NHS Constitution contains a right for patients to access their health records, which is covered by the Data Protection Act 1998.

> You have the right of access to your own health records. These will always be used to manage your treatment in your best interests

Some people can access their medical records online now and the plan is to make all medical records available online in the future. However, if this option is not available to you, you may need to ask your doctor for access to your medical records to get copies of your test results.

You can simply ask your doctor, during a consultation, to view your records and write them down or ask for a copy of your results and, in most cases, doctors are willing to allow this without any problem and free of charge. Alternatively, you can telephone your GP surgery or hospital to arrange a time to see your records and then you can make a note of your results. There may be a fee to access your health records (see below). However, sometimes, doctors receptionists or the doctors themselves are not very helpful in this respect.

So, what are your rights in respect of your health records? First of all, you need to be aware that your health records means any record of information relating to your physical or mental health that has been made by, or on behalf of, a health professional (NHS, 2014h).

For the purpose of the Data Protection Act, a registered health professional can be one of the following people -

- A medical practitioner - this could be a GP, consultant or hospital doctor,
- A dentist,
- An optician,
- A pharmaceutical chemist,
- A nurse, midwife or health visitor,
- An osteopath,
- A chiropractor,
- A clinical psychologist, child psychotherapist or speech therapist,
- A music therapist,
- A scientist employed by a health service body as head of department,
- Anyone registered as a member of a profession to which the Health Professionals Order 2001 for the time being extends (NHS, 2014h).

If you are refused access to your medical records by your doctor, then you may need to make what is called a "subject access request" (SAR). A subject access request is simply a letter or email to the relevant person which will depend on which health records you want to see - your GP surgery, your optician, your dentist or the hospital trust's health records manager or patient services manager.

Its a good idea to find out which department and person you need to send the request to and to make sure you know exactly which information you want as a fee can be charged for every request - if you forget something, you may have to pay again.

The person who deals with the requests will then decide whether your request can be approved. They can refuse your request if, for example, they believe that releasing the information may cause serious harm to your physical or mental health or that of another person.

Under the Data Protection Act, requests for access to records should be dealt with within 40 days although Government guidance for healthcare organisations says they should aim to respond within 21 days.

When requesting your personal information from an organisation, make sure you include the following information -

- your full name, address and contact telephone number,
- details of the specific information you require and any relevant data i.e. your medical records (between 2006 & 2009) held by Dr 'A' at 'B' hospital (NHS, 2014h).

Although you may be asked why you want to access your health records, there is no obligation for you to tell them.

Do I Have to Pay for Accessing my Records?

You can access your health records free of charge if -

- the records have been updated in the previous 40 days and,

- you don't require a copy.

If the records have not been updated in the last 40 days and you don't require a copy, the maximum charge is £10. This charge applies whether the records are stored -

- on computer,
- partly on computer and partly in another form, for example, paper records such as letters or hand-written clinical notes, or images such as X-ray film,
- entirely in another form.

If you do want a copy, the maximum £10 charge for viewing will be included in the fee for obtaining a copy. You will not be charged twice for one access request.

If you want a copy of the health records, the fee will depend on how the records are stored -

- on computer: maximum £10
- partly on computer and partly in another form: maximum £50
- entirely in another form: maximum £50 (NHS, 2014h).

If you request your information to be sent to you in the post, the maximum charges include postage and packaging.

Accessing Health Records of Someone Else

There are specific rules for applying for access to someone else's records and these rules apply if you would like someone else to access your records.

Health records are confidential so you can only access someone else's records if you're authorised to do so.

To access someone else's health records, you must -

- be acting on their behalf with their consent, or
- have legal authority to make decisions on their behalf (power of attorney), or
- have another legal basis for access (NHS, 2014a).

Lasting Power of Attorney

A Lasting Power of Attorney (LPA) is a legal document that allows a person to appoint someone else to make decisions on their behalf. The person appointed is called an attorney.

There are two types of LPA relating to -

- health and welfare, or
- property and financial affairs (NHS, 2014a).

An attorney appointed on a health and welfare LPA can only make decisions when -

- the person lacks the mental capacity to make decisions, and
- the LPA document has been registered with the Office of the Public Guardian (NHS, 2014a).

Applying for access to someone elses health records

Depending on which health records you want to see, submit your request in writing or by email to -

- the person's GP surgery,
- the person's optician,
- the person's dentist,
- the health records manager at the hospital trust where the person was treated,
- any other body that holds personal information (NHS, 2014a).

If you are applying for records on behalf of another individual in exercise of their rights, this is known as a Subject Access Request (SAR).

If possible, send a copy of the person's written permission with your request. In cases where it is not possible to obtain written consent, other arrangements may need to be made to confirm that the patient has given consent.

The health records manager, GP or other healthcare professional will decide whether the request can be approved. They can refuse to supply some of your request if, for example -

- it is likely to cause serious physical or mental harm to the patient or another person,
- the information you have asked for contains information that relates to another person.

Under the Data Protection Act, requests for access to records should be met within 40 days. However, government guidance for healthcare organisations says they should aim to respond within 21 days (NHS, 2014a).

Where patients are unable to give consent

If a patient is unconscious or unable to give consent or communicate a decision about their health records due to a mental or physical condition, their health professionals must take decisions about the use of information.

These decisions need to take into account the patient's best interests and any previous wishes or decisions they may have expressed. The views of relatives or carers as to the likely wishes of the patient should also be taken into account.

If a patient is unable to consent, information should only be given that is in the patient's best interests, and then only as much as is needed to support their care (NHS, 2014a).

Fees to access someone else's health records

You may have to pay a fee to access someone else's health records, so ask if there is a charge before you apply to see them (NHS, 2014a).

Note

The above is only applicable in England and Wales. Scotland and Northern Ireland have different requirements, as do other countries outside the UK.

Adrenal Fatigue

Are you feeling run down and stressed? Struggling to keep up with life and all its demands? Having trouble sleeping? You might have read about "adrenal fatigue" as a reason for your symptoms. Although some popular health books and alternative medicine websites state that adrenal fatigue is a real diagnosis, this is not proven by medical science (Chubinskaya et al., 2015).

- "Adrenal fatigue" is not a real medical condition. There are no scientific facts to support the theory that long-term mental, emotional, or physical stress drains the adrenal glands and causes many common symptoms.
- Adrenal insufficiency is a real disease diagnosed through blood tests.
- There is no test that can detect adrenal fatigue.

Supplements and vitamins made to "treat" adrenal fatigue may not be safe. Taking these supplements when you don't need them can cause your adrenal glands to stop working and may put your life in danger.

What is "adrenal fatigue"?

The term "adrenal fatigue" has been used to explain a group of symptoms that are said to occur in people who are under long-term mental, emotional, or physical stress. Supporters of adrenal fatigue say that you may be more likely to develop this condition if, for example, you have a stressful job; are a shift worker, working student, or single parent; or if you abuse alcohol or drugs.

Symptoms said to be due to adrenal fatigue include tiredness, trouble falling asleep at night or waking up in the morning, salt and sugar craving, and needing stimulants like caffeine to get through the day. These symptoms are common and non-specific, meaning they can be found in many diseases. They also can occur as part of a normal, busy life.

No scientific proof exists to support adrenal fatigue as a true medical condition. Doctors are concerned that if you are told you have this condition, the real cause of your symptoms may not be found and treated correctly.

What is the theory behind adrenal fatigue?

Supporters of adrenal fatigue believe the problem begins when many different life stresses become too much for the body to handle. Our adrenal glands — small organs located above the kidneys — usually deal with stress by producing hormones like cortisol. According to the theory of adrenal fatigue, when people are faced with long-term stress, their adrenal glands cannot keep up with the bodys need for these hormones. When this happens, symptoms of "adrenal fatigue" may appear. Whats the difference between adrenal fatigue and adrenal insufficiency?

While adrenal fatigue is not accepted by most doctors, adrenal insufficiency is a real medical condition that occurs when our adrenal glands cannot produce enough hormones. Adrenal insufficiency is caused by damage to the adrenal glands or a problem with the pituitary gland — a pea-sized gland in the brain that tells the adrenals to produce cortisol.

A person with adrenal insufficiency may be dehydrated, confused, or losing weight. He or she may feel weak, tired, or dizzy, and have low blood pressure. Other symptoms include stomach pain, nausea, vomiting, and diarrhoea.

Adrenal insufficiency is diagnosed through blood tests, and can be treated with medications that replace the hormones the adrenals would normally make.

How is adrenal fatigue "diagnosed"?

There is no test that can detect adrenal fatigue. Many times, a person will be told he or she has adrenal fatigue based on symptoms alone. Sometimes, a blood or saliva test may be offered, but tests for adrenal fatigue are not based on scientific facts or supported by good scientific studies, so the results and analysis of these tests may not be correct.

Are treatments for adrenal fatigue helpful or harmful?

Supporters of adrenal fatigue may advise you to improve your lifestyle by giving up smoking, alcohol, and drugs. Starting an exercise program, eating healthy foods, and following a daily routine for sleeping and waking will almost always make you feel better, no matter what the medical diagnosis.

You may also be told to buy special supplements or vitamins. These supplements claim to be made just for adrenal health. While regular vitamins and minerals may be good for your health, doctors are concerned that supplements or vitamins sold as a treatment for adrenal fatigue could hurt you. Many of these supplements have not been tested for safety.

The U.S. Food and Drug Administration (the government agency that oversees most food and medical products) does not oversee nutritional supplements and vitamins. This means there is no guarantee that what's on the label of a supplement is really what's inside the bottle. In some cases, supplements have very few, if any, active ingredients. In other cases, the dose of a particular ingredient may be too high. This is true if you purchase supplements from your local drug store or a specialty pharmacy (sometimes called a compounding pharmacy[89]).

If you take adrenal hormone supplements when you don't need them, your adrenal glands may stop working and become unable to make the hormones you need when you are under physical stress. When these supplements are stopped, a person's adrenal glands can remain "asleep" for months. People with this problem may be in danger of developing a life-threatening condition called adrenal crisis.

What should you do if you have been told you have adrenal fatigue?

Doctors urge you not to waste precious time accepting an unproven diagnosis such as "adrenal fatigue" if you feel tired, weak, or depressed. If you have these symptoms, you may have adrenal insufficiency, depression, obstructive sleep apnoea, or other health problems. Getting a real diagnosis is very important to help you feel better and overcome your health problem (Chubinskaya et al., 2015).

[89] a practice in which a licensed pharmacist, a licensed physician, or, in the case of an outsourcing facility, a person under the supervision of a licensed pharmacist, combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient

Adrenal Insufficiency

The most common symptoms of adrenal insufficiency are -

- chronic, or long lasting, fatigue,
- muscle weakness,
- loss of appetite,
- weight loss,
- abdominal pain.

Other symptoms of adrenal insufficiency can include -

- nausea,
- vomiting,
- diarrhoea,
- low blood pressure that drops further when a person stands up, causing dizziness or fainting,
- irritability and depression,
- craving salty foods,
- hypoglycaemia, or low blood sugar,
- headache,
- sweating,
- in women, irregular or absent menstrual periods,
- in women, loss of interest in sex.

Hyperpigmentation, or darkening of the skin, can occur in Addison's disease, although not in secondary adrenal insufficiency. This darkening is most visible on scars; skin folds; pressure points such as the elbows, knees, knuckles, and toes; lips; and mucous membranes such as the lining of the cheek.

The slowly progressing symptoms of adrenal insufficiency are often ignored until a stressful event, such as surgery, a severe injury, an illness, or pregnancy, causes them to worsen (NIDDK, 2014).

Note

- Adrenal insufficiency is an endocrine, or hormonal, disorder that occurs when the adrenal glands do not produce enough of certain hormones.
- Addison's disease, the common term for primary adrenal insufficiency, occurs when the adrenal glands are damaged and cannot produce enough of the adrenal hormone cortisol. The adrenal hormone aldosterone may also be lacking.
- Secondary adrenal insufficiency occurs when the pituitary gland fails to produce enough adrenocorticotropin (ACTH), a hormone that stimulates the adrenal glands to produce cortisol. If ACTH output is too low, cortisol production drops.

- The most common symptoms of adrenal insufficiency are chronic fatigue, muscle weakness, loss of appetite, weight loss, and abdominal pain. The slowly progressing symptoms are often ignored until a stressful event, such as surgery, a severe injury, an illness, or pregnancy, causes them to worsen.
- If not treated, an adrenal crisis can cause death.
- A diagnosis of adrenal insufficiency is confirmed through hormonal blood and urine tests. Imaging studies of the adrenal and pituitary glands can be useful in helping to establish the cause.
- Adrenal insufficiency is treated by replacing, or substituting, the hormones that the adrenal glands are not making.
- Problems can occur in people with adrenal insufficiency who are undergoing surgery, suffer a severe injury, have an illness, or are pregnant. These conditions place additional stress on the body, and people with adrenal insufficiency may need additional treatment to respond and recover.
- People with adrenal insufficiency should always carry identification stating their condition, "adrenal insufficiency", in case of an emergency, as well as the supplies necessary to administer an emergency corticosteroid injection (NIDDK, 2014).

Bio-equivalence

This section is a guideline only to approximately equivalent doses of some of the different hormones available in 2015. The intention is to help you see what is available and to then choose, with your healthcare provider, a hormone suitable for you.

Hormone	Dose
Micronised Oestradiol	2mg
Oestrogens, conjugated	0.625mg
Oestradiol valerate	2mg
Transdermal E2 patch	50mcg
Transdermal Estrogel	2 doses (1.5mg)
Transdermal Sandrena	1mg (Rashna, 2014)

Table 17.1 – Bio-equivalent doses of Oestrogen

Estradiol transdermal patch = a 50 mcg patch is equivalent to 0.05 mg, and 100 mcg patch is equivalent to 0.1 mg.

Product	Presentation	Composition
Low Dose		
Estrofem	tablet	1mg 17-β-oestradiol

Product	Presentation	Composition
Progynova	tablet	1mg oestradiol valerate
Ovestin	tablet	2mg oestriol
Premarin	tablet	0.3mg conjugated oestrogen
Climara 25, Femtran 25	transdermal patch	25mcg/24hrs 17-β-oestradiol (weekly application)
Estradot 25 or 37.5	transdermal patch	25 or 37.5mcg/24hrs 17-β-oestradiol (twice weekly application)
Estraderm 25 MX	transdermal patch	25mcg/24hrs 17-β-oestradiol (twice weekly application)
Medium dose		
Estrofem, Zumenon	tablet	2mg 17-β-oestradiol
Progynova	tablet	2mg oestradiol valerate
Premarin	tablet	0.625mg conjugated equine oestrogen
Climara 50, Femtran 50	transdermal patch	50mcg/24hrs 17-β-oestradiol (weekly application)
Estradot 50, Estraderm 50 MX	transdermal patch	50mcg/24 hours 17-β-oestradiol (twice weekly application)
Sandrena	transdermal gel	1mg oestradiol (daily application)
High Dose		
Climara 75	transdermal patch	75mcg/24hrs oestradiol (weekly application)
Estradot 75, Estradot 100	transdermal patch	75 or 100mcg/24 hours (twice weekly application)
Climara100, Femtran99	transdermal patch	100mcg/24hrs oestradiol (weekly application)
Estraderm 100 MX	transdermal patch	100mcg/24hours 17-β-oestradiol (twice weekly application)
Estraderm 100	transdermal patch	100mcg/24hours 17-β-oestradiol (twice weekly application)
Ovestin	cream	1mg/g oestradiol
Vagifem	pessary	25mcg oestradiol (AMS, 2014)

Table 17.2 – Bio-equivalent doses of Oestrogen used in menopause treatment

Generic	Brand	Form	Strength	Dosing Frequency
Oral Oestrogen				
Conjugated oestrogens	Premarin	tablets	0.3mg, 0.45mg, 0.625mg, 0.9mg, 1.25mg, 2.5mg	Once daily

Generic	Brand	Form	Strength	Dosing Frequency
Esterified oestrogens	Menest	tablets	0.3mg, 0.625mg, 1.25mg, 2.5mg	
Estradiol	Femtrace	tablets	0.9mg, 1.8mg	
Estradiol (micronized)	Estrace	tablets	0.5mg, 1mg, 2mg	
Synthetic conjugated oestrogens	Enjuvia	tablets	0.3mg, 0.45mg, 0.625mg, 0.9mg, 1.25mg	
Transdermal Oestrogen				
Estradiol	Alora	matrix patch	0.025mg/day, 0.05mg/day, 0.075mg/day, 0.1mg/day	Twice weekly
	Climara	matrix patch	0.025mg/day, 0.0375mg/day, 0.05mg/day, 0.06mg/day, 0.075mg/day, 0.1mg/day	Once weekly
	Divigel	topical gel	0.25mg/pkt, 0.5mg/pkt, 1mg/pkt	Once daily
	Elestrin	topical gel	0.87g/pump	Once daily
	Estraderm	reservoir patch	0.05mg/day, 0.1mg/day	Twice weekly
	Estrasorb	topical emulsion	1.74g/pouch	2 pouches once daily
	Estrogel	topical gel	1.25g/pump	1 pump once daily
	Evamist	topical spray	1.53mg/spray	Initially 1 spray daily, may increase to 2 - 3 sprays if needed
	Menostar	matrix patch	0.014mg/day	Once weekly
	Minivelle	patch	0.025mg/day, 0.0375mg/day, 0.05mg/day, 0.075mg/day, 0.1mg/day	Twice weekly
	Vivelle	matrix patch	0.05mg/day, 0.1mg/day	

Generic	Brand	Form	Strength	Dosing Frequency
	Vivelle-Dot		0.025mg/day, 0.0375mg/day, 0.05mg/day, 0.075mg/day, 0.1mg/day	
Vaginal Oestrogen				
Conjugated oestrogen	Premarin	cream	0.625mg/g	Daily
Estradiol	Estring	ring	7.5mcg/24hrs	Once every 90 days
	Femring	ring	0.05mg/day, 0.1mg/day	Once every 3 months
	Vagifem	vaginal tablets	10mcg	Once daily for 2 weeks, then twice weekly
Oral Progestogen				
Medroxyprogest acetate	Provera	tablets	2.5mg, 5mg, 10mg	Once daily
Progesterone (micronized)	Prometriu	capsules	100mg, 200mg, 300mg	(unknown, 2015d)

Table 17.3 – Hormone Replacement Therapies

Oral Oestrogens	Transdermal Oestrogens
•Plasma oestrogen peaks & troughs	•Serum E2 levels relatively constant
•First pass through GI tract & liver (requires higher dose)	•Does not pass through liver, therefore lower doses required
•Increased hepatic enzymes, inflammatory markers	•No change in inflammatory markers
•Increased triglycerides	•No change or decrease in triglycerides
•Increased blood pressure	•Decrease in blood pressure
•Reduced IGF-1	•No effect on GH/IGF-1
•Decreased LDL cholesterol and increased HDL	•Decreases LDL but no change in HDL

Table 17.4 – Oral oestrogens vs transdermal oestrogens - 1

Active ingredient	Brand	Source of oestrogen	Dose equivalents
Oral			
Equine conjugated oestrogen	Premarin	Pregnant mares urine	0.625mg

Active ingredient	Brand	Source of oestrogen	Dose equivalents
Synthetic conjugated oestrogen	Enjuvia	Plant derived: Soy/Yams	0.625mg
Esterified oestrogens	Menest	Plant derived: Soy/Yams	0.625mg
17-β-estradiol (micronized)	Estrace	Plant derived: Soy/Yams	1mg
17-β-estradiol	Femtrace	Plant derived: Soy/Yams	No equivalence data, only studied with placebo
Transdermal			
17-β-estradiol patch (reservoir)[90]	Estraderm	Plant derived: Soy/Yams	0.05mg
17-β-estradiol patch (matrix)[91]	Alora or Climara or Vivelle or Vivelle-Dot or Menostar	Plant derived: Soy/Yams	0.05mg
17-β-estradiol gel	Divigel	Plant derived: Soy/Yams, Sunflower seeds, Rapeseed, Poppy seeds, Pine trees	1g Divigel = 34pg/mL estradiol
17-β-estradiol gel	Elestrin	Plant derived: Soy, Rapeseed, Pine tree wood	1 pump (0.87g/d) = 0.0125mg estradiol, 2 pumps (1.7g/d) = 0.0375mg estradiol
17-β-estradiol gel	Estrogel	Plant derived: Oil seed, Soy, Pine tree wood	No comparison studies done in U.S., Rate of delivery is 35µg/day which is therapeutically equivalent to Climara 50µg/day

[90] Estradiol is contained in a drug reservoir and its release is controlled by a copolymer membrane, it contains more layers than a matrix patch

[91] Estradiol is embedded in the adhesive layer that is applied directly to the skin

Active ingredient	Brand	Source of oestrogen	Dose equivalents
17-β-estradiol emulsion	Estrasorb	Plant derived: Soy	2 packets (3.48g) = 0.05mg systemic oestrogen
17-β-estradiol spray	Evamist	Plant derived: Soy/Yams	No direct comparison trials. 1.53mg/spray. For 1 spray, 21µg gets to blood stream (29µg for 2 sprays, 40µg for 3 sprays). Premarin 0.625mg = just over 3 sprays of Evamist (unknown, 2015f).

Table 17.5 – Oral And Transdermal Estrogen Dose Equivalents - 2

Blood levels

Blood tests are taken to monitor what is happening in your bodies, and how your bodies are coping with the drugs. Much discussion takes place in various forums, so I have included this section in order to try and help make sense of the results. However, it should be noted that, different testing laboratories use different machines for testing the blood, and there seems to be no consistent standard, this accounts for the disparity of some of the ranges below, and also why you can have such widely differing figures. The solution may be to ask your doctor what the "normal range" is for the particular test that they are using on your sample.

Test	S.I. units	Conventional units
Follicle Stimulating Hormone (FSH)	0.5–5.0 u/l (males only)	
	1–12 u/l (males)	0.5–5.0 MIu/ml
Full Blood Count (FBC)		
Liver Function Test (LFT)	80–280 u/l	
Luteinising Hormone	3–8 iu/l (males)	
	3–12 iu/l (females)	
Estradiol	300 pmol/l (males)	

Test	S.I. units	Conventional units
	200 pmol/l (postmenopausal females)	
Sex Hormone Binding Globulin (SHBG)	18–50 nmol/L (males)	
	22–126 nmol/L (females)	
	6–45 nmol/l (males)	
	30–120 nmol/l (females)	
Testosterone	9–42 nmol/l (males)	2.6–12.1 ng/ml
	1–2.5 nmol/l (females)	0.3–0.7 ng/ml (O'Sullivan, 2013)

Table 17.6 – Reference ranges for various blood tests

Test	Specimen	Conventional units	SI units
Estradiol, females			
Day 1–10 of menstrual cycle	Serum	14–27 pg/mL	50–100 pmol/L
Day 11–20 of menstrual cycle	Serum	14–54 pg/mL	50–200 pmol/L
Day 21–30 of menstrual cycle	Serum	19–40 pg/mL	70–150 pmol/L
Estradiol, males	Serum	10–30 pg/mL	37–110 pmol/L (Merck, 2013)

Table 17.7 – Estradiol reference ranges of adults

Hormone	M→F	F→M
Dehydroepiandrosterone sulphate (DHEAS)	0.5–4 µg/ml	0.5–5 µg/ml
Luteinizing hormone (LH)	0.1–10 mU/ml	1–9 mU/ml
Follicle stimulating hormone (FSH)	1–10 mU/ml	1–8 mU/ml
Estradiol (E2N)	50–200 pg/ml	5–35 pg/ml
Bioavailable estradiol (BAE)	25–100 pg/ml	unknown
Progesterone	0.1–1.5 ng/ml	0.1–1 ng/ml
Testosterone (T)	0.1–1 ng/ml	5–15 ng/ml
Bioavailable testosterone (BAT)	0–0.15 ng/ml	1–3 ng/ml
SHBG	20–100 nmol/l	10–60 nmol/l (unknown, 2014b)

Table 17.8 – Reference values for hormone therapy of transsexuals

Hormone		Female	Male
Blood urea nitrogen BUN		10–20 mg/dL	
DHEAS	15–19 years	63–373	88–483
	20–29 years	65–380	280–640
	30–39 years	45–270	120–520
	40–49 years	32–240	95–530
	50–59 years	26–200	70–310
	60–69 years	13–130	42–290
	70 years and older	10–90	28–175
Estradiol (E2)	still menstruating	85–498 pg/mL	
	Postmenopause	<5–54 pg/mL	7–42 pg/mL
FSH	still menstruating	4.7–21.5 mIU/ml	
	Postmenopause	25.8–134.8 mIU/mL	1.5–12.4 mIU/ml
LH	menstruating	14.0–95.6 mIU/mL	
	postmenopause	7.7–58.5 mIU/mL	1.7–8.6 mIU/mL
Progesterone	still menstruating	0.8–3.0 ng/mL	
	Postmenopause	<0.2–0.8 ng/mL	0.2–1.4 ng/mL
SHBG	non-pregnant	20–130 nmol/L	10–80 nmol/L
Testosterone (free) [92]	18–30 years	1–5 pg/mL	32–168 ng/mL
	31–40 years	1–6 pg/mL	
	41–50 years	1–4 pg/mL	
	51 years and older	Less than 3 pg/mL	
Testosterone (total)	18–39 years	9–55 ng/dL	300–1080 ng/dL
	40–59 years	9–55 ng/dL	300–890 ng/dL
	60 years and older	5–32 ng/dL	300–720 ng/dL
alternative test	19–49 years old	8–48 ng/dL	249–836 ng/dL
	50 years and older	2–41 ng/dL	193–740 ng/dL (of Iowa (UIHC), 2014)

Table 17.9 – Normal reference values for adults

[92] This refers to males 18 years and older

The problem with "blood levels" is that all they are measuring is the amount of hormone in your blood stream at the time that the sample was obtained. It can give you, and the doctor, an indication as to whether the hormone being used is getting into the blood stream, and in the case of implanted hormones whether the implant needs to be renewed. But the blood levels do not predict what the results of the hormone will be on your body. What really is of concern to us is the results of the hormones we take, their effects and their side-effects on our bodies. And this cannot be measured by "blood levels".

Although in 2012 it was stated - *"The aim of therapy is to achieve a plasma estradiol level in the upper follicular range (400–600 pmol/litre) (Middle and Kane, 2009), and testosterone level in the normal female range 2.8 nmol/litre)"* (H. Turner and WJA, 2009) (Seal et al., 2012) which at least gives us some figures so that we know what the doctors and endocrinologists are aiming towards.

However, in 2013, the Royal College of Psychiatrists downgraded this to *"a representative range for the upper half of the follicular range is 300–400 pmol/l or 80–140 pg/ml"* (Psych, 2013).

They then go on to say *"Levels higher than this **may** be associated with the established side-effects of excessive oestrogen, particularly thromboembolism, hypertension and myocardial infarction. Physiological levels should be able to produce the desired phenotypic changes, particularly if the circulating androgen levels and their effects are suppressed"*(Psych, 2013). I have highlighted the word "may", as it is not an absolute, definite fact, just something that might happen, and again might not happen! Or in other words, Your Mileage May Vary, meaning it might be different for you (YMMV)[93]!

Blood tests

At various times of taking hormones we have to have blood taken, and these are some of the blood tests that blood is taken for -

- FBC,
- U&E's,
- LFT,
- ALT,
- AST,
- TFT[94],
- kidney and lipid (cholesterol) profiles,
- serum prolactin,
- blood sugar level,
- blood clotting time,

[93] Your Mileage May Vary, meaning it might be different for you

[94] Thyroid function test

- SHBG,
- testosterone levels,
- estradiol levels (unknown, 2005)

These are some of the more usual blood tests requested.

Any of these further tests could be required -

- calcium and phosphorus (skeletal health)
- serum androgen levels (unknown, 2005)

Alanine aminotransferase - ALT

An alanine aminotransferase (ALT) test measures the amount of this enzyme in the blood. ALT is found mainly in the liver, but also in smaller amounts in the kidneys, heart, muscles, and pancreas. ALT was formerly called serum glutamic pyruvic transaminase (SGPT).

ALT is measured to see if the liver is damaged or diseased. Low levels of ALT are normally found in the blood. But when the liver is damaged or diseased, it releases ALT into the bloodstream, which makes ALT levels go up. Most increases in ALT levels are caused by liver damage (WebMD, 2014a).

Aspartate aminotransferase - AST

An aspartate aminotransferase (AST) test measures the amount of this enzyme in the blood. AST is normally found in red blood cells, liver, heart, muscle tissue, pancreas, and kidneys. AST formerly was called serum glutamic oxaloacetic transaminase (SGOT).

Low levels of AST are normally found in the blood. When body tissue or an organ such as the heart or liver is diseased or damaged, additional AST is released into the bloodstream. The amount of AST in the blood is directly related to the extent of the tissue damage. After severe damage, AST levels rise in 6 to 10 hours and remain high for about 4 days (WebMD, 2014c).

Full Blood Count - FBC

The normal range describes the range where 95% of the normal healthy population will lie. This also means that there is 5% of the normal healthy population will fall outside the "normal range", however they too are normal. Normal ranges are a guide. There are many instances where the FBC will fall outside the "normal range" and yet these could be described as totally normal for the given clinical situation, for example, it is normal for patients who have had a splenectomy to have a moderately raised lymphocyte count or a patient on haemofiltration to have a raised

eosinophil count. These variations would show as outside the normal range, however they are normal for the situation. It is very useful therefore for biomedical scientists and haematology clinicians to have appropriate clinical details added to the request so that interpretation and best clinical advice can be given on the report where appropriate (unknown, 2013b).

Parameter	Male	Female
Haemoglobin g/L	135–180	115–160
WBC x109/L	4.00–11.00	4.00–11.00
Platelets x109/L	150–400	150–400
MCV fL	78–100	78–100
PCV	0.40–0.52	0.37–0.47
RBC x1012/L	4.5–6.5	3.8–5.8
MCH pg	27.0–32.0	27.0–32.0
MCHC g/L	310–370	310–370
RDW	11.5–15.0	11.5–15.0
Neutrophils	2.0–7.5	2.0–7.5
Lymphocytes	1.0–4.5	1.0–4.5
Monocytes	0.2–0.8	0.2–0.8
Eosinophils	0.04–0.40	0.04–0.40
Basophils	< 0.1	< 0.1 (O'Sullivan, 2013)

Table 17.10 – Adult normal ranges of the full blood count

Reference Values for Commonly Ordered Tests

Analyte	Specimen	Conventional units	SI units
Adrenocorticotropin (ACTH)	P	6.0–76.0pg/mL	1.3–16.7pmol/L
Aminotransferases	S		
•Aspartate (AST, SGOT)		0–35U/L	0–0.58µkat/L
•Alanine (ALT, SGPT)		0–35U/L	0–0.58µkat/L
Ammonia (as NH_3)	P	10–80µg/dL	6–47µmol/L
Amylase	S	60–180U/L	0.8–3.2µkat/L
Anion gap	S	7–16mmol/L	7–16mmol/L
Antinuclear antibody	S	Negative at 1:40 dilution	N/A
Antithrombin III	P		
•Antigenic		22–39mg/dL	220–390mg/L
•Functional		80–130%	0.8–1.30U/L
Arterial blood gases (sea level)	WB, arterial		

Analyte	Specimen	Conventional units	SI units
•Bicarbonate (HCO_3		21–30mEq/L	21–28mmol/L
•Partial pressure of carbon dioxide (PCO2)		35–45mmHg	4.7–5.9kPa
•pH		7.38–7.44	7.38–7.44
•Partial pressure of oxygen (PO_2)		80–100mmHg	11–13kPa
Bilirubin	S		
•Total		0.3–1.0mg/dL	5.1–17.0µmol/L
•Direct		0.1–0.3mg/dL	1.7–5.1µmol/L
•Indirect		0.2–0.7mg/dL	3.4–12.0µmol/L
Bleeding time		2.0–9.5min	2.0–9.5min
Calcitonin	S		
•Male		3–26pg/mL	3–26ng/L
•Female		2–17pg/mL	2–17ng/L
Calcium	S	9.0–10.5mg/dL	2.2–2.6mmol/L
Calcium, ionized	WB	4.5–5.6mg/dL	1.1–1.4mmol/L
Carbon dioxide			
•Content (sea level)	P	21–30mEq/L	21–30mmol/L
•Partial pressure (PCO2) (sea level)	WB, arterial	35–45mmHg	4.7–5.9kPa
Carcinoembryonic antigen (CEA)	S	0–3.4ng/mL	0–3.4µg/L
Chloride	S	98–106mEq/L	98–106mmol/L
Cholesterol (totals)*	P		
•Desirable		<200mg/dL	<5.17mmol/L
•Borderline high		200–239mg/dL	5.17–6.18mmol/L
•High		>240mg/dL	>6.18mmol/L
Low-density lipoprotein (LDL) cholesterol	P		
•Desirable		<100mg/dL	<2.59mmol/L
•Near or above normal		100–129mg/dL	2.59–3.34mmol/L
•Borderline high		130–159mg/dL	3.36–4.11mmol/L

Analyte	**Specimen**	**Conventional units**	**SI units**
•High		160–189mg/dL	4.13–4.88mmol/L
•Very high		>190mg/dL	>4.91mmol/L
High-density lipoprotein (HDL) cholesterol	P		
•Low		<40mg/dL	<1.03mmol/L
•High		>60mg/dL	>1.55mmol/L
Copper	S	70–140µg/dL	11–22µmol/L
Cortisol	S		
•Fasting, 8am–12noon		5–25µg/dL	138–690nmol/L
•Noon–8pm		5–15µg/dL	138–414nmol/L
•8pm–8am		0–10µg/dL	0–276nmol/L
Creatine kinase (totals)	S		
•Male		60–400U/L	1.00–6.67µkat/L
•Female		40–150U/L	0.67–2.50µkat/L
•MB isoenzyme		0–7ng/mL	0–7µg/L
Creatinine	S	<1.5mg/dL	<133µmol/L
Erythrocyte count	WB		
•Male		4.50–5.90 Œ $10^6/mm^3$	4.50–5.90 Œ $10^{12}/L$
•Female		4.00–5.20 Œ $10^6/mm^3$	4.00–5.20 Œ $10^{12}/L$
Erythrocyte sedimentation rate	WB		
•Male		0–17mm/hr	0–17mm/hr
•Female		1–25mm/hr	1–25mm/hr
Ferritin	S		
•Male		30–300ng/mL	30–300µg/L
•Female		10–200ng/mL	10–200µg/L
Fibrinogen	P	150–400mg/dL	1.5–4.0g/L
Folate (folic acid)	S, P		
•Normal		3.1–17.5ng/mL	7.0–39.7nmol/L
•Borderline deficient		2.2–3.0ng/mL	5.0–6.8nmol/L
•Deficient		<2.2ng/mL	<5.0nmol/L
•Excess		>17.5ng/mL	>39.7nmol/L
Folic acid	RC	150–450ng/mL/cells	340–1020nmol/L/cells

Analyte	Specimen	Conventional units	SI units
Follicle-stimulating hormone (FSH)	S, P		
•Female, menstruating			
✣ Follicular phase		3.0–20.0 mIU/mL	3.0–20.0 IU/L
✣ Ovulatory phase		9.0–26.0 mIU/mL	9.0–26.0 IU/L
✣ Luteal phase		1.0–12.0 mIU/mL	1.0–12.0 IU/L
•Female, postmenopausal		18.0–153.0 mIU/mL	18.0–153.0 IU/L
•Male		1.0–12.0 mIU/mL	1.0–12.0 IU/L
Glucose	P		
•Fasting, normal		75–115mg/dL	4.2–6.4mmol/L
•Fasting, diabetes mellitus		>125mg/dL	>7.0mmol/L
•2-hour postprandial		120mg/dL	<6.7mmol/L
Glucose-6-phosphate dehydrogenase, erythrocyte	WB	No gross deficiency	N/A
γ-Glutamyltransferase	S	1–94U/L	1–94U/L
Haptoglobin	S	16–199mg/dL	0.16–1.99g/L
Hematocrit	WB		
•Male		41.0–53.0%	0.41–0.53
•Female		36.0–46.0%	0.36–0.46
Hemoglobin			
•Plasma	P	1–5mg/dL	0.01–0.05g/L
•Whole blood, male	WB	13.5–17.5g/dL	8.4–10.9mmol/L
•Whole blood, female	WB	12.0–16.0g/dL	7.4–9.9mmol/L
Hemoglobin electrophoresis	WB		
•Hemoglobin A		95–98%	0.95–0.98
•Hemoglobin A_{1c}		3.8–6.4%	0.038–0.064 Hg fraction
•Hemoglobin A_2		1.5–3.5%	0.015–0.035
•Hemoglobin F		0–2.0%	0–0.02
•Hemoglobins other than A, A_2, or F		Absent	Absent

Analyte	Specimen	Conventional units	SI units
Iron (hematology and coagulation values)	S	30–160µg/dL	5.4–28.7µmol/L
Iron-binding capacity (hematology and coagulation values)	S	228–428µg/dL	40.8–76.7µmol/L
Iron (clinical chemistry values)	S	50–150µg/dL	9–27µmol/L
Iron-binding capacity (clinical chemistry values)	S	250–370µg/dL	45–66µmol/L
Lactate	P, venous	5–15mg/dL	0.6–1.7mmol/L
Lactate dehydrogenase isoenzymes	S		
•Fraction 1 (of total)		14–26%	0.14–0.25
•Fraction 2		29–39%	0.29–0.39
•Fraction 3		20–26%	0.20–0.25
•Fraction 4		8–16%	0.08–0.16
•Fraction 5		6–16%	0.06–0.16
Lactate dehydrogenase	S	100–190U/L	1.7–3.2µkat/L
Lead (adult)	S	<10–20µg/dL	<0.5–1µmol/L
Leukocyte count (WBC)	WB	4.5–11.0 x 10^3/mm3	4.5–11.0 x 10^9/L
Lipase	S	0–160U/L	0–2.66µkat/L
Magnesium	S	1.8–3.0mg/dL	0.8–1.2mmol/L
Mean corpuscular hemoglobin (MCH)	WB	26.0–34.0pg/cell	26.0–34.0pg/cell
Mean corpuscular hemoglobin concentration (MCHC)	WB	31.0–37.0g/dL	310–370g/L
Mean corpuscular volume (MCV)	WB	80–100µm^3	80–100fl
Osmolality	P	285–295mOsm/kg serum water	285–295mmol/kg serum water
Oxygen			

Analyte	Specimen	Conventional units	SI units
•Content (sea level)	WB (arterial)	17–21 vol%	
	WB (venous, arm)	10–16 vol%	
•Saturation (sea level)	WB (arterial)	97%	0.97mol/mol
	WB (venous, arm)	60–85%	0.60–0.85mol/mol
•Partial pressure (PO_2)	WB	80–100mmHg	11–13kPa
Partial-thromboplastin time (activated)	P	22.1–35.1sec	22.1–35.1sec
Phosphatase	S		
•Acid		0–5.5U/L	0.90nkat/L
•Alkaline		30–120U/L	0.5–2.0nkat/L
Phosphorus, inorganic	S	3–4.5mg/dL	1.0–1.4mmol/L
Platelet count	WB	150–350 Œ $10^3/mm^3$	150–350 Œ $10^9/L$
Potassium	S	3.5–5.0mEq/L	3.5–5.0mmol/L
Progesterone	S, P		
•Female, menstruating			
✣ Follicular		<0.2ng/mL	<0.6nmol/L
✣ Midluteal		3–20ng/mL	9.54–63.6nmol/L
•Male		<0.2–1.4ng/mL	<0.60–4.45nmol/L
Prolactin	S		
•Male		0–15ng/mL	0–15µg/L
•Female		0–20ng/mL	0–20µg/L
Prostate-specific antigen (PSA)	S		
•Female		<0.5ng/mL	<0.5µg/L
•Male			
✣ ≤40 years		0–2.0ng/mL	0–2.0µg/L
✣ >40 years		0–4.0ng/mL	0–4.0µg/L
Protein	S		
•Total		5.5–8.0g/dL	55–80g/L
•Fractions			
✣ Albumin		3.5–5.5g/dL (50–60%)	35–55g/L

Analyte	Specimen	Conventional units	SI units
✣ Alpha$_1$		0.2–0.4g/dL (4.2–7.2%)	2–4g/L
✣ Alpha$_2$		0.5–0.9g/dL (6.8–12%)	5–9g/L
✣ Beta		0.6–1.1g/dL (9.3–15%)	6–11g/L
✣ Gamma		0.7–1.7g/dL (13–23%)	7–17g/L
✣ Globulin		2.0–3.5g/dL (40–50%)	20–35g/L
Protein C	P		
•Total antigen		70–140%	0.70–1.40
•Functional		70–140%	0.70–1.40
Protein S	P		
•Total antigen		70–140%	0.70–1.40
•Functional		70–140%	0.70–1.40
•Free antigen		70–140%	0.70–1.40
Prothrombin time	P	11.1–13.1sec	11.1–13.1sec
Reticulocyte count	WB	0.5–2.5% red cells	0.005–0.025 red cells
Rheumatoid factor	S, JF	<30.0 IU/mL	<30.0 kIU/L
Sodium	S	136–145mEq/L	136–145mmol/L
Testosterone	S		
•Total (morning)			
✣ Female		6–86ng/dL	0.21–2.98nmol/L
✣ Male		270–1070ng/dL	9.36–37.10nmol/L
Thyroid hormone function tests	S		
•Thyroid-stimulating hormone (TSH)		0.5–4.7µU/mL	0.5–4.7mU/L
•Thyroxine			
✣ Total (T$_4$)		4.5–10.9µg/dL	58–140nmol/L
✣ Free (fT$_4$)		0.8–2.7ng/dL	10.3–35.0pmol/L
•Triiodothyronine			
✣ Total (T$_3$)		60–181ng/dL	0.92–2.78nmol/L
✣ Free (fT$_3$)		1.4–4.4pg/mL	0.22–6.78pmol/L
Transferrin	S	230–390mg/dL	2.3–3.9g/L
Triglycerides	S	<160mg/dL	<1.8mmol/L

Analyte	Specimen	Conventional units	SI units
Urea nitrogen	S	10–20mg/dL	3.6–7.1mmol/L
Uric acid	S		
•Male		2.5–8.0mg/dL	150–480µmol/L
•Female		1.5–6.0mg/dL	90–360µmol/L
Vitamin A	S	20–100µg/dL	0.7–3.5µmol/L
Vitamin B_{12}	S, P		
•Normal		>250pg/mL	>185pmol/L
•Borderline		125–250pg/mL	92–185pmol/L
•Deficient		<125pg/mL	<92pmol/L (Kratz, Ferraro, and Sluss, 2004)
Key: JF=joint fluid, P=plasma, RC=red cells, S=serum, WB=whole blood			

Table 17.11 – Reference Values for Commonly Ordered Tests

Body fat

Subcutaneous body fat begins to be laid down in the foetus from about 34 weeks from conception, and it increases from then to birth, and from birth to 9 months. From 9 months the subcutaneous fat decreases until 6–8 years when it begins to increase again. This early decrease is less in girls than in boys, so that after 1 year girls have more subcutaneous fat than the boys. From 7 years, the increase in fat occurs in both sexes. At adolescence, the fat in the limbs (as measured at the triceps) of boys decreases and is not regained until the late 20s; girls show a slight slowing of the fat increase, but no loss. Also at this time, the trunk fat stops increasing in boys; whilst in girls it shows a steady increase. Girls show fat deposits in a secondary sexual distribution, in the breasts, over the upper arms, lower abdomen and thighs at puberty. Post-pubertal boys do not have this pattern of fat distribution; adult men are more likely to fat around the abdominal wall (BNF, 2016a), the so-called middle-age spread.

As can be seen it takes many years for the fat to assume a male-type position, and for it to assume a female-type position it also takes several years under the influence of hormones. For us it does not take years (because our subcutaneous fat is not being laid down, but rather redistributed) but it does take some time, so don't expect it to happen overnight. The average male is reputed to have about 17% body fat whilst the average female is reputed to have 22% body fat. This difference has to be made up from somewhere, and normally it is the diet. You may find that your diet changes whilst taking the hormones, with you eating more carbohydrates and fats. You should be aware of this, but also be careful not to put on too much excess weight, otherwise youll have to start dieting.

Doctor Eugene Schrang of Neenah, Wisconsin, USA, sets an upper weight limit for his SRS patients of just over 14 stones (the actual figure he uses is 200 pounds). Not a lot if you're 6-foot tall, but quite a bit if you're only 5-foot tall. If you are over his weight limit he may delay surgery until you have reached his target.

Breast Development

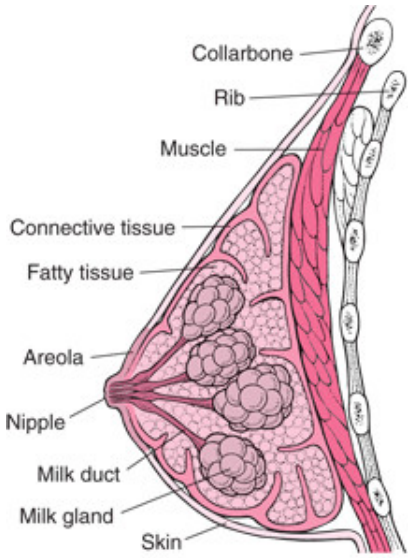

Figure 17.1 – Anatomy of the breast

In transwomen (being male-to-female transsexual people), cross-sex hormone therapy is administered to induce feminization. Breast development is an important part of feminization for most transwomen.

Breast development is measured on the "Tanner Scale", see the graphic below.

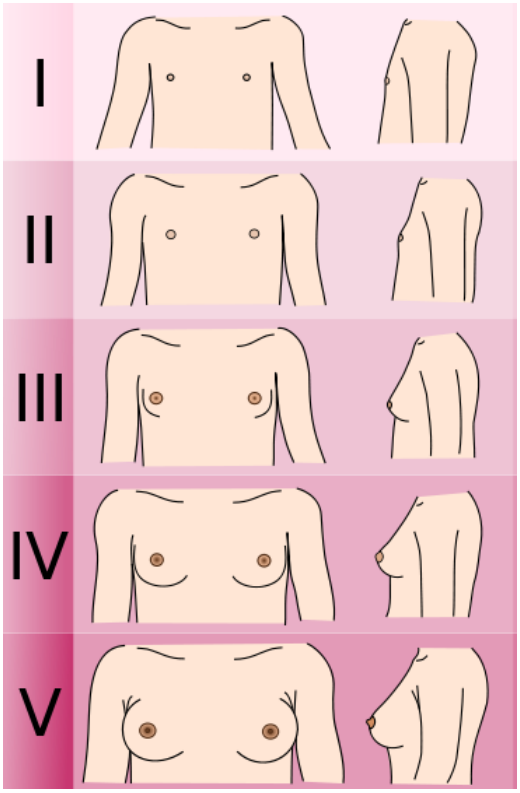

Figure 17.2 – The growing breast

Tanner I - no glandular tissue - areola follows the skin contours of the chest (prepubertal) (typically age 10 and younger),

Tanner II - breast bud forms, with small area of surrounding glandular tissue - areola begins to widen (10–11.5 years),

Tanner III - breast begins to become more elevated, and extends beyond the borders of the areola, which continues to widen but remains in contour with surrounding breast (11.5–13 years),

Tanner IV - increased breast size and elevation - areola and papilla form a secondary mound projecting from the contour of the surrounding breast (13–15 years),

Tanner V - breast reaches final adult size - areola returns to contour of the surrounding breast, with a projecting central papilla (15+ years) (Marshall and Tanner, 1969).

As you can see above it takes at least 5 years for a Cis-Female to reach a fully mature adult breast, being "Tanner V". Most transwomen will not reach "Tanner V", and those that do generally have had orchiectomy and are under 23 years old. The reason for this is the human growth hormones that your body relies on during puberty to speed growth, peak at 16–18, and then drop off drastically after 22–24 years of age.

From the experiences of other folk, it seems that most breast development will be within the first 18 months and then slow almost to a stop. This may change if you change your oestrogen dosage and method of deliverance. Mine changed when I moved from tablets to patches. When this happens you then need to determine what is your optimum dosage per week/fortnight/month, mine seems to be 400 mcgs per week (200mcg

patches twice a week). Below that dosage I feel unmotivated and lethargic, as if "there's something missing from my life" and generally unwell and unhappy. But at my optimum dosage I'm happy and productive, and life is good.

Anyway, back to breast growth, as I said mine changed when I moved from tablets to patches, and again when I achieved my optimum dosage. On each of the last two occasions I had a growth spurt, and they grew slightly. But, you must have some body fat on you, if you're as skinny as a rake and with your ribs being very easily seen, then you won't have much fat to build your breasts!

If you have had an orchiectomy or breast implants, then breast growth may have a spurt as well. It is also possible that you're breast growth may not have ended when you have breast implants, which could account for the growth seen post-operatively.

Most transwomen will not have fully developed breasts, and this is normal. Most will be "Tanner III" or perhaps "Tanner IV". And the available evidence suggests that breast development is insufficient for the majority of transwomen and that the type and dosage of hormonal therapy seems to not have an important role on the final breast size.

"Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast development in transwomen is extremely sparse and based on low quality of evidence. Current evidence does not provide evidence that progestogens enhance breast development in transwomen. Neither do they prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions" (Wierckx, L Gooren, and T'sjoen, 2014).

Earlier research in 2012 suggests that 60% of transsexual women request a mammoplasty, and that depression was noted in approximately 30% of their subjects (Seal et al., 2012).

For the transgendered woman, breast development will vary greatly, as it does with the genetic female population. However, breast development will typically be less than what is experienced in the genetic female population.

With the transgendered woman, breast tissue growth is basically promoted by oestrogens and anti-androgens. Under most circumstances, breast development exceeding a B cup is rare. Development will take at least 2 years to reach maximum size.

- Before your breasts start to grow, your chest will be flat and your nipples may be small.
- Then, small bumps (called buds) will start under your nipples, after about two to three months of hormone therapy.
- These buds may feel tender or sensitive at first, but this will stop as time passes.
- Your nipples and the area around them (the areola) may change in colour and your nipples will sometimes get hard and stick out.

- As time passes, your breast buds will get rounder and fuller and grow into the shape of your breast.

This early stage of development is caused by an increase in the ductal system behind the nipple and is part of the transition process and will usually normalize in a matter of months (University, 2014).

Are my breasts "normal"?

- Lots of people feel self-conscious about their breasts, but there is no one normal way for breasts to look.
- Breasts come in all different sizes, shapes, and colours.
- It is totally normal for one breast to be a bit bigger than the other. Sometimes the size of your breasts will equal out over time, but sometimes not.
- Its very common for breasts to grow at different rates while they're developing.
- There are as many different breasts as there are faces, or hands, or belly buttons!
- Some transwomen have hair around their nipples. This is completely normal. If the hair bothers you, it's best to cut it with small scissors. Plucking or shaving the hair can cause infection.
- If your nipples point inward instead of out, you have "inverted nipples" . Between 10%-20% of all females have inverted nipples on at least one breast. This is normal and will not affect your health in any way. If you have inverted nipples, it's important to keep them clean to avoid getting an infection in the folds of skin around your nipple.
- see Stretch marks.

Breast disorders

Breast symptoms (eg, masses, nipple discharge, pain) are common, accounting for more than 15 million visits to the doctor each year. Although $>$ 90% of symptoms have benign causes, breast cancer is always a concern. Because breast cancer is common and may mimic benign disorders, the approach to all breast symptoms and findings is to conclusively exclude or confirm cancer (Kosir, 2013b).

Breast disorders may be noncancerous[95] or cancerous[96]. Most are noncancerous and not life threatening. Often, they do not require treatment. In contrast, breast cancer can mean loss of a breast or of life. Thus, for many women, breast cancer is their worst fear. However, potential

[95] benign

[96] malignant

problems can be detected early when women regularly examine their breasts themselves, are examined regularly by their doctor, and have mammograms as recommended. Early detection of breast cancer is essential to successful treatment (Kosir, 2016).

Symptoms

Symptoms related to the breast are common. These symptoms include breast pain (see *Breast Pain (Mastalgia*)), lumps (see *Breast Lumps*), and a discharge from the nipple, see Nipple discharge. Also, the breast's skin may become pitted, puckered, red, thickened, or dimpled (Kosir, 2016).

Breast symptoms do not necessarily mean that a woman has breast cancer or another serious disorder. For example, monthly breast tenderness that is related to hormonal changes before a menstrual period does not indicate a serious disorder.

However, women should examine their breasts once a month, see Breast Self Examination, and should see their doctor if they observe any change in a breast, particularly any of the following -

- A lump that feels distinctly different from other breast tissue,
- A lump that is stuck to the skin or chest wall,
- A lump that does not go away,
- Swelling that does not go away,
- Pitting, puckering, reddening, thickening, or dimpling in the skin of the breast,
- Scaly skin around the nipple,
- Changes in the shape of the breast,
- Changes in the nipple, such as turning inward,
- Discharge from the nipple, especially if it is bloody and/or occurs spontaneously (that is, without the nipple's being squeezed or stimulated by other means) (Kosir, 2016).

Common Breast Symptoms

Symptom	Causes	Comments
Breast pain	Hormonal changes related to menstrual periods, pregnancy, or use of hormonal drugs	Pain that occurs throughout both breasts is usually caused by hormonal changes related to menstrual periods.
	Cysts	Breast infections [97]
	Fibrocystic changes	

[97] Breast infections are very rare except during the first few weeks after childbirth

Symptom	Causes	Comments
	Large breasts that stretch supporting tissues	
	Very rarely, breast cancer	
Breast lumps	Breast infections, including abscesses*	Lumps in the breasts are relatively common and are usually not cancerous
	Cysts	Because cancerous and noncancerous lumps are hard to distinguish during a physical examination, tests are usually done
	Fibroadenomas	
	Fibrocystic changes	
	Galactocele (a clogged milk duct)	
	Scar tissue that develops after an injury	
	Breast cancer	
Nipple discharge	Most commonly, noncancerous milk duct tumours (intraductal papilloma)	A nipple discharge occurs normally sometimes - for example during milk production after childbirth
	Breast cancer	Abnormal discharges vary in appearance depending on the cause
	Breast infections, including abscesses*	
	Fibrocystic changes	
	Other disorders, such as pituitary, brain, or thyroid disorders	
	Certain drugs	(Kosir, 2015)

Table 17.12 – Common breast symptoms

Evaluation - History

History includes the following -

- Duration of symptoms,
- Relation of symptoms to menses and pregnancy,
- Presence and type of pain, discharge, and skin changes,
- Use of drugs, including hormone therapy,

- Personal and family history of breast cancer,
- Date and results of last mammogram (Kosir, 2013b).

Breast examination

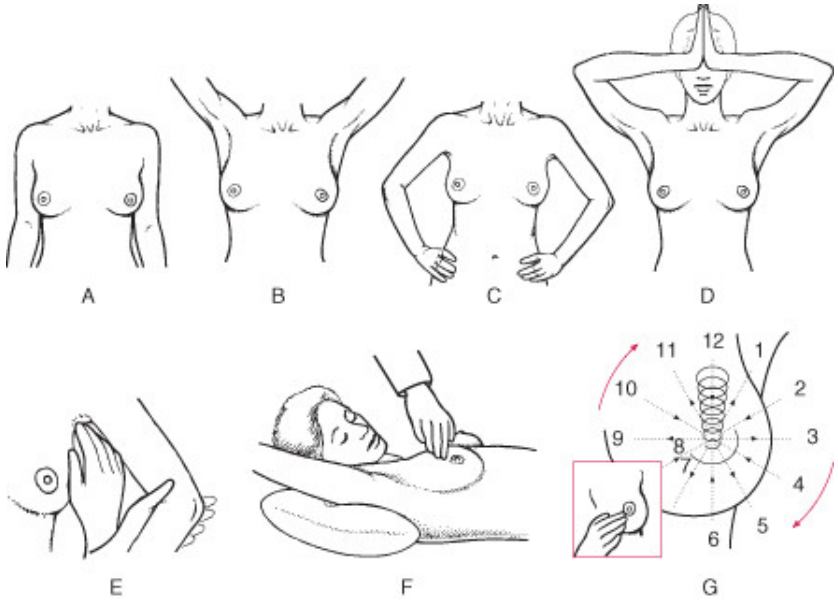

Figure 17.3 – Various positions for breast examination

Principles of examination are similar for physician and patient. Breasts are inspected for asymmetry in shape, nipple inversion, bulging, and dimpling. Although size differential is common, each breast should have a regular contour. An underlying cancer is sometimes detected by having the patient press both hands against the hips or the palms together in front of the forehead. In these positions, the pectoral muscles are contracted, and a subtle dimpling of the skin may appear if a growing tumour has entrapped a Cooper ligament. The nipples are squeezed to check for a discharge and determine its source (eg, whether it is multiductal).

Positions include the patient seated or standing (A) with arms at sides; (B) with arms raised over the head, elevating the pectoral fascia and breasts; (C) with hands pressed firmly against hips; or (D) with palms pressed together in front of the forehead, contracting the pectoral muscles. (E) Palpation of axilla; arm supported as shown, relaxing the pectoral muscles. (F) Patient supine with pillow under the shoulder and with the arm raised above the head on the side being examined. (G) Palpation of breast in a circular pattern from the nipple outward.

The axillary and supraclavicular lymph nodes are most easily examined with the patient seated or standing, see position (E). Supporting the patient's arm during the axillary examination allows the arm to be fully relaxed so that nodes deep within the axilla can be palpated.

The breast is palpated with the patient seated and again with the patient supine, the ipsilateral arm above the head, and a pillow under the ipsilateral shoulder, see position (F). The latter position is also used for breast self-examination; the patient examines the breast with her contralateral hand. Having the patient roll to one side, so that the breast on the examined side falls medially, may help differentiate breast and chest wall tenderness because the chest wall can be palpated separately from breast tissue.

The breast should be palpated with the palmar surfaces of the 2nd, 3rd, and 4th fingers, moving systematically in a small circular pattern from the nipple to the outer edges, see position (G). Precise location and size (measured with a caliper) of any abnormality should be noted on a drawing of the breast, which becomes part of the patient's record. A written description of the consistency of the abnormality and degree to which it can be distinguished from surrounding breast tissue should also be included. Detection of abnormalities during physical examination may mean that a biopsy is needed, even if imaging shows no abnormalities (Kosir, 2013e). Also see Breast Self Examination.

Testing

Imaging tests are used for screening and for evaluation of breast abnormalities.

Screening mammography is recommended yearly for women $\geq$ 50 years old and usually yearly or every 2 years for women $\geq$ 40 year, also see Screening. Mammography is more effective in older women because with aging, fibroglandular tissue in breasts tends to be replaced with fatty tissue, which can be more easily distinguished from abnormal tissue. Low-dose x-rays of both breasts are taken in 1 (oblique) or 2 views (oblique and craniocaudal). Only about 10 to 15% of abnormalities detected result from cancer. Accuracy of mammography depends partly on the techniques used and experience of the mammographer; false-negative results may exceed 15%. Some centres use computer analysis of digitized mammography images to help in diagnosis. Such systems are not recommended for stand-alone diagnosis, but they appear to improve sensitivity for detecting small cancers by radiologists.

Diagnostic mammography is used to evaluate masses, pain, and nipple discharge. It can determine size and location of a lesion and provide images of surrounding tissues and lymph nodes. Diagnostic mammography requires more views than screening mammography. Views include magnified views and spot compression views, which provide better visualization of suspect areas. Mammography can also be used to guide biopsy and, after surgery, to image the breast and the excised mass to help determine whether excision was complete.

Ultrasonography can be used to diagnose breast abnormalities and to stage breast cancer. If mammography detects one or more masses, ultrasonography is used to further evaluate them (eg, to determine whether they are solid or cystic). Ultrasonography is also used to evaluate abnormalities detected by MRI. Ultrasonography can be used before staging to identify abnormal axillary nodes that may require core biopsy.

MRI can be used to diagnose breast abnormalities and, before surgery, to accurately determine tumour size, chest wall involvement, and number of tumours. MRI is also used to identify abnormal axillary lymph nodes (to help stage breast cancer). For women at high risk of breast cancer (eg, with a BRCA gene mutation or a calculated lifetime risk of breast cancer of $\geq$ 15 to 20%), screening should include MRI in addition to clinical breast examination and mammography. MRI is not considered appropriate for screening women with average or slightly increased risk (Kosir, 2013e)

Screening

Screening includes mammography, clinical breast examination (CBE) by health care practitioners, MRI (for high-risk patients), and monthly breast self-examination (BSE).

Mammography, done annually, is recommended for women $\geq$ 50; it reduces mortality rate by 25 to 35% in this age group. Mammography is more accurate in older women, partly because with aging, fibroglandular tissue in breasts tends to be replaced with fatty tissue, which can be more easily distinguished from abnormal tissue. However, there is considerable disagreement about screening for women 40 to 50 years; recommendations include annual mammography (American Cancer Society), mammography every 1 to 2 yr (National Cancer Institute), and no periodic mammography (American College of Physicians). Concerns about screening too soon or too often include increased radiation exposure and overdiagnosis of tumours (eg, ductal carcinoma in situ (DCIS)) that may not develop into invasive cancer during the patients lifetime. Young age at the time of radiation exposure increases the risk of cancer. On balance, most experts recommend screening mammography every 1 to 2 years for women aged 40 to 50.

Only about 10 to 15% of abnormalities detected on screening mammography result from cancer, and false-negative results may exceed 15%. Accuracy depends partly on the techniques used and experience of the mammographer. Some centres use computer analysis of digitized mammography images (full-field digital mammography) to help in diagnosis. Such systems may be slightly more sensitive for invasive cancers in women $<$ 50 when results are interpreted by radiologists, but probably not when interpreted primarily via computer detection.

CBE is usually part of routine annual care for women $>$ 35; it can detect 7 to 10% of cancers that cannot be seen on a mammogram. In the US, CBE augments rather than replaces screening mammography. However, in some countries where mammography is considered too expensive, CBE is the sole screen; reports on its effectiveness in this role vary.

MRI is thought to be better than CBE or mammography for screening women with a high (eg, $>$ 15%) risk of breast cancer, such as those with a BRCA gene mutation. For these women, screening should include MRI as well as mammography and CBE. MRI has higher sensitivity but may be less specific. Because specificity is lower, MRI is not considered appropriate for screening women with average or slightly increased risk.

BSE alone has not been shown to reduce mortality rate, but evidence of its usefulness is mixed, and it is widely practiced. Because a negative BSE may tempt some women to forego mammography or CBE, the need for these procedures should be reinforced when BSE is taught. Patients should be instructed to do BSE on the same day each month. For menstruating women, 2 or 3 days after their period ends is recommended because breasts are less likely to be tender and swollen (Kosir, 2013d).

Breast Masses (Breast Lumps)

The term breast mass is preferred over lump for a palpably discrete area of any size. A breast mass may be discovered by patients incidentally or during breast self-examination or by the clinician during routine physical examination. Masses may be painless or painful and are sometimes accompanied by nipple discharge or skin changes.

Causes

Although cancer is the most feared cause, most (about 90%) breast masses are nonmalignant. The most common causes include

- Fibrocystic changes,
- Fibroadenomas (Kosir, 2013a).

Fibrocystic changes (previously, fibrocystic disease) is a catchall term that refers to mastalgia, breast cysts, and nondescript masses (usually in the upper outer part of the breast); these findings may occur in isolation or together. Breasts have a nodular and dense texture and are frequently tender when palpated. Fibrocystic changes cause the most commonly reported breast symptoms and have many causes. Fibrocystic changes are not associated with increased risk of cancer.

Repeated stimulation by oestrogen and progesterone may contribute to fibrocystic changes, which are more common among women who had early menarche, who had their first live birth at age $>$ 30, or who are nulliparous.

Fibroadenomas are typically smooth, rounded, mobile, painless masses; they may be mistaken for cancer. They usually develop in women during their reproductive years and may decrease in size over time. Juvenile fibroadenoma, a variant, occurs in adolescents, and unlike fibroadenomas in older women, these fibroadenomas continue to grow over time. Simple fibroadenoma does not appear to increase risk of breast cancer; complex fibroadenoma may increase risk slightly.

Breast infections (mastitis) causes pain, erythema, and swelling; an abscess can produce a discrete mass. Infections are extremely rare except during the puerperium (postpartum) or after penetrating trauma. They may occur after breast surgery. Puerperal mastitis, usually due to Staphylococcus aureus, can cause massive inflammation and severe breast pain, sometimes with an abscess. If infection occurs under other circumstances, an underlying cancer should be sought promptly.

Galactocele is a round, easily movable milk-filled cyst that usually occurs up to 6 to 10 months after lactation stops. Such cysts rarely become infected.

Cancers of various types can manifest as a mass. About 5% of patients have pain (Kosir, 2013a).

Evaluation - History

History of present illness should include how long the mass has been present and whether it comes and goes or is painful. Previous occurrence of a mass and the outcome of its evaluation should be queried.

Review of systems should determine whether nipple discharge is present and, if present, whether it is clear, milky, or bloody. Symptoms of advanced cancer (eg, weight loss, malaise, bone pain) should be sought.

Past medical history should include risk factors for breast cancer, including previous diagnosis of breast cancer, history of radiation therapy to the chest area before age 30 (eg, for Hodgkin lymphoma). Family history should note breast cancer in a 1st-degree relative (mother, sister, daughter) and, if family history is positive, whether the relative carried one of the 2 known breast cancer genes, BRCA1 or BRCA2 (Kosir, 2013a).

Physical examination

Examination focuses on the breast and adjacent tissue. The breast is inspected for skin changes over the area of the mass and for nipple discharge. Skin changes include erythema, rash, exaggeration of normal skin markings, and trace oedema sometimes termed peau dorange (orange peel). The mass is palpated for size, tenderness, consistency (ie, hard or soft, smooth or irregular), and mobility (whether it feels freely mobile or fixed to the skin or chest wall). The axillary, supraclavicular, and infraclavicular areas are palpated for masses and adenopathy (Kosir, 2013a).

Red flags

Certain findings are of particular concern -

- Mass fixed to the skin or chest wall,
- Stony hard, irregular mass,
- Skin dimpling,
- Matted or fixed axillary lymph nodes,
- Bloody nipple discharge,
- Thickened, erythematous skin (Kosir, 2013a).

Interpretation of findings

Painful, tender, rubbery masses in women who have a history of similar findings and who are of reproductive age suggest fibrocystic changes.

Red flag findings suggest cancer. However, the characteristics of benign and malignant lesions, including presence or absence of risk factors, overlap considerably. For this reason and because failure to recognize cancer has serious consequences, most patients require testing to more conclusively exclude breast cancer (Kosir, 2013a).

Testing

Initially, physicians try to differentiate solid from cystic masses because cysts are rarely cancerous. Typically, ultrasonography is done. Lesions that appear cystic are sometimes aspirated (eg, when they cause symptoms), and solid masses are evaluated with mammography followed by imaging-guided biopsy (see Diagnosis). Some physicians evaluate all masses with needle aspiration; if no fluid is obtained or if aspiration does not eliminate the mass, mammography followed by imaging-guided biopsy is done (Kosir, 2013a).

Fluid aspirated from a cyst is sent for cytology only under the following circumstances -

- It is turbid or grossly bloody.
- Minimal fluid is obtained.
- A mass remains after aspiration (Kosir, 2013a).

Patients are reexamined in 4 to 8 weeks. If the cyst is no longer palpable, it is considered benign. If the cyst has recurred, it is reaspirated, and any fluid is sent for cytology regardless of appearance. A third recurrence or persistence of the mass after initial aspiration (even if cytology was negative) requires biopsy (Kosir, 2013a).

Treatment

Treatment is directed at the cause.

A fibroadenoma is usually removed if it grows or causes symptoms. Fibroadenomas can usually be excised using a local anesthetic, but they frequently recur. Patients who have fibroadenomas that are not excised should be checked periodically for changes. After patients have had several fibroadenomas established as benign, they may decide against having subsequent ones excised. Because juvenile fibroadenomas tend to grow, they should be removed.

Acetaminophen, NSAIDs, and athletic bras (to reduce trauma) can be used to relieve symptoms of fibrocystic changes. Vitamin E and evening primrose oil may be somewhat effective (Kosir, 2013a).

Key Points

- Most breast masses are not cancer.
- Clinical features of benign and malignant disease overlap so much that testing should usually be done (Kosir, 2013a).

Nipple discharge

Fluid that leaks from one or both nipples is called a nipple discharge. Each breast has several (15 to 20) milk ducts. A discharge can come from one or more of these ducts.

Nipple discharge can occur normally during the last weeks of pregnancy and after childbirth when breast milk is produced. A nipple discharge can also be normal in women who are not pregnant or breastfeeding, especially during the reproductive years. For example, in women, fondling, suckling, irritation from clothing, or sexual arousal can stimulate a nipple discharge, as can stress. However, a nipple discharge in men is always abnormal.

A normal nipple discharge is usually a thin, cloudy, whitish, or almost clear fluid that is not sticky. However, the discharge may be other colours, such as gray, green, yellow, or brown. During pregnancy or breastfeeding, a normal discharge is sometimes slightly bloody. Abnormal discharges vary in appearance depending on the cause. An abnormal discharge may be accompanied by other abnormalities, such as dimpled skin, swelling, redness, crusting, sores, and a retracted nipple. (A nipple is retracted if it pulls inward and does not return to its normal position when it is stimulated.) If a discharge from only one breast occurs on its own (without any stimulation of the nipple), it may be abnormal (Kosir, 2016).

Nipple discharge can be serous[98] (yellow), mucinous[99] (clear and watery), milky, sanguineous[100] (bloody), purulent[101] , multicolored and sticky, or serosanguineous[102] (pink). It may occur spontaneously or only in response to breast manipulation (Kosir, 2013b).

Pathophysiology

[103] Nipple discharge may be breast milk or an exudate produced by a number of conditions.

Breast milk production in nonpregnant and nonlactating women (galactorrhea) typically involves an elevated prolactin level, which stimulates glandular tissue of the breast. However, only some patients with elevated prolactin levels develop galactorrhea.

Causes

Most frequently, nipple discharge has a benign cause, see Some Causes of Nipple Discharge. Cancer (usually intraductal carcinoma or invasive ductal carcinoma) causes < 10% of cases. The rest result from benign ductal disorders (eg, intraductal papilloma, mammary duct ectasia, fibrocystic changes), endocrine disorders, or breast abscesses or infections. Of these causes, intraductal papilloma is probably the most common; it is also the most common cause of a bloody nipple discharge without a breast mass.

Endocrine causes involve elevation of prolactin levels, which has numerous causes.

Causes

Several disorders can cause an abnormal discharge. A discharge from one milk duct or from one breast is likely to be caused by a problem with that breast, such as a noncancerous or cancerous breast tumour. A discharge from both breasts or from several milk ducts in one breast is more likely to be caused by a problem outside the breast, such as a hormonal disorder or use of certain drugs.

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[98] producing or containing serum

[99] relating to, resembling or containing mucin

[100] containing blood

[101] containing, discharging, or causing the production of pus

[102] composed of serum and blood

[103] The physiological processes associated with disease or injury

Common causes

Usually, the cause is a benign disorder of the milk ducts -

- A benign tumour in a milk duct (intraductal papilloma),
- Dilated milk ducts (mammary duct ectasia),
- Fibrocystic changes, including pain, cysts, and general lumpiness,
- An abscess or infection.

Intraductal papilloma is the most common cause. It is also the most common cause of a bloody nipple discharge when there is no lump in the breast.

Less common causes

Certain disorders stimulate the production of breast milk in women who are not pregnant or breastfeeding. In most of these disorders, the level of prolactin (a hormone that stimulates production of breast milk) is elevated. Taking certain drugs can have the same effect.

Cancer causes fewer than 10% of cases.

Some Causes of Nipple Discharge

Cause	Suggestive findings	Diagnostic approach
Benign breast disorders		
Intraductal papilloma[104] (most common cause)	Unilateral bloody (or guaiac[105]-positive) or serosanguinous discharge	Evaluation as for breast mass
Mammary duct ectasia	Unilateral or often bilateral bloody (or guaiac-positive), serosanguinous, or multicoloured (purulent, gray, or milky) discharge	Evaluation as for breast mass
Fibrocystic changes	A mass, often rubbery and tender, usually in premenopausal women	Possibly a history of other masses
	Evaluation as for breast mass	

[104] a benign growth on the skin or mucous membrane

[105] used as a reagent in laboratory tests for the presence of occult blood

Cause	**Suggestive findings**	**Diagnostic approach**
Abscess or infection	Acute onset with pain, tenderness, or erythema	Clinical evaluation
	With abscess, a tender mass and possibly purulent discharge	If discharge does not resolve with treatment, evaluation as for breast mass
Breast cancer		
Most often, intraductal carcinoma or invasive ductal carcinoma	May have a palpable mass, skin changes, or lymphadenopathy; Sometimes bloody or guaiac-positive discharge	If suspected, evaluation as for breast mass
Hyperprolactinemia		
Many causes	Often bilateral, milky not bloody discharge with multiple ducts involved and no masses; Possibly menstrual irregularities or amenorrhea; If a pituitary lesion is the cause, possibly signs of CNS mass (visual field changes, headache) or other endocrinopathy	Prolactin level, TSH[106], review of drug use; If prolactin or TSH is elevated, MRI of head (Kosir, 2013b).

Table 17.13 – Some causes of nipple discharge

Warning signs

Nipple discharge is a cause for concern when it

- Occurs without the nipple's being squeezed or stimulated by other means (when it occurs spontaneously),
- Occurs in women aged 40 or older,
- Comes from only one breast,
- Is bloody or pink,
- Is accompanied by a lump that can be felt,
- Occurs in a boy or man.

[106] thyroid-stimulating hormone

When to see a doctor

If a nipple discharge continues for more than one menstrual cycle or if any of the warning signs are present, women should see a doctor. Delay of a week or so is not harmful unless there are signs of infection such as redness, swelling, and/or a discharge of pus. Women with such symptoms should see a doctor within 1 or 2 days (Kosir, 2016).

What the doctor does

Doctors first ask questions about the woman's symptoms and medical history. Doctors then do a physical examination. What they find during the history and physical examination often suggests a cause of the discharge and the tests that may need to be done (see Table below).

Evaluation

History

History of present illness should include whether the current discharge is unilateral or bilateral, what its color is, how long it has lasted, whether it is spontaneous or occurs only with nipple stimulation, and whether a mass or pain is present.

Review of systems should seek symptoms suggesting possible causes, including fever (mastitis or breast abscess); cold intolerance, constipation, or weight gain (hypothyroidism); amenorrhea, infertility, headache, or visual disturbances (pituitary tumour); and ascites or jaundice (liver disorders).

Past medical history should include possible causes of hyperprolactinemia, including chronic renal failure, pregnancy, liver disorders, and thyroid disorders, as well as history of infertility, hypertension, depression, breastfeeding, menstrual patterns, and cancer. Clinicians should ask specifically about drugs that can cause prolactin release such as oral contraceptives, antihypertensive drugs (eg, methyldopa, reserpine, verapamil), H-antagonists (eg, cimetidine, ranitidine), opioids, and dopamine D-antagonists (eg, many psychoactive drugs, including phenothiazines and tricyclic antidepressants).

Physical examination

Physical examination focuses on the breasts. The breasts are inspected for symmetry, dimpling of the skin, erythema, swelling, color changes in the nipple and skin, and crusting, ulceration, or retraction of the nipple. The breasts are palpated for masses and evidence of lymphadenopathy in the axillary or supraclavicular region. If there is no spontaneous discharge,

the area around the nipples is systematically palpated to try to stimulate a discharge and to identify any particular location associated with the discharge. A bright light and magnifying lens can help assess whether the nipple discharge is uniductal or multiductal.

Red flags

Certain findings are of particular concern -

- Spontaneous discharge,
- Age 40,
- Unilateral discharge,
- Bloody or guaiac-positive discharge,
- Palpable mass,
- Male sex (Kosir, 2013b).

Interpretation of findings

Important differentiating points are whether a mass is present, whether the discharge involves one or both breasts, and whether the discharge is bloody (including guaiac-positive).

If a mass is present, cancer must be considered. Because cancer rarely involves both breasts or multiple ducts at presentation, a bilateral, guaiac-negative discharge suggests an endocrine cause. However, if the discharge is guaiac-positive, even if bilateral, cancer must be considered.

Presence of a breast mass, a bloody (or guaiac-positive) discharge, a spontaneous unilateral discharge, or history of an abnormality on a mammogram or an ultrasound scan requires follow-up with a surgeon who is experienced with breast disorders.

For other suggestive findings, see Some Causes of Nipple Discharge.

Testing

If endocrine causes are suspected, the following are measured -

- Prolactin level,
- Thyroid-stimulating hormone (TSH) level.

If discharge is guaiac-positive, the following is done -

- Cytology.

If there is a palpable mass, evaluation as for breast mass is done, usually beginning with -

- Ultrasonography

Lesions that appear cystic are sometimes aspirated, and solid masses or any that remain after aspiration are evaluated with mammography followed by imaging-guided biopsy.

If there is no mass but cancer is otherwise suspected or if other tests are indeterminate, the following is done -

- Mammography

Abnormal results are evaluated by biopsy guided by imaging. If mammography and ultrasonography do not identify a source and the discharge is spontaneous and comes from a single duct or breast, ductography (contrast-enhanced imaging of the milk duct) can be done.

Treatment

Treatment is based on the cause.

If the cause is benign and the discharge is persistent and annoying, the terminal duct can be excised on an outpatient basis.

Key Points

- Nipple discharge is most often benign.
- Bilateral, multiductal, guaiac-negative discharge is usually benign and has an endocrine etiology.
- Spontaneous, unilateral discharge requires diagnostic testing; this type of discharge may be cancer, particularly if it is bloody (or guaiac-positive).
- Presence of a breast mass, a bloody (or guaiac-positive) discharge, or history of an abnormality on a mammogram or an ultrasound scan requires follow-up with a surgeon who is experienced with breast disorders (Kosir, 2013b).

Mastalgia (Breast Pain)

Mastalgia (breast pain) is common and can be localised or diffuse and unilateral or bilateral.

Causes

Localised breast pain is usually caused by a focal disorder that causes a mass, see Breast Masses (Breast Lumps), such as a breast cyst, or an infection (eg, mastitis, abscess). Most breast cancers do not cause pain.

Diffuse bilateral pain may be caused by fibrocystic changes or, uncommonly, diffuse bilateral mastitis. However, diffuse bilateral pain is very common in women without breast abnormalities. The most common causes are -

- Hormonal changes that cause breast tissue proliferation (eg, during the luteal phase or early pregnancy, in women taking oestrogens or progestins),
- Large, pendulous breasts that stretch Cooper ligaments.

Evaluation - History

History of present illness should address the temporal pattern of pain and its nature (focal or diffuse, unilateral or bilateral). The relation between chronic or recurrent pain and menstrual cycle phase should be ascertained.

Review of systems should seek other symptoms suggesting pregnancy (eg, abdominal enlargement, amenorrhea, morning nausea) or fibrocystic changes (eg, presence of many masses).

Past medical history should cover disorders that could cause diffuse pain (eg, fibrocystic changes) and use of oestrogens and progestins.

Physical examination

Examination focuses on the breast and adjacent tissue, looking for abnormalities such as skin changes including erythema, rash, exaggeration of normal skin markings, and trace oedema sometimes termed peau dorange (orange peel), and signs of infection, such as redness, warmth, and tenderness.

Red flags

The following are of particular concern -

- Signs of infection.

Interpretation of findings

Absence of abnormal findings suggests that pain is due to hormonal changes or large, pendulous breasts. Abnormal findings may suggest other specific problems.

Testing

Pregnancy testing should be done if pain is unexplained and has lasted less than several months, particularly if other symptoms or signs are consistent with pregnancy.

Other testing is indicated infrequently – only if physical findings suggest another problem that requires testing.

Treatment

For menstrual-related mastalgia, acetaminophen or an NSAID is usually effective. If pain is severe, a brief course of danazol or tamoxifen may be given. These drugs inhibit oestrogen and progesterone. If oestrogen or a progestin is being taken, stopping may be necessary.

For pregnancy-related breast pain, wearing a firm, supportive brassiere, taking acetaminophen, or both, can help.

Recent evidence suggests that evening primrose oil, vitamin E, or both used together may reduce the severity of mastalgia.

Key Points

- Diffuse, bilateral breast pain is usually caused by hormonal changes or large, pendulous breasts and causes no abnormal physical findings (Kosir, 2013c).

Breast Implants

Some folk decide after several years of hormone treatment that they need breast implants. This can be done locally, in general, and may not need expensive foreign trips, and depending on the surgeon/clinic you may not need a general anaesthetic. But, this needs to be discussed with the surgeon and clinic concerned. As many as 20% of women who receive breast implants for breast augmentation have to have their implant removed within 8–10 years (FDA, 2014).

But what you may be told at the time, and have since forgotten, is that your implants need to be replaced after ten to fifteen years, but times vary massively for different people and this could be much longer or shorter! You may "wear" them for longer, but then you are increasing the chances for leaks or a rupture!

Saline implant rupture

People with a rupture of their saline implants can present with -

- pain in the breast,
- potential permanent changes in nipple sensitivity,
- implant leakage leading to loss of breast shape,
- redness of the skin,
- tenderness,
- increasing pain,
- There may also be capsular contracture leading to capsulitis[107] (Linder, 2014).

Silicone implant rupture

People with a rupture of their silicone implants can present with -

- pain,
- swelling,
- redness of the skin,
- possible tingling in the breast
- possible scar tissue formation,
- pain inside the breast, caused by hardening of the capsule around the breast (Linder, 2014).

On the other hand, some people may show no signs of a silicone implant rupture and the results may be found on simply diagnostic radiograph, including an MRI!

> "It has been found that the incidence of implant rupture will increase over time and that the silicone gel implants are not lifetime devices. The incidence of silicone breast implant rupture has been found to be approximately 15% rupture rate between the third and 10th year after implantation. Findings showed an overall rupture rate of approximately 5.3 ruptures per 100 implants per year. The rate of ruptures certainly has been shown to significantly increase with increasing implant age,"

said Doctor Stuart Linder (Linder, 2014).

[107] Inflammation of a capsule (e.g., of a joint or the ocular lens) or a pseudocapsule (e.g., that formed around a breast implant)

Breast Screening

What is breast screening?

- Breast screening (also known as 'mammography') is an x-ray examination of the breasts,
- Breast screening can show breast cancers at an early stage, when they are too small for you or your doctor to see or feel,
- A mammogram takes a few minutes and involves a tiny dose of radiation, so the risk to your health is very small,
- Your whole visit to the breast screening unit should take about half an hour (Programmes, 2006).

Who is screened and when?

- Breast screening is free on the NHS in the UK and a government-funded scheme in the Republic of Ireland.
- In the UK, women aged between 50 and 70 are invited for screening every three years. This is being extended to women aged 47 to 73 in some areas of England.
- In Ireland, women aged 50 to 64 are invited every two years
- Women at high risk due to their family history or anyone who detects unusual changes to their breasts may be screened after being referred by their doctor (Campaign, 2014).

Why do I need breast screening?

One in nine women will develop breast cancer at some time in their life. Breast cancer is more common in women over 50. Breast screening can help to find small changes in the breast before there are any other signs or symptoms. If changes are found at an early stage, there is a good chance of a successful recovery (Programmes, 2006).

Should all women have breast screening?

We invite all women aged between 50 and 70 for breast screening every three years.

Breast cancer risk rises as women get older. So even though women over the age of 70 are not automatically invited for breast screening, you are still encouraged to go for screening every three years. You can contact your local breast screening unit to make an appointment.

Whatever age you are, if you are ever worried about any breast problem, please contact your doctor who may refer you for a specialist opinion if necessary (Programmes, 2006).

What is the NHS Breast Screening Programme?

The programme make sure that if you are aged between 50 and 70 we will invite you for breast screening. We will get your name from your health authority record. This record is made up from your doctor's list so it is important that your doctor always has your correct name and address.

In most parts of the country we will invite doctors' practices for screening in turn. So you will not necessarily get your invitation in the year that you turn 50. As long as you are registered with a doctor we will invite you for breast screening before your 53rd birthday (Programmes, 2006).

Where do I go for breast screening?

The screening centre may be in a hospital or clinic, or it may be in a mobile unit. Please do not use talcum powder or spray-on deodorant on the day you go fro breast screening as this may affect the mammogram (Programmes, 2006).

What exactly happens during breast screening?

When you arrive, feel free to ask any questions you have about breast screening.

When you have undressed and are ready and comfortable, a specialist female member of the screening staff will explain mammography to you and ask you a few questions. She will put your breasts, one at a time, between two special plates and take the x-rays.

Mammography takes a few minutes and your breasts are only pressed between the two plates for a few seconds each. There is no evidence that this procedure harms the breast (Programmes, 2006).

Do I have to undress?

Yes, you will be asked to undress completely down to your waist, so it is a good idea to wear a separate top instead of a dress (Programmes, 2006).

Does breast screening hurt?

Some women find mammography uncomfortable and some find it painful as the breasts have to be held firmly in position and pressed to take a good x-ray. If you do experience pain it usually only lasts for as long as the mammogram, although it may continue for some time in a small number of women (Programmes, 2006).

When do I get my results?

When you have had the mammogram, the specialist female member of the screening staff will tell you how and approximately when you will get your results. Make sure you have received this information before you leave the unit (Programmes, 2006).

What does it mean if I am called back?

Some women (about one in every 20 that are screened) are called back because the appearance of the x-ray suggests that more tests are needed. Do not be surprised if we call you back and then tests show that there is nothing to worry about. Most women will not have any problems and we will call them back again in three years' time as part of the routine screening process (Programmes, 2006).

What if I need treatment?

If we call you back and you need treatment, a team will look after you. They will make sure that you get a high quality of acre and treatment at all times.

Breast cancer treatment is always being improved and reviewed. As part of this process, we may invite you to take part in a trial where we will compare the effects of different treatments. You do not have to take part in any trial that we offer you (Programmes, 2006).

Risks and limitations of breast screening

- Screening involves exposure to small amounts of radiation - although the risks here are very small.
- Sometimes mammograms detect a tumour that might not have caused any harm to the woman over their lifetime - this is called "over-diagnosis", and is one of the main criticisms of breast screening programmes.
- Screening is able to detect breast cancer but it won't prevent the disease, so it's vital that people are breast aware, especially between screening appointments.
- Occasionally some patients are recalled because of unclear mammograms or for more tests (Campaign, 2014).

How reliable is breast screening?

Mammography is the most reliable way of detecting breast cancer early but, like other screening tests, it is not perfect. For example -

- some cancers are very difficult to see on the x-ray,
- some cancers, even though they are there, cannot be seen on the x-ray at all,
- the person reading the x-ray may miss the cancer (this will happen occasionally, no matter how experienced the reader is) (Programmes, 2006).

Does breast screening prevent breast cancer?

No, breast screening only helps find breast cancer if it is already there. You should be aware of any changes in your breasts because breast cancer can develop at any time. Some women will develop breast cancer before their first mammogram or between mammograms.

There is a simple five-point breast awareness code that all women should remember.

- Know what is normal for you,
- look at and feel your breasts,
- know what changes to look for (lumps, pain, discharge from the nipple or anything else unusual),
- tell your doctor about any changes immediately,
- go for breast screening every three years if you are over 50.

There are many reasons for changes in the breast. Most of them are harmless but you should get all of them checked as there is a small chance that they could be the first sign of cancer.

Breast awareness and regular mammograms together offer you the best chance of finding breast cancer early (Programmes, 2006).

What happens to my x-rays once they have been read?

The breast screening unit will keep your mammogram for at least eight years. They can then compare your latest mammogram with the ones you have had before.

We regularly review all screening records, including mammograms, as part of our aim to offer you a quality service and to help increases the expertise of specialist staff. This means that staff who work elsewhere in the health service will need to see your records. When a review shows that you should have been cared for differently, we will contact you. We will offer you more information about the review of your case if you want to know it.

For more information about the records we keep, you can contact **NHS Direct** on **0845 4647** (Programmes, 2006).

Summary

To help you decide whether or not to come for breast screening, the main benefits and difficulties of screening for breast cancer are explained below -

- Most breast cancers are found at an early stage when there is a good chance of a successful recovery.
- Around half the cancers that are found at screening are still small enough to be removed from the breast. This means that the whole breast does not have to be removed.
- Breast screening saves an estimated 1,400 lives each year in the UK.
- Breast screening reduces the risk of the women who attend dying from breast cancer.
- We will call back some women for more investigations if we are not sure about their mammogram. After more tests, we will find that many of these women will not have cancer. If you are called back it can cause worry.
- Screening may miss some breast cancers.
- Not all breast cancers that are found at screening can be cured.
- Many women find mammography uncomfortable or painful, but normally just for a brief period of time (Programmes, 2006).

More information and support

If you have any questions about the service, you can -

- ask your doctor,
- contact your local screening office,
- visit our cancer-screening programme website at `www.cancerscreening.nhs.uk`, or
- visit NHS Direct at `www.nhsdirect.nhs.uk` (Programmes, 2006).

Non-invasive breast cancer

- Breast screening can also detect some non-invasive conditions such as DCIS,
- DCIS is when cancerous changes develop within the breast ducts that do not break out into the surrounding tissue
- Most cases of DCIS are detected by screening, rather than self-examination or referral by a doctor
- It is difficult to estimate how often DCIS will develop into invasive breast cancer, but it is believed that if left untreated, DCIS will develop into invasive breast cancer in up to 50% of cases
- For that reason doctors usually recommend that DCIS is treated as they cannot predict how they will develop (Campaign, 2014).

A personal experience.

When I was called for my first breast screening I knew more or less what to expect. It was done in a purpose-built trailer in a secluded spot of my local hospitals car park, and had a very warm and relaxing atmosphere. I was asked to undress my top-half and then went into the x-ray room. I stood in front of this odd-shaped machine and very carefully and sensitively the radiographer placed my breast between two metal plates so that it was squashed flat to get a good "picture"! The x-ray was then taken, but there is no noise or anything to tell you that it has completed, just the radiographer coming back in to set up for the other breast. The whole process took between twenty to thirty minutes.

About a fortnight later I received a letter recalling me for a repeat scan as they were unhappy with my scans. This again took place at my local hospital, but indoors in the specialist "breast care" suite. This time it was more difficult because not being very tall I have a limited arm length and found that I had to stretch to hold onto the handles I was requested to. This time it was more painful on the breast as it was squashed more than before, plus I was over-extending in my reach. It took longer this time to set up for each scan, to get me positioned absolutely right to get the optimum scan, which was eventually done. I was left in position whilst the resulting scan was shown to a senior radiographer to see if they needed to redo one, and I was so uncomfortable and in pain that I was on the point of refusing to cooperate and refusing any more scans when I was told that the scans were OK and I could get dressed now. There was then a period of waiting, before the radiographer came out and took me into a "quiet room" and told me that my scans were OK with no signs of cancer or any other problem, and I was free to go.

The second visit of mine was more intense, and uncomfortable, verging on the painful. I was glad when it was over and I had the "all clear", especially as there is a history of breast cancer in my family.

Coming out

If you need or want to tell someone that you are trans, it can seem rather daunting. First take time to consider who you plan to inform and, if you will be telling more than one person, what order it would be best to speak to them. Try to work out the likelihood that the people you are planning to tell might reveal your situation to other people and how you would deal with that. Remember that often the people that you are telling will never have had to think about gender identity issues before. The way you describe your situation during the initial conversation with them can have a big impact on how well they react and what they think about you.

It is a good idea to plan what you are going to say and to try to anticipate difficult questions they might ask so that you can have clear explanations ready. The more calmly, confidently and positively you present the news to people the more likely that they will react well. When people are not sure what to think about a situation they tend to follow the lead of whoever is appearing the most self-assured in their viewpoint. Similarly, having someone present that already knows and is supportive can also be very helpful in encouraging others there to also be supportive.

If you are a transsexual person who has already transitioned and want to tell people about your history then you might be particularly keen for them to consider it to be something relatively minor so that it does not change their relationship with you. In this case, it can help to keep the conversation as light and upbeat as possible and to present it as more of an interesting quirky little fact than a terrible confession.

People may react to the news that you are trans in all kinds of different ways. They could be completely unfazed and fully supportive of you, or they might be really curious, surprised or confused. Unfortunately, some people might become upset about it or even angry and blaming towards you.

If you think you might get a bad reaction from someone then ensure that you tell them at a time and place where you can then leave quickly and easily to give them space to calm down. Don't panic if they are negative initially, there is a good chance that given enough time to think it over they will gradually adjust and come to terms with it.

Sometimes the fact that someone really cares for you can mean that if you are telling them you intend to transition then they might become very concerned about the prejudice you may face or the risk of taking hormones or having surgery. They might worry that you are doing something too drastic and risky which could mess up your life.

Remember that it is hard for other people to understand the certainty you may feel about your gender identity and how you intend to express it. Try to appreciate that their concerned reaction is because they care about your future welfare. You will quite likely find that their opinions change for the better and their fears reduce over a few years as they start to better understand trans issues and they hopefully start to see your life becoming happier (LGBT, 2014b).

Also you need to bear in mind that you have spent some considerable time thinking things through for yourself, maybe many months, but the person you are telling has only just heard of it all. It might be quite a surprise to them, perhaps even a shock, and may take time for them to assimilate it all and come to terms with what may be a changed relationship with you. I'm thinking specifically of you telling your parents, which is never easy.

Consent and Informed Consent

Consent to treatment is the principle that a person must give their permission before they receive any type of medical treatment or examination. This must be done on the basis of a preliminary explanation by a clinician.

Consent is required from a patient regardless of the intervention from a physical examination to organ donation.

The principle of consent is an important part of medical ethics and the international human rights law.

It can be given -

- Verbally for example, by saying they are happy to have an X-ray.
- In writing for example, by signing a consent form for surgery.

Patients may passively allow treatment to take place – for example, by holding out an arm to show they are happy to have a blood test.

For consent to be valid, it must be voluntary and informed, and the person consenting must have the capacity to make the decision. These terms are explained below -

- **Voluntary** the decision to either consent or not to consent to treatment must be made by the person themselves, and must not be influenced by pressure from medical staff, friends or family.
- **Informed** the person must be given all of the information in terms of what the treatment involves, including the benefits and risks, whether there are reasonable alternative treatments and what will happen if treatment does not go ahead.
- **Capacity** the person must be capable of giving consent, which means they understand the information given to them, and they can use it to make an informed decision.

If an adult has the capacity to make a voluntary and informed decision to consent to or refuse a particular treatment, their decision must be respected (NHS, 2014c).

Informed consent has been defined as

> "**Mutual decision-making between the doctor and the patient**. This is the broadest definition of informed consent. It involves an open exchange of information, education on options and alternatives for care, and assisting the patient in making a decision that is consistent with his/her values"

(Pantilat, 2008).

Contact lenses and drug treatment

Many drugs given systemically can also have adverse effects on contact lens wear. These include oral contraceptives (particularly those with a higher oestrogen content), drugs which reduce blink rate (e.g. anxiolytics, hypnotics, antihistamines, and muscle relaxants), drugs which reduce tear production (e.g. antihistamines, some beta-blockers, diuretics, and tricyclic antidepressants), and drugs which increase tear production (including ephedrine and hydralazine). Other drugs that may affect contact lens wear include aspirin (salicylic acid appears in tears and may be absorbed by contact lenses thereby leading to irritation) (Mackenzie, Downie, and A. Williams, 2004). If you are at all unsure, ask your doctor or dispensing pharmacist whether the drug will affect your eyes or contact lenses.

Cranberry Juice

For many decades cranberry juice *(Vaccinium macrocarpon)* has been thought to reduce bacterial infections of the bladder. Studies in recent years have shown that cranberry juice inhibits adherence of Escheri coli cells to the cells that line the bladder. Two different constituents have been implicated, one being fructose and the other a large polymeric compound of unknown structure. Fructose is present in all fruits, but the large polymeric compound concerned is found only in cranberry and blueberry juices, and not those of grapefruit, orange, guava, mango and pineapple (Bandolier, 1994).

People have also recommended drinking cranberry juice although the evidence suggests that it is ineffective in treating urinary tract infections (Jepson, G. Williams, and Craig, 2012) although it may help to stop repeated infections (Kontiokari et al., 2001).

The evidence appears to show that cranberry juice does not work best on its own but as an adjunct to treatment with antibiotics, although further studies could help to clarify the evidence.

Recent research is starting to show a slightly different picture though. A very recent study shows that *acute beverage consumption of cranberry extract and/or juice provides ex vivo anti-adhesion activity* meaning that its harder for bacteria to stick to the bladder wall (Kaspar, Howell, and Khoo, 2015). Another study showed that an active ingredient of cranberrys, specifically "A-type proanthocyanidins", has anti-biofilm properties against Escherichia coli[108]. This means that the humble cranberry is more able to attack E.coli

[108] the name of a germ, or bacterium, that lives in the digestive tracts of humans and animals. There are many types of E. coli, and most of them are harmless. But some can cause bloody diarrhoea. Some strains of E. coli bacteria (such as a strain called O157:H7) may also cause severe anaemia or kidney failure, which can lead to death

thanks to its anti-biofilm properties (Ulrey et al., 2014). Another recent study showed that even just one drink of cranberry juice, in this case diluted with water, improved the biomarkers of antioxidant status and inhibited bacterial adhesion in urine (Mathison et al., 2014). See also Urinary Tract Infections.

Cycling Hormones?

There has been debate in recent years over whether to administer a constant dosage of hormones every day, or whether to mimic the natural menstrual cycle by reducing or stopping oestrogen for 7–10 days every 28 days, and adding or increasing a progestogen during that period. No advantage has been found to the cyclic method, and its principal effect seems to be to induce extreme mood swings similar to PMS[109]. There is some evidence that the non-cyclic approach produces slightly more rapid feminisation, and so a non-cyclic regime is widely regarded as preferable today.

Also in a genetic female, there is never the case in which oestrogen is ever stopped being produced so that some form of cycling occurs! Hormone levels will rise and fall, but they never stop and start. Therefore people's ideas and concept of "cycling" is, I find, hard to understand!

Depression

Depression is more than simply feeling unhappy or fed up for a few days.

We all go through spells of feeling down, but when you're depressed you feel persistently sad for weeks or months, rather than just a few days. Some people think that depression is trivial and not a genuine health condition. They're wrong. Depression is a real illness with real symptoms, and it's not a sign of weakness or something you can "snap out of" by "pulling yourself together".

Depression affects people in different ways and can cause a wide variety of symptoms.

They range from lasting feelings of sadness and hopelessness, to losing interest in the things you used to enjoy and feeling very tearful. Many people with depression also have symptoms of anxiety[110].

There can be physical symptoms too, such as feeling constantly tired, sleeping badly, having no appetite or sex drive, and complaining of various aches and pains.

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[109] premenstrual syndrome

[110] a feeling of unease, such as worry or fear, that can be mild or severe

The severity of the symptoms can vary. At its mildest, you may simply feel persistently low in spirit, while at its most severe depression can make you feel suicidal and that life is no longer worth living (NHS, 2014b).

If you experience some of these symptoms for most of the day, every day for more than two weeks, you should seek help from your GP.

Psychological symptoms include -

- continuous low mood or sadness,
- feeling hopeless and helpless,
- having low self-esteem,
- feeling tearful,
- feeling guilt-ridden,
- feeling irritable and intolerant of others,
- having no motivation or interest in things,
- finding it difficult to make decisions,
- not getting any enjoyment out of life,
- feeling anxious or worried,
- having suicidal thoughts[111] or thoughts of harming yourself[112].

Physical symptoms include -

- moving or speaking more slowly than usual,
- change in appetite or weight (usually decreased, but sometimes increased),
- constipation,
- unexplained aches and pains,
- lack of energy or lack of interest in sex (loss of libido[113], or sex drive),
- changes to your menstrual cycle,
- disturbed sleep (for example, finding it hard to fall asleep at night or waking up very early in the morning).

Social symptoms include -

- not doing well at work,
- taking part in fewer social activities and avoiding contact with friends,
- neglecting your hobbies and interests,
- having difficulties in your home and family life (NHS, 2014b).

[111] thoughts of intentionally ending your life

[112] thoughts of intentionally damaging or injuring your body. It is a way of coping with or expressing overwhelming emotional distress

[113] this is a common problem affecting up to one in five men — and even more women — at some point in their life

Drug names

Medicines normally have more than one name -

- a generic name, which is the active ingredient of the medicine,
- a brand name, which is the trade name the manufacturer gives to the medicine.

The generic name is the official medical name for the active ingredient of the medicine.

The brand name is chosen by the manufacturer, usually on the basis that it can be recognised, pronounced and remembered by health professionals and members of the public. An example would be Viagra - this is the well-known brand name given by Pfizer to the generic medicine sildenafil. (Brand names are capitalised; generic names are not.)

E-numbers

The ubiquitous "E-numbers" rear their head in the coatings of some medications, specifically Dutasteride, which contains E321, E172 and E171. Other medications may also contain E-numbers, only I may not have found the reference to them yet.

E-numbers are codes for substances which can be used as food additives for use within the European Union, with the "E" standing for "Europe". They are commonly found on food labels throughout the European Union. Safety assessment and approval are the responsibility of the European Food Safety Authority (wikipedia, 2014b).

Having a single unified list for food additives was first agreed upon in 1962 with colours. In 1964, the directives for preservatives were added, 1970 for antioxidants and 1974 for the emulsifiers, stabilisers, thickeners and gelling agents.

E321	Butylated hydroxytoluene (BHT)	antioxidant	Approved in the EU.
E171	Titanium dioxide	White	Approved in the EU. Approved in the US.
E172	Iron oxides and iron hydroxides	Brown	Approved in the EU. Approved in the US for sausage casings.

Table 17.14 – The e-numbers used in some tablets

Ethinylestradiol

There has long been discussion in various forums of the safety of this drug with regard to it seemingly having a higher thrombotic risk than any other hormone commonly taken. The main article cited has been "Mortality and Morbidity in Transsexual Patients With Cross-Gender Hormone Treatment" written by H Asscheman, LJG Gooren, and PLE Eklund (Asscheman, LJ Gooren, and Eklund, 1989), where they stated *"Combined treatment with estrogen and cyproterone acetate in 303 male-to-female transsexuals was associated with a 45-fold increase of thromboembolic events"*. The oestrogen used in this case was Ethinylestradiol.

But no explanation was given as to why this was so, and I have seen no explanation since, until this article in the "Journal of Clinical Endocrinology & Metabolism" of 2003 where they state that the reason for the high thrombotic risk of Ethinylestradiol is due to its molecular structure rather than to a first-pass liver effect (Toorians et al., 2003).

In view of the high risks involved with this drug, maybe it would be better to avoid using it wherever possible. And if it is prescribed for you by your GP then perhaps you could present them with copies of the two articles to show how risky it can be for you.

Exercise

What is it?

Exercise is part of the complete and total package for good health. Exercise is one of the most powerful lifestyle changes we have available to us. Regular and consistent exercise can do all of the following for you -

- Increase metabolic rate,
- Burn calories,
- Increase muscle mass,
- Improve fitness level,
- Reduce the risk of heart disease, osteoporosis, diabetes, breast cancer, osteoarthritis and depression,
- Give you strength and vitality,
- Release those endorphins in your brain,
- Lose or maintain weight,
- Feel more confident with yourself.

The kind of exercise you do is really up to you. Its not about the spandex; its about the movement!

What to do?

There are so many ways you can get exercise. You may not even realize you are doing itYou can chase kids, walk up the stairs at work, run a mile, lift weights, jump rope, take a yoga class, or scale a mountain. You can move anytime, anywhere, any way you like. If you are an on again, off again, exercise kind of gal, try to really commit yourself to a regular program. Set time aside. Studies show that people who exercise in the morning are more successful with staying on their exercise program. Find a pal. Pick an activity you enjoy. Make it fun (womeninbalance.org, 2016a).

Expiry dates

In the US a law was passed in 1979 stating that drug manufacturers were required to stamp an expiration date on their products. This is the date at which the manufacturer can still guarantee the full potency and safety of the drug.

Most of what is known about drug expiration dates comes from a study conducted by the Food and Drug Administration (FDA) at the request of the military. With a large and expensive stockpile of drugs, the military faced throwing out and replacing its drugs every few years. What they found from the study is that 90% of more than 100 drugs, both prescription and OTC, were perfectly good to use even 15 years after the expiration date.

So the expiration date doesn't really indicate a point at which the medication is no longer effective or has become unsafe to use. Medical authorities state expired drugs are safe to take, even those that expired years ago. A rare exception to this may be tetracycline, but the report on this is controversial among researchers. It's true the effectiveness of a drug may decrease over time, but much of the original potency still remains even a decade after the expiration date. Excluding nitroglycerin, insulin, and liquid antibiotics, most medications are as long-lasting as the ones tested by the military. Placing a medication in a cool place, such as a refrigerator, will help a drug remain potent for many years (harvard-health, 2015).

However, if you have any questions about the safety or effectiveness of any drug, ask your pharmacist. He or she is a good resource when it comes to getting more information about any of your medications.

From Amazon

Just browsing on Amazon and I found that they have just started selling Oestrogel as **Oestrogel Estradiol 80 Grams**. It can be found at http://www.amazon.co.uk/Thailand-oOestrogel-Estradiol-80-Grams/dp/B00Q5AH74G/ref=sr_1_2?ie=UTF8&qid=1416947663&sr=8-2&keywords=oestrogel This is the picture from the Amazon page -

Figure 17.4 – 17β-Estradiol

It is being sold for UK £21.00, and the supplier is listed as 'Thailand'.

And they also sell testosterone as pill, gel, or tablets. Try searching through your countries version of Amazon.

Further discussion of Vitamin D

Factor that influences Vitamin D level	Comment
Aging - (Older individuals lose their ability to adequately produce Vitamin D, regardless of sun exposure time)	Older individuals make less Vitamin D for many reasons; 7-dehydrocholesterol in the skin decreases over time so it is more difficult to make Vitamin D3 (for example, individuals above the age of 65 have a fourfold reduction in the capacity of the skin to produce Vitamin D3), liver and kidney function is not as efficient, and the gut's ability to just absorb Vitamin D from food or supplements is reduced
Belly Fat - (Obesity or greater amounts of visceral fat)	Obese individuals tend to have lower vitamin D concentrations because this vitamin gets absorbed by fat-tissue and is not easily released in the blood stream; another reason is that the volume of the blood is so large that it dilutes this nutritional test

Factor that influences Vitamin D level	Comment
Cholesterol-lowering medications - Statins	Preliminary research suggests that lowering cholesterol may increase vitamin D levels
Dietary vitamin D intake - (Natural or non-fortified sources)	The more vitamin D one gets from dietary sources, the higher the blood level. Fish and other seafood are the best naturally producing dietary sources, followed by mushrooms and egg yolks, which are both considerably lower sources
Dietary vitamin D intake - (Fortified vitamin D sources)	In the US and Canada, milk, soy milk, bread products, cereals, protein bars, and beverages are fortified with vitamin D. In Europe, margarine is one of the more common fortified sources of vitamin D. However, independent surveys have found that many of these products do not contain the amount of vitamin D on the label (usually less).
Frequency of vitamin D intake - (Daily versus weekly versus monthly)	Recent research has demonstrated that taking a daily pill has a higher probability of keeping a normal blood level of vitamin D compared to a once-weekly or once-monthly dosage equivalent formulation
Skin pigmentation	Darker skinned individuals have more melanin (increased skin pigmentation), which blocks the impact of UVB radiation and reduces the production of vitamin D. African-american individuals have a higher risk of vitamin D deficiency
Sunlight exposure due to outside activities	The more one's occupation or activities involve being outdoors, especially in the spring and summer, the greater the chance that you will have higher vitamin D levels
Sunscreen/sun-protective clothing and other measures	The higher the SPF of sunscreen, the more it blocks the ability of UVB light from the sun to increase vitamin D level. This is also the case with sun-protective clothing. Individuals that are completely covered by clothing for a variety of purposes (including religious) have lower vitamin D levels
Supplemental vitamin D - (Supplemental availability and type or form of vitamin D)	Multivitamins generally contain 400IU (10mcg) per capsule, and vitamin D individual tablets can now be purchased and are cost effective. However, many of these pills and liquids contain vitamin D2 and not vitamin D3

Factor that influences Vitamin D level	Comment
Ultraviolet-B (UV-B) light radiation (Wavelength=290 to 315nm; exposure based on where one lives)	UVB radiation from the sun is the primary source of vitamin D for most people. Thus, geographic location (where you live) has an impact on how much sun and vitamin D is produced (more sun or closer to the equator = more vitamin D). In latitudes of approximately 40 degrees north and south of the equator, vitamin D production in skin rarely occurs in winter (for example, Boston, MA, is 42 degrees north and Edmonton, Canada, is 53 degrees north)

Table 17.15 – The primary factors that can potentially determine an individual's vitamin D blood level from A to Z

It is becoming increasingly obvious that the majority of people living in the northern hemisphere are deficient in vitamin D. *"It is estimated that about a billion people worldwide have vitamin D levels considered insufficient (<75 nmol/L)"* (*Jeffrey, 2010*).

In fact *"Older patients with very low levels of vitamin D have about a 122% increased risk for dementia compared with those with higher levels, according to a large, prospective, population-based study"* (*Anderson, 2014*).

Maybe there is an idea that we should ask our health care providers/GP's for getting a blood test done to get baseline levels of vitamin D, with a view to perhaps commencing vitamin D supplementation. See also Vitamin D.

Gender

For many people, the terms "gender" and "sex" are used interchangeably, and thus incorrectly. This idea has become so common, particularly in western societies, that it is rarely questioned. We are born, assigned a sex, and sent out into the world. For many people, this is cause for little, if any dissonance. Yet biological sex and gender are different; gender is not inherently nor solely connected to ones physical anatomy.

Biological Gender (sex) includes physical attributes such as external genitalia, sex chromosomes, gonads, sex hormones, and internal reproductive structures. At birth, it is used to assign sex, that is, to identify individuals as male or female. Gender on the other hand is far more complicated. It is the complex interrelationship between an individuals sex (gender biology), ones internal sense of self as male, female, both or neither (gender identity) as well as ones outward presentations and behaviors (gender

expression) related to that perception, including their gender role. Together, the intersection of these three dimensions produces ones authentic sense of gender, both in how people experience their own gender as well as how others perceive it.

The Gender Spectrum

Western culture has come to view gender as a binary concept, with two rigidly fixed options: male or female, both grounded in a persons physical anatomy. When a child is born, a quick glance between the legs determines the gender label that the child will carry for life. But even if gender is to be restricted to basic biology, a binary concept still fails to capture the rich variation that exists. Rather than just two distinct boxes, biological gender occurs across a continuum of possibilities. This spectrum of anatomical variations by itself should be enough to disregard the simplistic notions of a binary gender system.

But beyond anatomy, there are multiple domains defining gender. In turn, these domains can be independently characterized across a range of possibilities. Instead of the static, binary model produced through a solely physical understanding of gender, a far richer tapestry of biology, gender expression, and gender identity intersect in a multidimensional array of possibilities. Quite simply, the gender spectrum represents a more nuanced, and ultimately truly authentic model of human gender.

Falling Into Line

Gender is all around us. Like water surrounding creatures in the sea, we are often unaware of its ever-present nature. Gender is actually taught to us from the moment we are born. Gender expectations and messages bombard us constantly. Upbringing, culture, peers, schools, community, media, and religion are some of the many influences that shape our understanding of this core aspect of self. How you learned and interacted with gender as a young child directly influences how you view the world today. Gendered interactions between parent and child begin as soon as the sex of the baby is known. In short, many aspects of gender are socially constructed, particularly with regard to gender expression.

Like other social constructs, gender is closely monitored and reinforced by society. Practically everything in society is assigned a gendertoys, colors, clothes and behaviors are just some of the more obvious examples. Through a combination of social conditioning and personal preference, by age three most children prefer activities and exhibit behaviors typically associated with their sex. Accepted social gender roles and expectations

are so entrenched in our culture that most people cannot imagine any other way. As a result, individuals fitting neatly into these expectations rarely if ever question what gender really means. They have never had to, because the system has worked for them.

About Gender-expansiveness

"Gender-expansive" is an umbrella term used for individuals that broaden commonly held definitions of gender, including its expression, associated identities, and/or other perceived gender norms, in one or more aspects of their life. These individuals expand the definition of gender through their own identity and/or expression. Some individuals do not identify with being either male or female; others identify as a blend of both, while still others identify with a gender, but express their gender in ways that differ from stereotypical presentations. A gender-expansive persons preferences and self-expression may fall outside commonly understood gender norms within their own culture; or they may be aligned with them even as ones internal gender identity doesnt align with the sex assigned at birth.

This diversity of gender is a normal part of the human experience, across cultures and throughout history. Non- binary gender diversity exists all over the world, documented by countless historians and anthropologists. Examples of individuals living comfortably outside of typical male/female expectations and/or identities are found in every region of the globe. The calabai, and calalai of Indonesia, two-spirit Native Americans, and the hijra of India all represent more complex understandings of gender than allowed for by a simplistic binary model.

Further, what might be considered gender-expansive in one period of history may become gender normative in another. One need only examine trends related to men wearing earrings or women sporting tattoos to quickly see the malleability of social expectations about gender. Even the seemingly intractable "pink is for girls, blue is for boys" notions are relatively new. While there is some debate about the reasons why they reversed, what is well documented is that not until the mid-twentieth century were notions of pink for girls or blue for boys so firmly ensconced. You can make the case that "pink is the new blue!"

Gender And Privilege

When someone is "typically gendered," they benefit from gender privilege. For individuals whose biological sex, gender expression, and gender identity neatly align, often referred to as "cisgender," there is a level of congruence as they encounter the world around them. Like many forms of social privilege, this is frequently an unexamined aspect of their lives. Forms they fill out, the clothing stores in which they shop, or identification papers they carry bring few if any second thoughts. Yet for a transgender

or otherwise gender-expansive person, each of these, and many more examples, is a constant reminder that they move about in a culture that really does not account for their own experience. Social privilege comes from an assumption that ones own perspective is universal; whether related to race, or language, or gender, privilege comes from being part of the "norm." Or, as Dorothy Soelle aptly described it: Privilege is being able to choose what you will not see.

To understand this more intuitively, think about the last time you were in a public setting and needed to use a restroom. For cisgender individuals, this rarely presents a problem or question (issues of cleanliness notwithstanding!). Yet for an individual who does not fit into narrowly defined expectations of gender presentation or identity, restroom use can present a whole host of challenges, sometimes even becoming a matter of life and death. The daily need to make judgments about what one does, or wears, or says based on other peoples perceptions of their gender is a burden that many people never encounter. These everyday reminders of being different are also constant reinforcement of being "other".

Perhaps the most fundamental aspect of a persons identity, gender deeply influences every part of ones life. In a society where this crucial aspect of self has been so narrowly defined and rigidly enforced, individuals who exists outside its norms face innumerable challenges. Even those who vary only slightly from the norm can become targets of disapproval. Yet this does not have to be the case forever. Through a thoughtful consideration of the uniqueness and validity of every persons experiences of self, we can develop greater acceptance for all. Not only will this create greater inclusion for individuals who challenge the norms of gender, it will actually create space for all individuals to more fully explore and celebrate who they are (genderspectrum, 2015).

Getting a urine sample

If you are asked to provide a urine sample you may be given a small, clear plastic, sample pot, with either a red or white screw-top lid. It may, or may not, contain a small amount of white powder, which if present is boric acid, a preservative. The pot is about three inches high and maybe $\frac{3}{4}$ of an inch wide.

Trying to wee into such a small pot is I have found, almost impossible. Right from being potty-trained as toddlers, we are taught that to get urine on our hands is a big no-no, and is something that should be avoided wherever possible, which means everywhere! So to stick the urine sample pot between our legs and to be expected to wee into it, whilst we are having a wee, just never happens. We are programmed not to do it!

But we still need a urine sample! The solution? Using a clean, dry, empty margarine container, remove the lid, and hold the container between your legs whilst sitting down and weeing. The big oblong container goes easily between the legs, and can be easily held in position yet keeping your hand away from the urine stream. The result should be an amount of fresh urine which can be easily poured into the sample pot, and the lid screwed on. Any excess urine can be disposed of down the toilet and the margarine container can be rinsed out and left to dry. Then wash your hands, as per usual.

Getting older

As you age, your immune system becomes less effective at protecting your body from infection and disease.

Cardiovascular (heart) disease

Cardiovascular disease is a broad term that includes coronary heart disease, heart attack and stroke. It is often referred to as heart disease. As you age, the risk of developing heart disease increases. Women older than 55 and men older than 45 are at higher risk of developing heart disease. If you have other members in your family who have heart disease - a father, a mother, an uncle or a sibling, for instance - your risk of developing heart disease will be higher than the person who doesn't have a family history.

While you can't control risk factors for heart disease such as your age and family history, there are many lifestyle risk factors you can control. These include -

- smoking,
- being overweight,
- lack of exercise,
- poor diet,
- excessive alcohol intake,
- high blood cholesterol and blood lipids or fats,
- diabetes,
- high blood pressure or hypertension.

Healthy heart habits

Lower your risk for heart problems by adopting the following lifestyle -

- eat a healthy diet,
- exercise regularly - especially aerobic or cardio exercise,
- quit or cut down on smoking,
- drink alcohol in moderation,

- avoid cocaine, crack cocaine, crystal meth, ecstasy, ketamine and GHB,

Bone disorders

Your bones are living and growing. The strength of your bones, or bone density, is determined by the amount of calcium, phosphorous and other minerals they contain.

Age is also a risk factor for bone problems, as is gender. Women, for instance, have a higher risk than men of osteoporosis, a bone disease that causes bones to become thin and fragile and to break easily, particularly at the hip, spine and wrist. This is partly because women have 30% less bone mass than men. But women are also particularly vulnerable to osteoporosis after menopause, when the hormone oestrogen — a key factor in maintaining bone strength in women — is no longer produced by the ovaries.

Also see Osteoporosis.

Prescriptions

I'm hearing anecdotal reports about folk in the USA who are being refused transdermal patches by their insurance provider because after the age of 64, you are 'at risk' when using them!

Grapefruit Juice

Grapefruit or grapefruit juice has been shown to affect the metabolism of many medications, increasing the risk of toxicity and adverse events. Characteristics of oral medications that may interact with grapefruit include extensive metabolism through the intestinal cytochrome P450 3A4 (CYP3A4) system, low bioavailability, and a narrow therapeutic index. Grapefruit juice interacts through the intestinal CYP3A4 system and can inhibit the concentration for 24–72hrs. This is not an exclusive list of medications that may interact with grapefruit. Caution should be taken by both patient and doctor and monitor adverse reactions when taking medications that may interact with grapefruit or its juice.

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
alkaloid[114]		

[114] any of a group of organic basic substances found in plants, many of which are pharmacologically active, e.g., atropine, caffeine, morphine, nicotine, quinine, and strychnine

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
colchicine	Colcrys	Increases the risk of colchicine-induced toxic effects, significant increase in colchicine plasma concentration is anticipated. Grapefruit and grapefruit juice should not be consumed during colchicine treatment.
Antiarrhythmics[115]		
amiodarone	Cordarone	Inhibits CYP3A4-mediated metabolism of oral amiodarone resulting in increase plasma levels of amiodarone. Avoid co-administration.
dofetilide	Tikosyn	Inhibitor of the CYP3A4 isoenzyme, thus could increase systemic dofetilide exposure. If co-administration is necessary, use with caution.
dronedarone	Multaq	Moderate inhibitor of CYP3A, results in a 3-fold increase in dronedarone exposure and a 2.5-fold increase in Cmax. Avoid co-administration.
Antihelminthic[116]		
praziquantel	Biltricide	1.6-fold increase in the Cmax and a 1.9-fold increase in the AUC of praziquantel.
antipsychotic[117]		
pimozide	Orap	Inhibits CYP3A4-mediated metabolism of pimozide. Avoid co-administration.
Calcium channel blockers[118]		
felodipine	Plendil	2-fold increase in felodipine AUC and Cmax. Avoid co-administration prior to and during treatment.
nifedipine	Procardia	2-fold increase in nifedipine AUC and Cmax with no change in half-life. Avoid co-administration.
nisoldipine	Sular	3-fold increase in nisoldipine Cmax and 2-fold increase in nisoldipine AUC. Avoid co-administration before and after dosing.

[115] used to control cardiac arrhythmia, including membrane-stabilizing drugs (e.g. quinidine, lidocaine, flecainide), beta-blockers, amiodarone and sotalol and calcium channel blockers (e.g. verapamil)

[116] used to destroy or cause the expulsion of parasitic intestinal worms

[117] effective in the treatment of psychotic disorders; also, an agent that so acts. Antipsychotics are a chemically diverse but pharmacologically similar class of drugs; besides psychotic disorders, some are also used to treat movement disorders, intractable hiccups, or severe nausea and vomiting

[118] medication that slows the movement of calcium into the cells of the heart and blood vessels. This, in turn, relaxes blood vessels, increases the supply of oxygen-rich blood to the heart, and reduces the heart's workload

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
verapamil	Verelan	May significantly increase concentrations of verapamil. Increased S- and R-verapamil AUC012 by 36% and 28%, respectively. Steady state Cmax and Cmin of S-verapamil increased by 57% and 16.7%, respectively compared to control. Cmax and Cmin of R-verapamil increased by 40% and 13%, respectively.
Cholesterol-lowering medications		
atorvastatin	Lipitor	Inhibits CYP3A4 and can increase plasma concentrations of atorvastatin, especially with excessive grapefruit juice consumption (>1.2L/day).
lovastatin	-	Inhibits CYP3A4 and can increase plasma concentrations of lovastatin. Avoid large quantities of grapefruit juice (>1 quart daily).
simvastatin	Zocor	Inhibits CYP3A4 and can increase plasma concentrations of simvastatin and may increase risk of myopathy. Avoid large quantities of grapefruit juice (>1 quart daily).
opioid[119]		
fentanyl	Fentora	May result in a potentially dangerous increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression.
Psychotropic agents[120]		
buspirone	-	4.3 fold increase in Cmax, 9.2 fold increase in AUC. Avoid drinking large amounts (200mL double-strength three times daily) of grapefruit juice.
triazolam	Halcion	Increases the Cmax of triazolam by 25%, increases AUC by 48%, and increases half-life by 18%. Use with caution.
steroid[121]		
budesonide	Entocort EC	After extensive intake of grapefruit juice, the systemic exposure for oral budesonide increased about two times. Ingestion of grapefruit or grapefruit juice should be avoided (Stump, Mayo, and Blum, 2006).

[119] a synthetic narcotic that has opiate-like activities but is not derived from opium

[120] a chemical compound that influences the human psyche

[121] any of a large number of hormonal substances with a similar basic chemical structure, produced mainly in the adrenal cortex and gonads

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice

Table 17.16 – Pharmacological effects of grapefruit juice with medications

Heamatological Reference Values

Analyte	Conventional units	SI units
Antithrombin III		
Antigenic	22–39mg/dL	220–390mg/L
Functional	80–130%	0.8–1.30 U/L
Bleeding time	2.0–9.5min	2.0–9.5min
Erythrocyte count		
Male	4.50–5.90 x 10^6/mm3	4.50–5.90 x 10^{12}/L
Female	4.00–5.20 x 10^6/mm3	4.00–5.20 x 10^{12}/L
Erythrocyte sedimentation rate		
Male	0–17mm/hr	0–17mm/hr
Female	1–25mm/hr	1–25mm/hr
Ferritin		
Male	30–300ng/mL	30–300ng/mL
Female	10–200ng/mL	10–200ng/mL
Fibrinogen	150–400mg/dL	1.50–4.00g/L
Folate (folic acid)		
Normal	3.1–17.5ng/mL	7.0–39.7nmol/L
Borderline deficient	2.2–3.0ng/mL	5.0–6.8nmol/L
Deficient	<2.2ng/mL	<5.0nmol/L
Excess	>17.5ng/mL	>39.7nmol/L
Folic acid	150–450ng/mL/cells	340–1020nmol/L/cells
Heamatocrit		
Male	41.0–53.0%	0.41–0.53%
Female	36.0–46.0%	0.36–0.46%
Haemoglobin		
Plasma	1–5mg/dL	0.01–0.05g/L
Whole blood, male	13.5–17.5g/dL	8.4–10.9mmol/L
Whole blood, female	12.0–16.0g/dL	7.4–9.9mmol/L
Haemoglobin electrophoresis		
Hemoglobin A	95–98%	0.95–0.98%
Hemoglobin A_{1c}	3.8–6.4%	0.038–0.064Hg fraction
Hemoglobin A_2	1.5–3.5%	0.015–0.035
Hemoglobin F	0–2.0%	0–0.02

Analyte	Conventional units	SI units
Hemoglobins other than A, A_2, or F	Absent	Absent
Iron (hematology and coagulation values)	30–160µg/dL	5.4–28.7µmol/L
Iron-binding capacity (hematology and coagulation values)	228–428µg/dL	40.8–76.7µmol/L
Iron (clinical chemistry values)	50–150µg/dL	9–27µmol/L
Iron-binding capacity (clinical chemistry values)	250–370µg/dL	45–66µmol/L
Leukocyte count (WBC)	4.5–11.0 x $10^3/mm^3$	4.5–11 x 10^9/L
Mean corpuscular hemoglobin (MCH)	26.0–34.0pg/cell	26.0–34.0pg/cell
Mean corpuscular hemoglobin concentration (MCHC)	31.0–37.0g/dL	310–370g/L
Mean corpuscular volume (MCV)	80–100µ/m3	80–100fl
Partial-thromboplastin time (activated)	22.1–35.1sec	22.1–35.1sec
Platelet count	150–350 x 103/mm^3	150–350 x 10^9/L
Prothrombin time	11.1–13.1sec	11.1–13.1sec
Reticulocyte count	0.5–2.5% red cells	0.005–0.025% red cells
Transferrin	230–390mg/dL	2.3–3.9g/L
Vitamin B_{12}		
Normal	>250pg/mL	>185pmol/L
Borderline	125–250pg/mL	92–185pmol/L
Deficient	<125pg/mL	<92pmol/L (mpr, 2012)

Table 17.17 – Heamatological Reference Values

Hormones and dementia

Recent research is showing that women randomized to continue hormone treatment experienced relative preservation of frontal and parietal cortical metabolism, compared with women randomised to discontinue hormone treatment. Women who discontinued 17-β-oestradiol-based hormone treatment, as well as women who continued conjugated equine estrogen (CEE)-based hormone treatment, exhibited significant decline in metabolism of the precuneus/posterior cingulate cortical (PCC) area. Significant decline in PCC metabolism was additionally seen in women taking concurrent progestins (with either 17-β-oestradiol or CEE). Together, these findings suggest that among postmenopausal subjects at risk for developing dementia, regional cerebral cortical metabolism is relatively preserved for at least two years in women randomized to continue hormone treatment, compared with women randomized to discontinue hormone treatment. In addition, continuing unopposed 17-β-oestradiol therapy is associated specifically with preservation of metabolism in PCC, known to undergo the most significant decline in the earliest stages of Alzheimer's disease (Rasgon et al., 2014).

This seems to show -

- take 17-β-oestradiol on its own
- don't take conjugated Oestrogens,
- don't take progestins, as these possibly lead to mental decline

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Hospital Records

- If your hospital treatment was before 1990, then it is extremely unlikely that your medical records are still available.
- If the hospital has moved its site in the intervening period, then they may have been disposed of, or just plain lost in the move.
- There is always the possibility that your consultant has taken the records out of the medical records section, perhaps for review or some other purpose, and they may have got mislaid, misfiled, or again lost. The consultants seem to be able to squirrel away medical records and x-rays not only into filing cabinets (the obvious place) but also windowsills, plastic crates (for ease of moving them to another hospital site for an outlying clinic), but also in cardboard boxes shoved under their desk. At least, thats been my experience.
- The records may be with a secretary for typing a letter.
- But, in general, the medical records (which also includes x-rays) should be kept for a period of ten years and indexed using your hospital number, surname and then initials, and generally stored in the medical records department.

This last point with the indexing system may mean that you have to 'out' yourself if the records are in your 'male' name instead of your present female name for transwomen. And vica versa in the case of transmen.

Other forms of medical records are our notes at our GP's, which in their paper form seem to follow us around the country when we move. Hopefully the use of electronic versions will enable them to get to your new doctors in a considerably quicker time than the paper version does. Dental records don't seem to follow us, but remain at the dentist who provided the treatment. Presumably there are time limits, and space constraints too, on the records storage there.

How to Take Your Tablets.

There is at present some discussion going on in various forums about the best way of taking your tablets. There is anecdotal evidence that sublingually[122] is best for some. Basically if the tablet can be easily crushed, i.e. it doesn't have a hard coating, ('enteric coated' is the technical term, meaning that the coating dissolves further into the gut rather than the stomach) then it can be taken sublingually. However, you may get a funny taste in your mouth for a while. The advantage of this method is that you will absorb more of the drug into your bloodstream far quicker than by swallowing the tablet, and it bypasses the liver thereby hopefully reducing the strain on the liver. However, some of the tablet will have dissolved into the saliva produced by the mouth, which is then swallowed as normal. So a proportion of the medication will still be administered orally. Please note, if you take Premarin by this method it dissolves very slowly, and once the enteric coating is dissolved, its equine origins will become very evident! It is not advisable to take Ethinylestradiol by this method, because it triggers the oestrogen receptors within the liver several times because of the hepato-intestinal recirculation (basically it circulates in the blood stream, and oestrogens are excreted with bile into the intestine. They then get absorbed back into the blood stream, travelling with the blood through the veins into the liver and again triggering oestrogen receptors, and starting its cycle off again).

Research of medications via different routes, indicate that pessaries may deliver around twice as much as oral medications, for any given dosage. Oral capsules reach the blood within the first hour (dependant on what the medication is and its absorption) and peak within hours afterwards. Pessaries peak over 6 hours or so but could be better taken as a split dose. Oral medications seem to be most effective taken with or just after food, since the oils in the food aid absorption and minimise any potential for gastric irritation.

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[122] Beneath the tongue

See also Methods of Delivery or Administration, and also Understanding "Enteric Coating".

Renewed Confidence in HRT

Since July 2002, there has been a huge downturn in the confidence of, and use of HRT. The concern about risks of HRT followed publication of results the Women's Health Initiative trial in 2002 and of the Million Women study in 2003. The massive publicity around the apparent risks shown by these studies understandably led to HRT being viewed as dangerous and that it should rarely be used.

Both these studies have since been reviewed and reanalysed and the revised outcomes, along with new studies which have now been published paints a much different picture - when used appropriately, **HRT provides more benefits than risks for most women**. Yet this message has not yet been widely circulated and I continue to hear of women who have distressing menopausal symptoms, have read thoroughly, weighed up the pros and cons and know that HRT is the best option for them but have to battle with their doctor to be allowed to take it.

To sort out the ongoing confusion, a global team of representatives of Menopause Societies and organisations associated with Women's Health met in November 2012 and have published a global consensus statement. The conclusions are clear -

- HRT is the most effective treatment for symptoms related to the hormonal changes of the menopause, and is beneficial for bone health and may decrease mortality and cardiovascular disease.
- Risks are acknowledged, but benefits will generally outweigh the risks for women under sixty, or within ten years of the menopause. The risks are generally small.
- Taking HRT is a decision which needs to be individualised, in consultation with a suitably qualified doctor.

This statement is extrememly important and must be widely circulated and discussed. Women should be able to be access accurate, non-biased information so that they can make informed choices and in managing the consequences of the hormonal changes of the menopause, HRT should once again be considered as a safe option (Heather, 2013).

Implants, Testosterone and Estradiol

In November 2012, MSD made the commercial decision to discontinue the production of Testosterone Implants. There were no alternative suppliers here in Europe. There is now availability of Testosterone 100 mg Implants from Smartway Pharmaceuticals Ltd (SP Ltd) in the UK. SP Ltd is the only distributor of the product across the world (excluding USA). The product is manufactured by Advanced Pharmaceutical Technology Inc in the USA, and SP Ltd is their main distributor for the Testosterone Implants.

There is also availability through SP Ltd for Estradiol 25 mg and 50 mg Implants. These are also manufactured by Advanced Pharmaceutical Technology Inc in the USA, and again, SP Ltd is their main distributor for these Implants.

Contact Details for Smartway Pharmaceuticals Ltd Name: Dhruv Patel Tel: +44 208 545 7730 Email: dhruv@smartwaypharma.co.uk (unknown, 2015g).

Importation of prescribed medication

It appears from emails that I have received that certain medications can be legally imported on a correctly completed prescription from your doctor. This is how it can be done (taking Prometrium as an example only) - if your GP is convinced of the case for the prescription, they should write on the standard prescription form, something along the lines of "Prometrium 100mg (progesterone BP 100mg in oil capsules), Laboratoires Besins Iscovesco, France (IDIS), twice daily". The Prescription Payments Authority has no problem with paying for such a prescription, however it is worth telling your GP and pharmacy that it has been imported before and cleared by the Prescription Payments Authority. It should be available for collection at your local pharmacy within about a week.

The ones that I have heard about are;-

Prometrium

Imported from the USA on a named patient basis, expensive!
Usual dosage 200–400mg daily.
Prometrium is micronised Progesterone, in oil, in capsules which can be taken orally. (Must be micronised (i.e. a special superfine powder) so that a reasonable amount of it can be absorbed before it is destroyed by gastric acids).

Progynon-Depot

Imported from Germany on a named patient basis. Injectable estradiol valerate which is 10mg/ml and 1ml in an ampoule.

Estradiol-Depot

Imported from Germany on a named patient basis. Injectable estradiol valerate which is 10mg/ml and 1ml in an ampoule.

Importing into ...

New Zealand

From anecdotal reports it seems extremely difficult, if not impossible, to import your needed hormones without a prescription. And not all doctors know much about TS's so they are reluctant to prescribe, which therefore makes it very difficult to get the required prescription!

Infection?

If you have unexplained pain "down below"? Specifically in your groin, then maybe you have an infection? Answering these questions may help in diagnosis, and if you are asked to provide a urine sample see Getting a urine sample. This can then be used for "dipstick-anaylsis". See also Urinary Tract Infections - UTI's.

- Do you have pain there?
- Is the area redder than the surrounding skin?
- Is the area sore?
- Does it itch?
- Is there any discharge?
- Is there an odour from it?

	Vaginal candidiasis (thrush)	**Bacterial vaginosis (BV)**
Cause	fungal infection	bacterial infection
Sexual transmission	very rarely	often
Symptoms		
Painful urination	mild to marked	absent to mild
Vulval irritation	external	not usual
Odour	absent	fishy, amine-like
Signs		

Labial redness	variable	no
Satellite lesions [123]	yes	no
Vaginal tenderness	yes	no
Discharge		
Consistency	sometimes curdy or cheeselike	homogenous, frothy
Colour	white	grey, white
pH	<4.5	>4.7 (VPS, 2015)

Table 17.18 – The difference between fungal and bacterial infections

Candida cystitis

Many people are asymptomatic. However, bladder invasion may result in frequency, urgency, dysuria[124], haematuria, and suprapubic pain. Candida cystitis may or may not be associated with the use of a Self-retaining catheter (SRC)[125]. Physical examination may reveal suprapubic pain; other findings are unremarkable (Hidalgo, 2014).

Diagnosis

A urinalysis should be performed; evidence of white blood cells (WBCs), red blood cells (RBCs), protein, and yeast cells is common; urine fungal cultures are useful (Hidalgo, 2014).

Using a speculum to help, swabs may be taken of the vaginal mucosa to help in diagnosis.

Treatment

Noncatheterized patients should be treated with oral fluconazole; in catheterized patients, the SRC should be removed or replaced; if the candiduria persists after the catheter change, then patients can be treated with oral fluconazole (Hidalgo, 2014).

Pain may be controlled with OTC paracetamol, but if this is ineffective, stronger analgesia may be required. Co-codamol has been found to be effective, plus stopping taking paracetamol.

[123] Smaller patches of similar-appearing rash to the main rash

[124] painful or difficult urination

[125] Self-retaining catheter

Injections

Knowing that some folk do their own injections, here are some instructions which might make it easier for you.

What is it?

- An intramuscular (IM) injection is the administration of medication through the cutaneous and subcutaneous layers, into the muscle.
- Solutions up to a volume of 5ml in large muscles, and 2ml in smaller muscles, may be used.
- The IM route is often used for medications that will not irritate soft tissue and can be suitably dissolved.
- The delivery of medication into skeletal muscles, with fewer pain receptors and good blood perfusion, minimises pain.

Giving Medicine By Intramuscular Injection

Supplies

- Medicine
- Syringe
- Filter/injection needles (Sabon et al., 1989) (Becton-Dickinson, 2014).
- Alcohol pad
- Sharps Box, or heavy plastic empty container with a wide mouth and secure cap. Used to put syringe and needle into after the injection is given.

Needle size

Most people inject with needles that are 1--1$\frac{1}{2}$ inches in length, ranging in thickness from 21G or 25G gauge, with a green or blue hub. The higher the gauge number, the smaller/thinner the needle. The 21G needle is 1$\frac{1}{2}$ inch (or 38 mm) long. The higher the number in front, the thinner the needle is; the second number is how long the needle is.

Draw with a green, inject with a blue!

Syringe size

Your syringe should be 1ml-5ml in total volume. B-D, who are "Becton-Dickinson", are a good company from which to buy them, and the Microlance 3 is a good needle (Becton-Dickinson, 2014). Syringes can be bought from Ryvemed http://www.ryvmed.com/syringesneedles.aspx or CalVetSupply http://www.calvetsupply.com/index.asp?PageAction=VIEWCATS&Category=233 Order 3ml syringes with $1\frac{1}{2}$ inch and a 22G needle.

Ampoule opener

Ampoules are dangerous to break open by hand or using a file or protective gauze. When the ampoule head is snapped off, the glass often breaks leaving sharp jagged edges which can cut the user's fingers. Slivers of glass or gauze fibres can also fall into the liquid drug.

The 'Clic Open Ampoule Opener' is easy to use, once you've learnt how to use it that is. It is a handy little gadget which snaps off the top of glass ampoules without leaving jagged edges. It can be used by anyone who needs to administer liquid drugs supplied in ampoules.

Clic-Open uses a tiny tungsten carbide cutter to score the glass before snapping the ampoule open.(Sepha, 2014)

1. Insert the ampoule head into the jaws of the CLIC-OPEN. Holding the ampoule steady, press only the upper jaw with the cutter onto the ampoule neck. Turn lightly to give a 1mm score.
2. Without squeezing the jaws together, but using the lower jaw only as an anchor, break open the ampoule at the score line.
3. Push in the plunger to eject the head of the ampoule into a waste container

Filter needles

You will require 'filter needles' to fill the syringes with. These can be obtained from many places, such as http://www.sepha.com/cl.htm You can order them in the US from here http://www.hcl-intl.com/mall/more.asp?fmmore=7371

Getting ready

1. Wash your hands with soap and water. Clean thoroughly between your fingers and under your nails. Dry your hands.
2. Gather the needed supplies.

Drawing up the medicine into the syringe - vials

1. Check the label on the medicine bottle to make sure the right medicine is used. Check the expiration date on the bottle. Do not use expired medicine. Inspect medication for any discolouration. **Do not** use if discoloured.
2. Remove the cap from the medicine bottle, if it is a new bottle. Clean the top of the bottle each time with an alcohol wipe. Do not touch the top of the bottle after it is cleaned with the alcohol.
3. Attach and / or tighten the needle onto the syringe.
4. Take the needle cap off the needle and place the cap on the table out of your way.
5. Pull back on the end of the plunger. Draw air into the syringe equal to the amount of medicine to be drawn up. Do not touch the plunger or the needle.
6. Insert the needle into the rubber stopper on top of the bottle.
7. Push down on the plunger to push the air into the bottle. Leave the syringe in the bottle.
8. Invert the bottle and syringe so the bottle is on top and the syringe below. Be sure to support the syringe and the bottle so the needle is not bent.
9. Pull down on the plunger allowing the medicine to fill the syringe. Stop at the amount ordered.
10. Check for bubbles in the syringe. If air bubbles are present:
11. Tap the barrel of the syringe with your finger to move any bubbles to the top of the syringe.
12. Push the plunger slightly up to move any air bubbles out of the syringe
13. Pull down on the plunger again and fill the syringe with the correct amount of medicine.
14. Check again for air bubbles and if present, repeat the steps above.
15. Remove the needle from the bottle.
16. Carefully replace the needle cap.
17. Replace the green needle with the blue needle.

Drawing up the medicine into the syringe - ampoules

1. Check the label on the ampoule and box of ampoules to make sure the right medicine is used. Check the expiration date. Do not use expired medicine. Inspect medication for any discolouration. **Do not** use if discoloured.
2. Inspect the glass ampoule for discolouration of contents and any cracks in the glass itself. If OK then clean the neck of the ampoule with the alcohol wipe.
3. Attach and / or tighten the needle onto the syringe.

4 Using your "Ampoule Opener" snap the top of the ampoule off and place the top and the "Ampoule Opener" down where they won't roll off and get trodden on.
5 Take the needle cap off the needle and place the cap on the table out of your way.
6 Insert the needle into the neck of the ampoule.
7 Pull up on the plunger allowing the medicine to fill the syringe. Stop at the amount ordered.
8 Remove the syringe from the ampoule, and point the needle upwards.
9 Check for bubbles in the syringe. If air bubbles are present -
10 Tap the barrel of the syringe with your finger to move any bubbles to the top of the syringe.
11 Push the plunger slightly up to move any air bubbles out of the syringe
12 Pull down on the plunger again and draw air into the syringe.
13 Check again for air bubbles and if present, repeat the steps above.
14 Carefully replace the needle cap.
15 Replace the green needle with the blue needle.

Selecting the site for injection

- Carefully select the site for injection so that major blood vessels and nerves are avoided.
- Use different sides to prevent repeated injections in the same area. Change sites with each injection.
- Do not use areas that are bruised, tender, scarred from surgeries or injury, or swollen.

Buttock (Gluteus Medius) site for IM injection

1. Find the **trochanter**. It is the knobby top portion of the long bone in your upper leg (femur). It is the size of a golf ball.
2. Find the **posterior iliac crest**. Many people have "dimples" over this bone.
3. Draw an imaginary line between the two bones.
4. After locating the centre of the imaginary line, find a point one inch toward your head. This is where (X) you will put the needle in.
5. Stretch the skin tight.
6. Hold the syringe like a pencil or dart. Insert the needle at a right angle to your skin (90°).

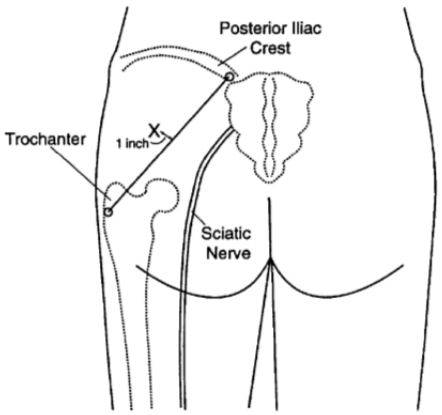

Figure 17.5 – X marks the injection site

Giving the IM injection

1. Choose the site you will use for the injection.
2. Clean your skin with an alcohol pad in a circular motion. Let the site dry for 30 seconds.
3. The needle should be long enough to penetrate the muscle and still leave at least one third of its length exposed to facilitate its removal should it snap from the hub.
4. 21 (green) and 23 (blue) gauge needles are most commonly used.
5. Pull the needle cap straight off the needle (do not twist). Set the cap aside.
6. Hold the syringe like a dart or pencil. Stretch the skin at the injection site. If you are thin, you may need to pinch the tissue using your thumb and index finger. Be careful not to touch the injection site itself.
7. Insert the needle at a 90°angle into the prepared injection site. Use a quick dart-like motion. The quicker you insert the needle, the less discomfort.
8. Release the skin. Hold onto the syringe so that it will not move. Pull back on the plunger to check for blood in the syringe. Remove the needle if you see blood in the syringe.
9. Inject the medicine by pushing down on the plunger at a moderate rate. Be sure to inject all the medicine in the syringe.

10 Where appropriate a 'Z-track' technique can be used. By stretching the skin downwards or sideways at the site before injection the track is closed when the skin is released, preventing leakage.

11 Hold the alcohol wipe near the injection site. Remove the needle and quickly press the alcohol pad onto the site. Hold the pad tightly for a minute. Check the area for any redness, bleeding or bruising. If bleeding occurs, wipe it off. It may be necessary to apply a elastoplast to the site.

12 Do not rub the site of the injection as you will increase the chance of leakage or bleeding.

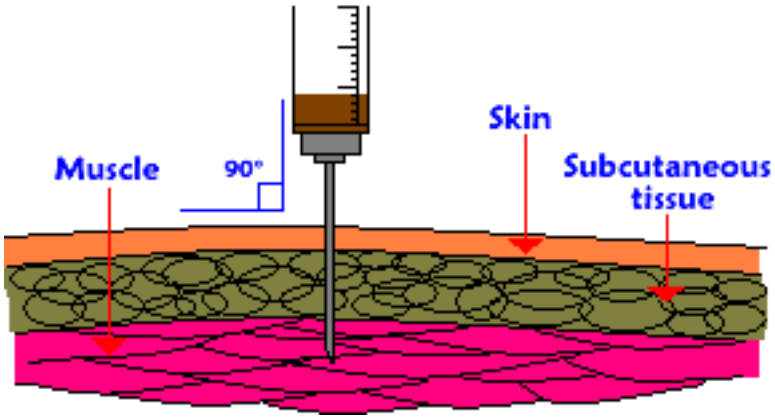

Figure 17.6 – This shows how to insert the needle

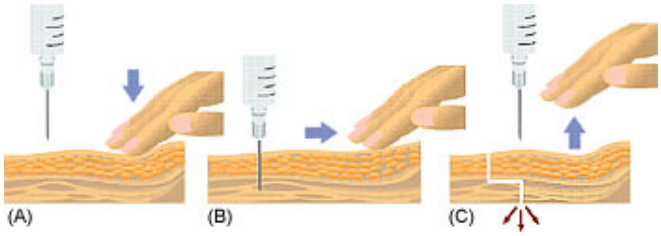

Figure 17.7 – This shows how the "Z-tracking" technique works

Safe disposal of sharps

- Immediately after use
- Never resheath or bend needles
- If possible, dispose of needle and syringe as a single unit
- Dont overfill sharps boxes

Discussion about IM injections

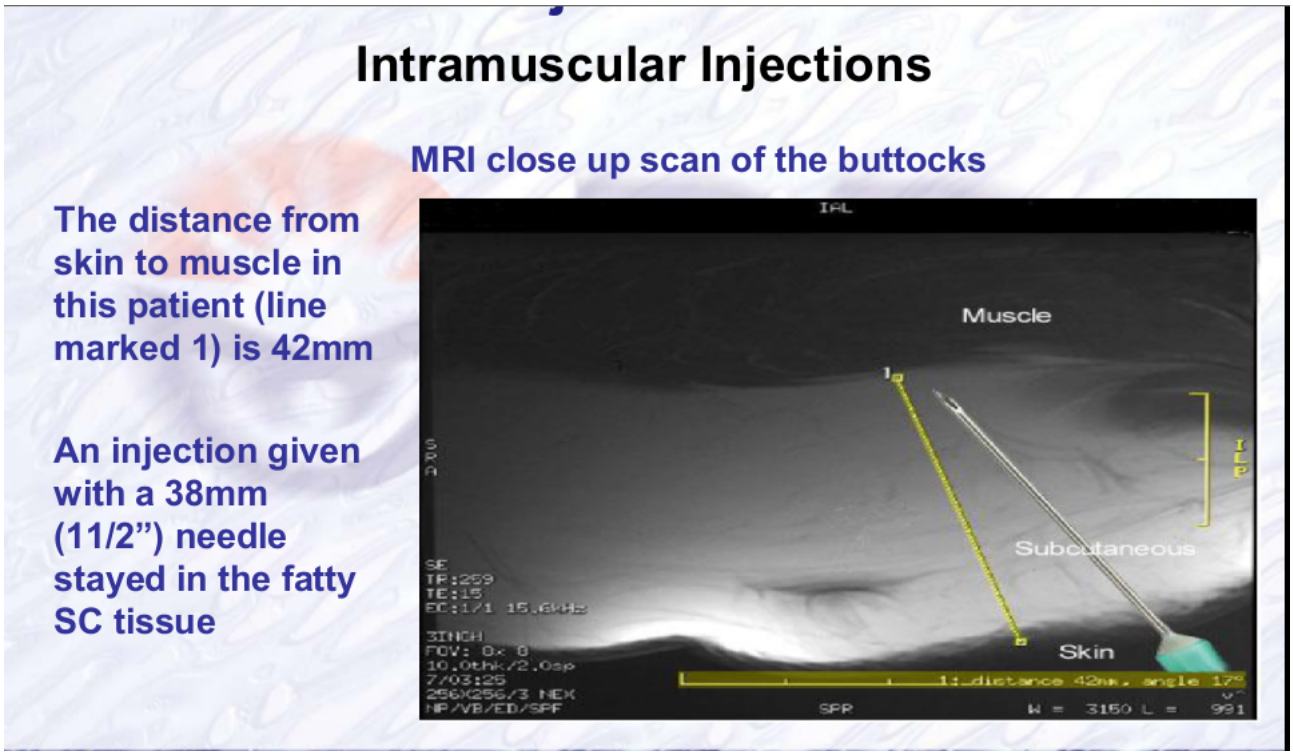

Figure 17.8 – A MRI scan of an IM injection

Recent research is suggesting using what is called the "Double Cross" method (unknown, 2014f).

- Divide the buttock with an imaginary cross
- Then divide the upper outer quadrant by another imaginary cross
- Inject into the upper outer quadrant of the upper outer quadrant

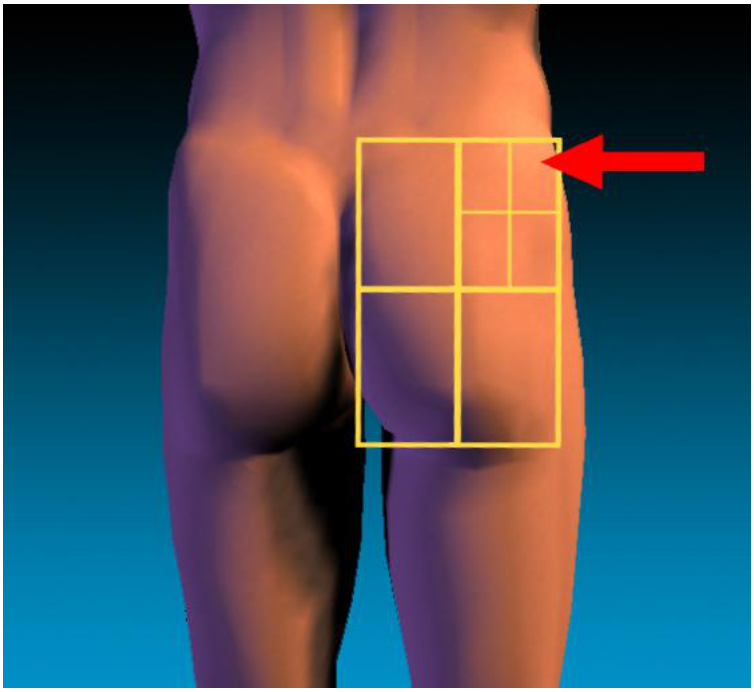

Figure 17.9 – This shows the site of the "Double Cross"

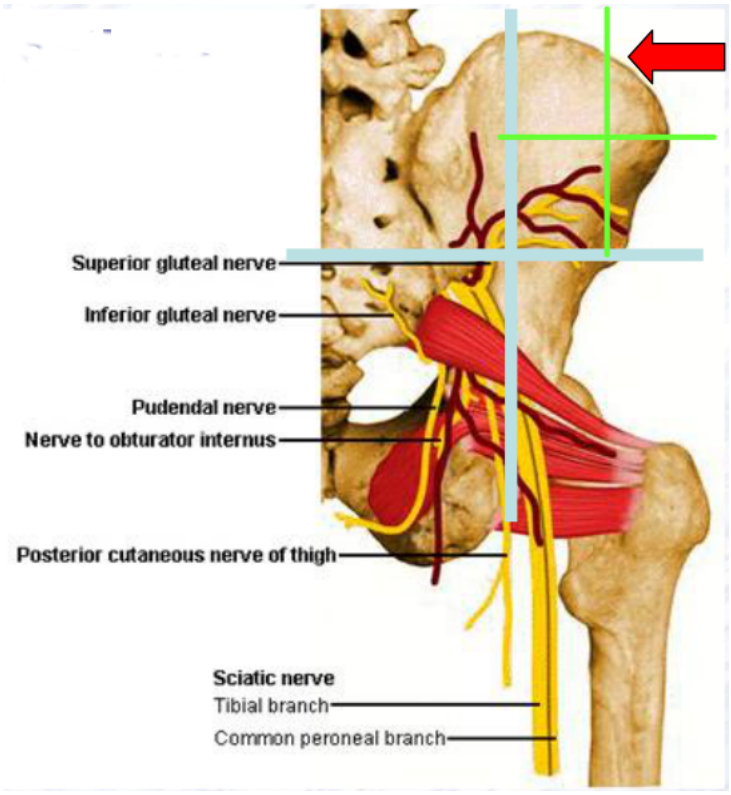

Figure 17.10 – The underlying anatomy of the "Double Cross"

Nursing implications

- IM injections can be an unpleasant experience for patients, making appropriate explanation and psychological support vital.
- Look at the skin to ensure there are no signs of infection, damage or poor blood supply. There must also be consideration of muscle mass to ensure patient safety and comfort.
- Where frequent IM injections are given the injection sites should be rotated to prevent damage, protect the administration route and maximise patient comfort. The use of a rotation chart may be considered.
- Oedematous limbs will not absorb medication as effectively as well-perfused limbs.
- The nurse must have a good knowledge of the appropriate technique and anatomy to avoid any damage to surrounding structures.
- IM injections should be avoided in patients with thrombocytopenia[126], in whom clotting problems may occur.
- Caution must be exercised to ensure that the medication is suitable for IM injection.

[126] a decreased number of platelets

Glass contamination in intramuscular injections

Research (Preston and Hegadoren, 2004) has shown that glass contamination may occur on opening of single dose glass ampoules, with possible subvisible particles of glass, rubber, fibre and other residues. The infusion of these particles has been linked with phlebitis[127], vascular occlusion[128] and subsequent embolism, formation of granulomas[129] and septicaemia[130] (Sabon et al., 1989). So therefore it is recommended to use a 'filler needle' to draw up the medication, then substitute it for an 'injecting needle' to do the actual injection with(Preston and Hegadoren, 2004)(Heiss-Harris and Verklan, 2005). B-D recommend a blunt 18G x $1\frac{1}{2}$ inch needle as your 'filler' needle (Becton-Dickinson, 2014).

What are the possible side-effects of estradiol injection?

Get emergency medical help if you have any of these signs of an allergic reaction - **hives**, **difficulty breathing**, **swelling of your face, lips, tongue, or throat** (drugs.com, 2014c).

[127] the inflammation of a vein

[128] blockage of a blood vessel, usually with a clot

[129] inflammation found in many diseases

[130] the presence of microorganisms or their toxins in the blood of a potentially fatal whole-body inflammation

Kegel exercises

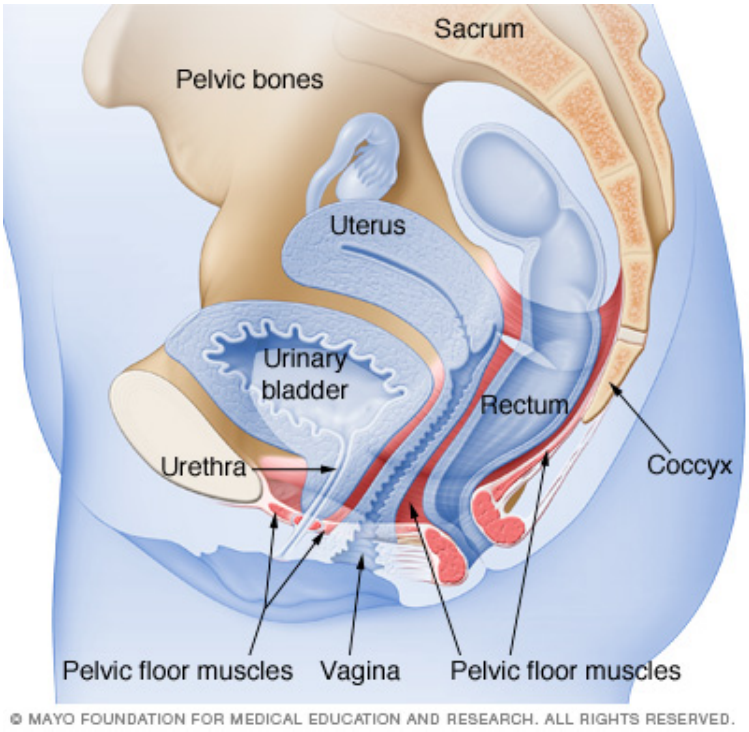

Figure 17.11 – Female pelvic floor muscles

Kegel exercises strengthen the pelvic floor muscles, which support the bladder, small intestine and rectum. You can do Kegel exercises, also known as pelvic floor muscle training, or pelvic floor exercises, discreetly just about anytime.

Start by understanding what Kegel exercises can do for you - then follow step-by-step instructions for contracting and relaxing your pelvic floor muscles (M. C. Staff, 2012).

Why Kegel exercises matter

Many factors can weaken your pelvic floor muscles, including pregnancy, childbirth, surgery, aging and being overweight.

You might benefit from doing Kegel exercises if you -

- Leak a few drops of urine while sneezing, laughing or coughing
- Have a strong, sudden urge to urinate just before losing a large amount of urine (urinary incontinence)
- Leak stool (faecal incontinence)

Kegel exercises can be done during pregnancy or after childbirth to try to prevent urinary incontinence. Kegel exercises - along with counselling and sex therapy - might also be helpful for women who have persistent difficulty reaching orgasm.

Keep in mind that Kegel exercises are less helpful for women who have severe urine leakage when they sneeze, cough or laugh. Also, Kegel exercises aren't helpful for women who unexpectedly leak small amounts of urine due to a full bladder (overflow incontinence) (M. C. Staff, 2012).

How to do Kegel exercises

It takes diligence to identify your pelvic floor muscles and learn how to contract and relax them. Here are some pointers -

- **Find the right muscles** - To identify your pelvic floor muscles, stop urination in midstream. If you succeed, you've got the right muscles.
- **Perfect your technique** - Once you've identified your pelvic floor muscles, empty your bladder and lie on your back. Tighten your pelvic floor muscles, hold the contraction for five seconds, and then relax for five seconds. Try it four or five times in a row. Work up to keeping the muscles contracted for 10 seconds at a time, relaxing for 10 seconds between contractions.
- **Maintain your focus** - For best results, focus on tightening only your pelvic floor muscles. Be careful not to flex the muscles in your abdomen, thighs or buttocks. Avoid holding your breath. Instead, breathe freely during the exercises.
- **Repeat 3 times a day** - Aim for at least three sets of 10 repetitions a day.

Don't make a habit of using Kegel exercises to start and stop your urine stream. Doing Kegel exercises while emptying your bladder can actually weaken the muscles, as well as lead to incomplete emptying of the bladder - which increases the risk of a urinary tract infection.

When to do your Kegels

Make Kegel exercises part of your daily routine. You can do Kegel exercises discreetly just about anytime, whether you're sitting at your desk or relaxing on the couch. You might make a practice of fitting in a set every time you do a routine task, such as checking email (M. C. Staff, 2012).

Over one-third of women start out squeezing the wrong muscles. Therefore, it is helpful to find the correct technique. You can check yourself by placing a finger in your vagina and squeezing around it. When you feel pressure around your finger, you are using the correct muscle. Try to keep everything relaxed except the muscles right around the vagina. At the same time, do not bear down or squeeze your thigh, back or abdominal muscles. And breathe slowly and deeply. At first you can do the exercises with your knees together (lying or sitting). Be sure you are doing them correctly before you start. They should be done for five minutes twice a day. You should squeeze

the muscle for a count of four and relax for a count of four. At first, you may not be able to do the exercises for a whole five minutes or hold the squeeze for a count of four. With practice it will become easier as the muscles get stronger (wikipedia, 2014c).

When you're having trouble

If you're having trouble doing Kegel exercises, don't be embarrassed to ask for help. Your doctor or other health care provider can give you important feedback so that you learn to isolate and exercise the correct muscles.

In some cases, biofeedback training might help. During a biofeedback session, your doctor or other health care provider inserts a small probe into your vagina or rectum. As you relax and contract your pelvic floor muscles, a monitor will measure and display your pelvic floor activity (M. C. Staff, 2012)

When to expect results

If you do Kegel exercises regularly, you can expect results - such as less frequent urine leakage - within about a few months. For continued benefits, make Kegel exercises a permanent part of your daily routine (M. C. Staff, 2012).

Warnings

- Always do kegels with an empty bladder. Doing kegels with a full bladder can weaken your pelvic floor and increases your risk of contracting a urinary tract infection.
- Don't do Kegels while using the bathroom, except to locate the muscles initially. Interrupting urine flow can result in urinary tract infections (various, 2014). Please also see Urinary Tract Infections - UTI's

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Lactation

Some people have experienced lactation[131] on stopping their hormones prior to surgery. This appears to be caused by a raise in prolactin levels which thereby stimulates the milk glands to produce colostrum and then milk.

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[131] their breasts discharging milk

Leg Cramps

I recently had several nights of extremely painful cramps in my calves and feet, and knowing that other folks have had similar ones too, I thought this might be relevant for them.

Cramp[132] in the legs is common, especially at night, but it may also occur after exercise. Only occasionally is it a symptom of some disease, in particular, salt depletion, muscle ischaemia[133], or myopathy[134]. In my case it was due to a lack of salt and not drinking enough fluids, which was easily remedied by increasing the amount of salt that I used at mealtimes by a small amount, perhaps no more than one teaspoonful extra per day, and obviously drinking more water.

Liver damage

The liver is the largest organ inside your body and it performs over 500 functions and is the primary "detox" center of your body, seperating the good stuff from the bad stuff and then passing on the good stuff to the rest of the body while sending the bad stuff to the gall bladder and kidneys for further processing and disposal (that is a very simplistic version of the process, by the way). And that literally means everything that winds up in your blood or stomach - alcohol, pesticides on foods you eat, chemicals absorbed through your skin, fumes inhaled, etc. We live in a very toxic world, and your liver is putting in a lot of overtime just trying to deal with it. Even things we normally don't think of as "toxic" can be if the liver is overworked or malfunctioning. A high protein diet can, for example, lead to unwanted ammonia in your bloodstream (it is a byproduct of metabolising proteins). Too much ammonia in the blood can lead to dementia, among other things. Okay, now that the scare is on and you're ready to live in a bubble, you should also know that the liver can do it's job even when 80% of it's tissues are damaged. That doesn't mean you shouldn't care what you do to it, though.

As part of its "detox duties" it also has to deal with a number of hormones. For example, it is supposed to clear out extra insulin. If it doesn't, the insulin remains in circulation and continues to do its job of lowering blood sugar. Failure to dispose of adrenaline (the "fight" or"flight" hormone) after it has outlived its usefulness may lead to chronic irritability and temper explosions.

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[132] a painful muscles spasm

[133] Insufficient blood supply for the need of a part of the body, usually as a result of a disease of the blood vessels supplying that part (medical-dictionary, 2014)

[134] any disease of muscle (medical-dictionary, 2014)

All products absorbed through digestion initially pass through the liver. This is why ingested hormones can potentially damage the liver. The liver is supposed to take care of "excess" hormone production. Ideally, if you are trying to infuse your system with hormones, you want them to make a complete circuit through your body, bonding to receptors along the way, before the blood gets to the liver. Otherwise there are just too many hormones for the liver to deal with. But it is also important to consider which hormones actually do damage. It is well-documented that synthetic anabolic steroids or testosterone derivitives damage the liver. I had difficulty understanding exactly how they damage it, but I gathered that the enzymes employed in breaking down the "natural" hormones into harmless compounds often "accidently" break synthetics down into toxic substances that cause cellular-level damage. But what about oestrogen? In some cases, even as little as two or three weeks of use have been documented to ruin the ability of the liver to detoxify natural oestrogen. The livers of women on B vitamin/protein deficient diets may have difficulty metabolising oestrogen to non-toxic estriol, leaving it instead in the form of liver toxic estradiol. Estradiol is the form associated with hyper emotional states including explosive temper and obsessive-compulsive tendencies (essentially, PMS).

The main problem with taking hormones orally is that the hormones are passed into the liver as part of the process of digestion. Not only will some of the hormones be destroyed in the process, the liver is designed to deal with small amounts of "left overs" and will be inundated by the large amount of hormones - some of which will likely be liver-toxic and cause cellular damage to the organ. Whatever the liver can't handle will ultimately be washed out the "downstream" side of the liver into the cardiovascular circuit where the hormones will be pushed all around the body, binding to receptors as they go, before the blood returns to the liver. The problem with this scenario is that it is the reverse of the process for hormones produced within the body.

So, obviously, if you are going to have oestrogen passing through your liver before it gets into the rest of your bloodstream, you'd avoid liver-toxic (i.e., liver damaging) effects if the hormones were "*estriol*" in form instead of "*estradiol*". Estriol is available and is also the main component of a supplement knowns as "Tri-Est" (Triple Estrogen) which is 80% Estriol, 10% Estradiol, and 10% Estrone. M2F Transsexuals report unsatisfactory feminization from estriol, as it is a relatively weak cell stimulator (i.e., it doesn't stimulate the growth of breast tissue as much as estradiol or estrone).

So how much is too much? That's unknown and would vary person to person and also depend on the concentrations of consumed. One thing you can do to mitigate this problem is to take estradiol transdermally (patch, lotion, or gel), sublingually (under the tongue), nasally (there is a spray

available), or by intramuscular injection. All of those methods allow the hormone to enter the bloodstream first which means there is better efficiency and only waste product hormones will go through the liver in much smaller amounts.

I have had great difficulty in determining exactly how damaging elevated estradiol levels may be to one's liver. A recent study published in "Oncology: International Journal of Cancer Research and Treatment", in a hospital-based case-controlled study of male liver cancer patients in Greece which looked specifically at the phenomena of elevated estradiol levels in such patients. It looked at 98 cancer patients and 111 control cases. It had been claimed that the elevated estradiol levels may have been responsible for the liver damage, however that claim was not supported by this study. When the researchers compensated for the fact that the cancer patients' livers were compromised, and therefore incapable of dealing with steroid hormones efficiently, the conclusion was that the elevated estradiol levels were a consequence of the liver damage, not the cause of it (Kuper et al., 2001).

Part of the difficulty in determining what the actual liver damage risk is posed by estradiol is that there are too many variables to simply say you have X% chance of harming your liver if you take oral estradiol. If your liver is already compromised by pre-existing liver disease, or you have a predisposition to liver-related complications, or if you mega-dose (as mentioned above) thus consuming "toxic" levels, you're obviously going to have a far greater risk than someone without such factors (hemingways, 2004c).

See the section on Progesterone below for liver toxicity information regarding that hormone.

Male pattern baldness

Male pattern baldness, or androgenic alopecia, typically affects the front and top of the scalp first where the most genetically-susceptible hair follicles reside. DHT is the primary contributing factor in male pattern baldness. Female hair loss can be very complicated and DHT could be just one of the possible causes. In women DHT is influenced by a decrease in oestrogen and hair loss tends to result in thinning, rather than complete balding.

DHT inhibits and reduces the proper growth of hair in the follicles in a process called 'miniaturisation'. "Miniaturisation" affects genetically-susceptible hair follicles resulting in lighter, finer hairs. DHT attaches itself to receptor cells of the part of these follicles called dermal papillas (the

root), preventing the necessary nourishment for the hair getting through for proper growth. DHT causes the hair follicles to shrink. The growing "anagen" stage of the hair is shortened and the resting "telogen" stage is extended. Eventually these hairs stop growing.

Androgenetic alopecia (AGA; male-pattern baldness) is a hereditary and androgen-dependent progressive thinning of the scalp hair that follows a defined pattern (Stanczyk, 2006). While the genetic involvement is pronounced but poorly understood, major advances have been achieved in understanding the principal elements of androgen metabolism that are involved. DHT may be related to baldness. High concentrations of 5 alpha-reductase have been found in frontal scalp and genital skin and androgen-dependent processes are predominantly due to the binding of DHT to the androgen receptor (AR). Since the clinical success of treatment of AGA with modulators of androgen metabolism or hair growth promoters is limited, sustained microscopic follicular inflammation with connective tissue remodeling, eventually resulting in permanent hair loss, is considered a possible cofactor in the complex etiology of AGA (mayomedical, 2016).

Male pregnancy

Male pregnancy is the carrying of one or more embryos or foetuses by the male of any species inside their bodies. The majority of all pregnancies in the animal kingdom are carried by female organisms. In most heterogamous species[135], the males produce the spermatazoa[136] and rarely host the zygote[137].

Speculation on inducing pregnancy in men

British physician Robert Winston speculates that it may be possible to surgically induce abdominal ectopic pregnancy in men (unknown, 1999). In his book **"The IVF Revolution"**, Winston speculates that an embryo could be implanted in a man's abdomen – with the placenta attached to an internal organ such as the bowel – and that the baby would later be delivered by Caesarean section. However, other experts expressed great concerns about the safety of such a procedure.

[135] In reproductive biology, heterogamy or heterogamous is often used as a synonym of heterogametic, meaning the presence of two unlike chromosomes in a sex. For example, XY males and ZW females are called the heterogamous sex

[136] one of the minute, usually actively motile gametes in semen, which serve to fertilize the ovum; a mature male reproductive cell

[137] the cell produced by the union of two gametes, before it undergoes cleavage

Pregnancy among transsexual and intersex people

Some intersex[138] people with XY chromosomes develop entirely female bodies and, if the individual develops a uterus, in-vitro fertilization is possible (Almonacid, 2012a).

Some female-to-male transsexuals who interrupt their hormone treatments can become pregnant, while still identifying and living as male - this is possible for individuals who still have functioning ovaries. One example is Matt Rice, a transman who is the former partner of writer Patrick Califia. Rice bore a child by artificial insemination. Although the individual is genetically and physiologically female, from an identity standpoint this may be considered by some a "male pregnancy" (Almonacid, 2012b).

Measuring Your Transition

While undergoing a regimen of hormonal feminization, keeping a diary or log of physical progress and medication/hormone usage can be very helpful in making the most of your physical transition. It not only helps you to remember the milestones, but also helps your medical team too.

Taking Body Measurements

Body size measurements should be taken on approximately a monthly basis. For best results, use a cloth (tailor's) tape measure. Keep the tape level and take measurements using the same areas depicted by the model shown below. Measurements should be taken standing straight with your body remaining relaxed, and drawing the tape until it is barely snug. Take measurements nude, or wearing a slip or nightwear made of a thin material. Keep in mind that maintaining consistency in the way that you take these measurements will assure your changing body is accurately represented in your measurements.

- Measure under the armpits, above the area of the breasts.
- Measure around the widest part of the back, straight across the fullest part of the bust. (See below for details on how to measure the breast)
- Measure under the area of the breast.
- Measure your waist approximately one inch above the navel. This is the female natural waistline, the smallest part of her waist. During successful hormonal feminization, this will become your natural waistline.
- Measure around the fullest part of your hips. Put your thumbs at your natural waist and rest your hands on your hips. The tips of your fingers should be the area at which to take the hip measurement.

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[138] having the biological characteristics of both the male and female sexes

- Measure at a point just above the pubic area and over the area of your buttocks.
- Measure the fullest area of your left upper thigh.

Breast Measurement

The main measurement area of concern is the breast. Often the medical literature as well as physicians not familiar with transgender practice will suggest measuring the breast itself. This technique calls for measuring each breast – taking a measurement of the breast along the horizontal and vertical axes. While treating the breast as a hemisphere and taking measurements accordingly works well for the genetic female, it offers little for the transitioning female. Let's take a look at why -

For the genetic female, no de-virulizing takes place. The muscles in the upper body do not diminish as they do in the transgender woman and breast growth is normally significant. So for the genetic female, taking a measurement of the breast, itself, is the most telling. **But, this traditional technique is not very useful for transwomen**.

For the transwoman, breast growth occurs along with the diminishment of upper body muscle mass. So the traditional technique which measures only the breast area does not take into account the competing forces of breast growth and decreasing upper body mass, and provides little in the way of useful information.

For the most accurate and reliable means of measuring the breast area for the transgender woman, we recommend measuring the breasts and the surrounding upper body area as a single measurement, as shown above.

Look for the Differences

Often during transition, the breast area values (numbers) do not show much change. At first glance, one may feel that not much change is happening. **Usually, more changes are occurring than you realize**. Keep in mind that your muscles are diminishing as fat is redistributing itself towards a normal female form. The change in breast size is seen by looking at the numeric differences between the chest, bust and rib cage measurements. Additionally, the overall decrease in one's frame size (size decrease due to overall loss of muscle mass) is seen in these measurements.

The true degree of breast growth in the transgendered woman is often hidden by the fact that the chest wall diminishes as quickly as the breasts enlarge. Therefore, the overall breast measurement may stay the same even though it has enlarged by an inch or more because the chest wall has diminished by that amount.

Medroxyprogesterone Acetate and osteoporosis

Medroxyprogesterone may cause osteoporosis especially when used over long periods of time. This bone loss may not be reversible. Do not use this medication for longer than 2 years. Talk with your doctor about your specific risk of bone loss (drugs.com, 2014c).

Conflicting data concerning the effects of medroxyprogesterone on bone mineral density have been reported.

In one study, women 25 to 51 years of age receiving medroxyprogesterone 150 mg intramuscularly every three months for five or more years for long-term contraception had a reduction in bone mineral density compared with premenopausal controls. However, bone mineral density in the treatment group was still significantly greater than that observed in postmenopausal controls.

A study of 200 women who received medroxyprogesterone 150 mg intramuscularly every three months for a median duration of 12 years (range 2 to 26 years) reported that bone density was significantly reduced in medroxyprogesterone users. However, bone mineral density in women starting depot medroxyprogesterone after the age of 20 years and using it for 15 or fewer years was greater than the remainder of the cohort.

A study to determine the potential for postmenopausal fracture due to residual effects of depot medroxyprogesterone in former users reported the risk to be small and unlikely to have substantial impact in postmenopausal women. No significant differences in bone density were found, however, women who had used depot medroxyprogesterone for >2 years had a trend toward lower bone densities.

Bone density in 185 women receiving long-term depot medroxyprogesterone for a mean of 5 years (range of 1–16 years) was only minimally below the normal population despite decreased oestrogen levels (drugs.com, 2014c).

Memory enhancing effects of oestrogen

The association between administered oestrogen and performance on verbal memory and other cognitive tasks was examined. Male-to-female transsexuals undergoing oestrogen treatment for sex reassignment (n = 29) scored higher on "Paired Associate Learning" (PAL) compared to a similar transsexual control group, awaiting oestrogen treatment (n = 30) (P ą 0.05). No differences between groups receiving and not receiving oestrogen were detected on a control memory task (Digit Span) or on other cognitive tasks including "Mental Rotations and Controlled Associations". There were no group differences in age. Group differences in mood or in general intellectual ability also did not explain the findings. Results

suggest a specific influence of oestrogen in men on verbal memory tasks, similar to that seen in prior studies of women. They are discussed in terms of differential processing demands of the two memory tasks and possible differences between oestrogenic influences on "Mental Rotations and Controlled Associations" in men versus women (Miles et al., 1988).

Oestrogen treatments may sharpen mental performance in women with certain medical conditions, but researchers at the University of Florida suggest that recharging a naturally occurring oestrogen receptor in the brain may also clear cognitive cobwebs(unknown, 2013c). Oestrogen also appears to protect against Alzheimer's disease and dementia. Also see Oestrogen and Alzheimer's Disease.

Menopause

Female menopause

The rise and fall of women's sex hormones

Question	Oestrogen	Progesterone	Testosterone
What does this hormone do?	• Stimulates growth of breast tissue • Maintains vaginal blood flow and lubrication • Causes lining of the uterus to thicken during the menstrual cycle • Keeps vaginal lining elastic • Many other functions, including preserving bone	Prepares lining of the uterus for a fertilised egg and helps maintain early pregnancy	Although known as the "male" hormone, testosterone is also important to womens sexual health: • Plays a key role in womens oestrogen production • Contributes to libido • May help maintain bone and muscle mass

Question	Oestrogen	Progesterone	Testosterone
How do menopause and age affect this hormone?	During perimenopause, levels fluctuate and become unpredictable. Eventually, production falls to a very low level	Production stops during menstrual cycles when there is no ovulation and after final menstrual period	• Levels peak in a woman's 20s and decline slowly thereafter. By menopause, level is at half of its peak. • Ovaries continue to make testosterone even after oestrogen production stops • Testosterone production from adrenal glands also declines with aging but continues after menopause
What symptoms may result at midlife?	• High levels can result in bloating, breast tenderness, heavy bleeding • Low levels can result in hot flashes, night sweats, palpitations, headaches, insomnia, fatigue, bone loss, vaginal dryness	Lack of progesterone can cause periods to become irregular, heavier, and longer during perimenopause	Effects of testosterone decline are uncertain (menopause.org, 2010)

Table 17.19 – The rise and fall of women's sex hormones

Male menopause

Male menopause is a term used to describe a stage in a male's life where his testosterone levels start to decline. During this time, men experience many symptoms similar to those of menopausal women, such as depression, weight gain, and loss of libido. As male menopause is a much more gradual period of change than in women, some medical professionals will instead use the terms 'andropause', or 'testosterone deficiency' to describe it.

Unlike female menopause, not all males experience male menopause, tending to more affect men with pre-existing medical conditions such as heart disease or obesity. However, like female menopause, there are ways to manage symptoms experienced by lowered testosterone, and maintain a healthy and happy lifestyle.

Although 'andropause' is the more correct term for this stage in male life, 'male menopause' is more commonly used. Those who have researched the changes that occur in men, and men at midlife recognise that both men and women experience many of the same symptoms, including the following -

- Decreased potency (inability to obtain and maintain an erection),
- Reduced libido (sexual desire),
- Increased irritability and anger,
- Fatigue and loss of energy,
- Aches, pains, and stiffness,
- Depression with symptoms that differ from those seen in women,
- Night sweats or 'hot flashes',
- Weight gain (healthspan, 2016a).

> "Male menopause begins with hormonal, physiological, and chemical changes that occur in all men generally between the ages of forty and fifty-five, though it can occur as early as thirty-five, or as late as sixty-five. These changes affect all aspects of a mans life. Male menopause is, thus, a physical condition with psychological, interpersonal, sexual, social, and spiritual dimensions."

The scientific basis for andropause, or male menopause is becoming more widely accepted. Marc Blackman, M.D. formerly chief of endocrinology and metabolism at Johns Hopkins Medical Center said:

> "The male menopause is a real phenomenon, and it does similar things to men as menopause does to women, although less commonly, and to a lesser extent."

Treatment options

The first step in seeking treatment is to get an accurate diagnosis. If there is any indication that a man is experiencing symptoms of male menopause, you can follow up with additional blood tests to rule out other causes, as well as assess testosterone and other hormone levels.

Treatments that may be used include the following -

- Changes of diet,
- Increased exercise,
- Counselling to address issues of sexuality, intimacy, and emotional support,
- Help with irritability, anger, and depression,
- Exploring issues of career, and what is perceived as a 'life's calling',
- Dealing with increasing stress levels,
- Hormone balance and enhancement

Although it is important to work with men via all seven of these approaches, many clinicians find that diet and exercise are particularly crucial. Even healthy diets can be missing key nutrients that are necessary for health and well-being. A sedentary lifestyle increases hormonal disruptions, and can contribute to your experience of any menopausal symptoms (healthspan, 2016a).

Male menopause, also known as 'andropause' is a very real medical condition, contrary to what some people may believe, that can be experienced by men anytime from their mid-twenties. Andropause originates from a gradual decline in testosterone over approximately thirty years.

This hormonal imbalance can lead to a number of symptoms, one of which being a loss of libido. This is a very common symptom experienced by men going through andropause, and is sometimes a difficult one to talk about, as there tends to be a great amount of pressure on men to conform to the normal stereotype of having a high sex drive, and sometimes pre-conceived ideas that this is something that males do not experience issues with as much as women do.

Why do men experience low libido?

Men going through andropause experience many symptoms such as -

- fatigue,
- depression,
- irritability,
- hot flushes,
- loss of muscle mass, and
- low libido.

Men normally experience a low libido due to a severe testosterone deficiency, which may also be accompanied by problems getting or maintaining an erection. More specifically, testosterone deficiency can happen when there is a signalling issue between the brain and testes, which can cause a drop in the amount of testosterone that is produced. It can be due to the brain sensing there is too much testosterone in the body, and signalling the testes to cut production. Another reason testosterone deficiency may occur is that the body simply can't produce enough testosterone due to a defect in the testes.

How diet can help

It would be beneficial to limit your intake of sugar, caffeine, white flour, and excessively starchy carbohydrates, as these can lead to hormonal imbalances. Diets high in omega 3 (oily fish, flaxseed and walnuts), organic foods, lean animal and plant proteins, whole grains and antioxidants (fruits and vegetables) and other healthy fats (nuts, seeds, avocados, coconut oil, olive oil, organic grass fed meat and organic butter) are generally beneficial for hormonal balance, as these are high in the vitamins and minerals needed to balance hormonal levels.

The best foods to increase to help testosterone production are foods containing zinc (lamb, seafood, nuts and seeds), vitamin D (fish, eggs and dairy), vitamin C (fruits and vegetables), and B vitamins (wholegrains, vegetables, eggs and meat).

Supplements for increasing libido

Fenugreek - Fenugreek may increase sexual arousal, testosterone levels, and enhance athletic performance in men. It is believed the main mechanism behind fenugreek and its ability to increase libido is via two enzymes called aromatase and 5-reductase, which modify cholesterol in the production of testosterone. The recommended dose for fenugreek is 500mg per day.

Ginseng (Korean) - This herb can work to increase testosterone levels when they are too low, due to chemical compounds in the ginseng plant called 'saponins', which may have an effect on sexual performance, and a man's ability to get and maintain erections. This increase in testosterone may lead to an increase in libido also. The recommended dose for this herb to increase libido would be 1,000mg three times a day.

L-arginine - As this herb helps to increase blood flow and oxygen throughout the body, especially blood flow to the penis, it thus increases endurance and sexual performance. A dose beneficial for andropausal males would be a minimum of 240mg per day, for at least two months.

Gingko biloba - Gingko biloba is thought to increase blood flow to the genital area, which supports obtaining and getting an erection. It also thought to increase testosterone levels in the body. The optimal dose for gingko to increase testosterone levels would be between 60-120mg per day.

Zinc - Adequate zinc is vital for hormonal balance and libido. Without zinc the pituitary gland cannot release the hormones that stimulate the testes to produce testosterone. Zinc also helps to minimise irritability, depression and sleep issues, which may in turn influence libido. A good dose is 25 mg three times daily of zinc citrate or picolinate.

Lifestyle changes

Reducing stress is important as this can decrease testosterone levels, and also have an effect on libido. It can become a vicious cycle when you are feeling pressure to perform, which makes you more stressed. Also low testosterone may lead to a low mood in itself, so this will exacerbate things further. Practising meditation, yoga or doing relaxation exercises, or even having a relaxing bath, massage, or listening to some soothing music may help to combat stress.

Resistance training that helps to increase muscle mass will help to increase testosterone levels, as does high intensity exercise. Exercise also has a positive effect on mood due to its effect on serotonin and endorphin levels in the brain, which are responsible for feelings of happiness, and may have an effect on libido, too, due to increased blood flow to your organs, and regulation of the stress hormone cortisol, which can help balance testosterone levels.

You should also minimise your use of household cleaning products and toiletries containing chemicals such as parabens and aluminium. Reduce the amount of time you spend around electromagnetic equipment such as mobile phones and wireless computers, as these can cause an imbalance on a cellular level and disrupt hormones.

Please check with your GP before taking any supplements, especially if you are on any medication, due to risk of a contraindication with herbs such as black cohosh, dong quai, and gingko biloba, which should be avoided in some cases (healthspan, 2016b).

Menopausal symptoms

I've been asked what are menopausal symptoms, so, these are what you may feel when your hormone dosage is too low. If you get one or two of these then you need to discuss with your prescribing doctor to get an increase in your hormone medication.

- hot flushes,
- emotional volatility,
- breast shrinkage,
- libido discomfort including morning erections for pre-ops,
- facial hair growth.

For contrast here are the menopausal symptoms which may occur in women -

Hot flashes - Hot flashes are the most common symptom of menopause. According to some studies, hot flashes occur in as many as 75% of perimenopausal women. Hot flash symptoms vary among women. Commonly, a hot flash is a feeling of warmth that spreads over the body, lasting from around 30 seconds to a few minutes. Flushed (reddened) skin, palpitations (feeling a strong heartbeat), and sweating often accompany hot flashes. Hot flashes often increase skin temperature and pulse, and they can cause insomnia, or sleeplessness. Hot flashes usually last 2 to 3 years, but many women can experience them for up to 5 years or longer. An even smaller percentage may have them for more than 15 years.

- Urinary incontinence and burning on urination

Vaginal changes - Because oestrogen affects the vaginal lining, peri-menopausal women may also have pain during intercourse and may note a change in vaginal discharge.

Breast changes - Menopause may cause changes in the shape of the breasts.

- Thinning of the skin

Bone loss - Rapid bone loss is common during the perimenopausal years. Most women reach their peak bone density when aged 25 to 30 years. After that, bone loss averages 0.13% per year. During perimenopause, bone loss accelerates to about a 3% loss per year. Later, it drops off to about a 2% loss per year. No pain is usually associated with bone loss. However, bone loss can cause osteoporosis, a condition that increases the risk of bone fractures. These fractures can be intensely painful and can interfere with daily life. They also can increase the risk of death.

Cholesterol - Cholesterol profiles also change significantly at the time of menopause. Total cholesterol and LDL ("bad") cholesterol levels increase. Increased LDL cholesterol is associated with an increased risk of heart disease.

Heart disease risk - increases after menopause, although it is unclear exactly how much is due to aging and how much is caused by the hormonal changes that occur at the time of menopause. Women who undergo premature menopause or have their ovaries removed surgically at an early age are at an increased risk of heart disease.

Weight gain - A three year study of healthy women nearing menopause found an average gain of five pounds during the three years. Hormonal changes and aging are both possible factors in this weight gain (Stoppler and Shiel Jr, 2014).

Hot flushes

Your first hot flush can be a startling experience. It may begin like a headache, with a pressure in the head, or as a sudden sensation of intense warmth. The "flush" increases in intensity until a feeling of heat or burning occurs in the face, neck, and chest. Your skin may redden and increase in temperature by as much as seven degrees. You may feel an urgent need to remove a sweater, jacket, or nightgown, and cool yourself by grabbing for a fan, throwing off the bedcovers, or standing by an open window. An outbreak of sweating, particularly affecting the upper body, may immediately follow the hot flush. Sweating cools down the skin temperature, causing you to have the shivers. Less common symptoms which may accompany a hot flush include palpitations, weakness, fatigue, faintness, and vertigo.

Hot flushes vary in frequency, intensity, and duration for every individual expereincing them. The average length of a hot flush is 4 minutes, though it can last from a moment to as long as 10 minutes. Frequency varies from 1 to 2 an hour to 1 to 2 a week (WebMD, 2014d) (Healthwise-Staff, 2013).

Hot flash or hot flush?

A "hot flush" is a UK variant of English, whereas a "hot flash" is North American. In this situation both are right, and are used interchangeably.

Methods of Delivery or Administration

In descending order of approximate efficiency in delivery into the bloodstream.

Intramuscular injection - 100% efficient
Transdermal (patch, gel, or cream) - 90%
Sublingual or nasal spray - 80%
Oral - 10% (unknown, 2014e)

See also How to Take Your Tablets, and also Understanding "Enteric Coating".

Medication taken orally (swallowed as compared to under the tongue) first enters into the digestive tract/stomach and is then processed by the liver. This is what is known as *"the first-pass effect"*. When taken under the tongue or through the skin, your medication directly enters the blood stream. In the case of estradiol, the conversion into its less oestrogenic metabolites is minimised, allowing the more potent estradiol to remain present to a greater degree. And this method produces less strain on the liver.

Mood swings and depression

Hormones also alter your brain chemistry. This can lead to wild mood swings, uncontrollable emotional outbursts, and in some people HRT can cause severe depression or suicidal tendencies. If you are taking HRT medications and experience any of these side-effects you should discuss them with your physician as they indicate a negative reaction to the drugs. There may be alternatives you could take that would be better tolerated. Some gender patients commit suicide and some of those deaths may have been attributable to HRT medications.

Use of hrt drugs with anti-depressants/anti-anxiety medications

It is extremely common for gender patients to be concurrently using an anti-depressant medication with their HRT drugs. What doctors are not telling their patients, and is (to the best of my knowledge) generally not stated in the prescribing or patient information for the drugs, is the possible negative interactions between anti-depressant and hormone replacement therapy medications.

Oestrogen - acts upon neurotransmitters in the same way as MAOI anti-depressants by increasing 5-HT-2 serotonin receptor binding as well as activating additional serotonin receptors and the overall concentration of serotonin. It also increases norepinephrine binding to receptors and the turnover (breakdown and replacement) rate for norepinephrine.

Progesterone - acts upon neurotransmitters in a similar manner to SSRI anti-depressants. It inhibits re-uptake of serotonin by receptors and also inhibits the breakdown of the neurotransmitter thus increasing concentrations of it. Progesterone also increases the serum levels of norepinephrine but inhibits binding of it to receptors. Synthetic progestins appear to have a similar chemical action on neurotransmitters and have been directly linked to HRT-associated depression.

- As a quick primer on these neurotransmitters -

Serotonin - low levels of activity (absorbtion) are associated with depression, high levels of activity are association with anxiety disorders. SSRI's increase the amount of serotonin by inhibiting how much the body can act on the body via receptors. For those with a naturally low amount the increase in intracellular concentration can alleviate depression. For those with a naturally high amount the inhibition of the receptors prevents some of the concentrated amount from acting on the body, reducing anxiety.

Norephinephrine - one of the metabolites of dopamine, this chemical is part of the body's system for responding to stress. Low levels of norepinephrine are associated with sluggishness, mental stress, and depression while high levels increase heart-rate, respiration, and increase energy levels (sometimes leading to nervousness or anxiety).

- Serotonin and Norepinephrine levels are apparently linked and, in a healthy individual, are kept in balance to prevent episodes of depression or anxiety. The fluctuations in hormone levels experienced by women during their cycle (and the drop in hormones at menopause) adversely affect BOTH of these neurotransmitters, leading to mood disorders. SSRI and MAOI drugs prescribed to treat depression and anxiety problems also affect BOTH serotonin and norepinephrine levels.
- Few transgendered people seem to be aware of the MAOI and SSRI effects of oestrogen and progesterone, nor are they aware of potential adverse interactions between their HRT and anti-depressant/anti-anxiety medications. If you were taking an MAOI or SSRI for depression or anxiety before beginning HRT you may need to adjust your dosage once you are taking hormones (I'm inclined to say you'll probably have to reduce it, but you should talk to your doctor first). If, after you've been on HRT for a while, you are experiencing anxiety or depression an adjustement to your HRT regimen may be in order, and as a last resort the addition of an MAOI or SSRI.
- Depression and anxiety disorders plague the majority of transgendered people, for which many are taking either SSRIs or MAOIs. Evidence suggests that the suicide rate alone among transgendered people is a whopping 50 percent and you now have to wonder how many of those suicides were chemically induced because patients (or even their doctors) were unaware of the action hormone therapy has on serotonin and norepinephrine. Since oestrogen, progesterone, SSRIs, and MAOIs do not appear to be listed as contraindications in patient and prescribing information, even though they act on the same neurotransmitters, seems a horrible oversight (hemingways, 2004a).

Oestrogen and Alzheimer's Disease

Alzheimer's disease is a progressive neurodegenerative disorder characterized by memory loss and disordered cognition. Women have a higher Alzheimer's incidence than men, indicating that the declining oestrogen levels during menopause may influence Alzheimer's pathogenesis. However, the mechanism underlying oestrogens neuroprotective effect is not fully clarified and is complicated by the presence of several distinct oestrogen receptor (ER) types and the identification of a growing number of ER splice variants. Thus, a deeper analysis of ERs could elucidate the role of oestrogen in age-related cognitive changes (Lan, Zhao, and S. Li, 2015). Also see Memory enhancing effects of oestrogen.

Alzheimer disease is a crippling neurodegenerative disorder. It is more common in females after menopause. Oestrogen probably has a protective role in cognitive decline. A large amount of research has been carried out to see the benefits of hormone replacement therapy with regards to Alzheimer still its neuroprotective effect is not established. Recent studies suggest a reduced risk of Alzheimer's and improved cognitive functioning of post-menopausal women who used 17β-estradiol in the critical period. Use of 17β-estradiol in young and healthy post-menopausal women yields the maximum benefit when the neurons are intact or neuronal stress has just started. Hence intervention in the critical period is key in the prevention or delay of Alzheimer's in post-menopausal women (Jamshed, Ozair, and Aggarwal, 2014).

Midlife vascular risk factors influence later cognitive decline and Alzheimer's disease. The decrease in serum estradiol levels during menopause has been associated with cognitive impairment and increased vascular risk, such as high blood pressure, which independently contributes to cognitive dysfunction and Alzheimer's. We describe the extent to which vascular risk factors relate to cognition in healthy, middle-aged, recently postmenopausal women enrolled in the Kronos Early Oestrogen Prevention Cognitive and Affective Study (KEEPS-Cog) at baseline. KEEPS-Cog is a double-blind, randomized, placebo-controlled, parallel group, clinical trial, investigating the efficacy of low-dose, transdermal 17β-estradiol and oral conjugated equine oestrogen on cognition. All results are cross-sectional and represent baseline data only. Analyses confirm that the KEEPS-Cog cohort (n = 571) was middle aged (mean 52.7 years, range 42-59 years), healthy, and free of cognitive dysfunction. Higher systolic blood pressure was weakly related to poorer performance in auditory working memory and attention (p = 0.004; adjusted for multiple comparisons p = 0.10). This relationship was not associated with endogenous hormone levels, and systolic blood pressure was not related to any other cognitive domain. Blood pressure levels may be more sensitive than other vascular risk factors in detecting subtle differences in cognitive task performance in healthy, recently menopausal women. Lower blood pressure early in menopause may affect cognitive domains known to be associated with Alzheimer's (Wharton et al., 2014).

It would seem therefore, that our increased oestrogen intake may help diminish the possibility of us developing Alzheimer's Disease in later life. But there is still much to be learnt in this area.

Online Pharmacies

These sites have been found to be safe for folk to use, and to be 'reputable' sites, but YMMV!

www.inhousepharmacy.biz
www.clickdrugstore.net
www.healthpluspharmacy.com
www.1drugstore-online.com
www.24x7pharmacy.com
www.importeddrugs.com
www.medicapharma.com
www.dru-online.com
www.healthcarepharma.com
www.healthworldpharmacy.com
www.pharmagroup.com
www.pharmatico.com
www.medscorp.com
www.e-pharmacy.net
www.12buys.com
http://unitedpharmacies.com
http://cutpricechemist.com/
http://www.alldaychemist.com/index.php
www.noprescriptiondrugs.com/npdnew/medlist.htm
http://medsmex.com/store3/customer
www.goldpharma.com
http://www.brandmedicines.com
http://www.fairvaluepharmacy.com

Pelvic examination

What is a pelvic examination?

It's a check-up, done by a doctor, or nurse, in which your vagina and the adjoining organs of your pelvis, are assessed.

The phrase 'pelvic examination' means the same thing as ' vaginal examination'.

There are two components of a pelvic examination -

- manual,
- visual.

The examiner does the manual check with her gloved fingers. And the visual check is done with a small device called a 'speculum', which allows him or her to see right up to the end of your vagina.

In practice, the visual part of a pelvic examination isn't always necessary. So you may just have a manual check-up.

What happens during a pelvic examination?

First of all, the reasons for needing the examination will be explained to you. You should be offered the option of having a chaperone to sit or stand beside you if you wish. This could be a friend, but very often a doctor will call in a nurse or some other female member of staff.

To begin with, you should remove your pants and tights, and anything else you happen to be wearing below the waist. There is no need to remove a skirt, unless it's very tight.

You will then be asked to get up on a couch, on which a sheet of fresh, clean paper should have been unrolled. Most doctors and nurses would ask you to lie flat on your back, but a few will request that you lie on your left side, facing away from them. They then do the examination from behind.

Next (assuming you're on your back), you'll be asked to draw your knees up and spread them wide apart. If necessary, the nurse or doctor will make a brief visual check of your vulva (that is, the external part of your genitals).

Manual examination - Then she will gently slip two fingers of her gloved hand into your vagina, and feel all around it, going up as far as its end. She may well put her other hand flat on your lower abdomen. During all this, most women experience mild discomfort only.

Visual inspection - This is carried out by slipping the instrument called a speculum into your vagina. It's about four inches (10cms) long, and it has two parts - rather like a duck's bill. Once it's inside, the nurse or doctor will open up the two halves, and this makes it fairly easy for her to see the upper part of your vagina.

It's fair to say that most women do not like having a speculum inserted.

It's uncomfortable, and some patients actually feel pain, particularly if they are tensed up, or if the vagina is inflamed for some reason (like an infection).

However, an experienced nurse or doctor should be able to insert it (and take it out) without causing you a lot of discomfort.

A lot of patients dislike the coldness of a speculum. A knowledgeable medic will warm it under the hot tap before inserting it!

Finally, you might need to have a bacteriology swab taken from your vagina or urinary opening, in order to send a sample of secretions to the lab. This should not hurt, and you may even be unaware that it is being done.

Is it normal to be worried or embarrassed?

Yes. Most of us find it embarrassing to have highly personal examinations. This is very understandable. Yet there are situations where procedures such as a pelvic examination are necessary.

Why do I need a pelvic examination?

A pelvic examination would be considered a routine investigation in women complaining of lower abdominal pain, and it's very often necessary when a patient has a vaginal discharge, or any other evidence of infection (Delvin, 2013).

When I had one, for a recurring UTI, I felt a slight tugging on my vagina as the speculum was opened but felt no discomfort from the whole scenario.

Permanent sterility and sexual dysfunction

For biological males taking female hormones there is a risk of permanent sterility. This can happen rather quickly (some reports say in as little as three weeks), but it is generally considered irreversible after six months of hormone use. This effect may be reversible before that time-frame however, and some are capable of reviving fertility even after the six month mark. Individual reaction to hormones, which medications are used, and quantity will all be factors.

I would strongly suggest that if you are concerned about losing fertility and/or sexual function you should reconsider medicating with hormones altogether. If your plans include having a child of your own, M2Fs should consider banking sperm and F2Ms storing eggs before beginning a counter-sexual hormone therapy. F2Ms and M2Fs will also need to consider that post-operatively they will not have a womb and any use of the stored eggs or banked sperm would require a surrogate (if you're lucky that might be your girlfriend or wife).

Pharmacodynamics

The study of the actions of the drugs and their effects is called pharmacodynamics. Before a drug can be effective, it must be absorbed and distributed throughout the body. Drugs taken orally may be absorbed by the intestines at different rates, some being absorbed rapidly, some more slowly. Even rapidly absorbed drugs can be prepared in ways that slow the degree of absorption and permit them to remain effective for 12 hours or longer. Drugs administered either intravenously or intramuscularly bypass problems of absorption, but dosage calculation is more critical.

Pharmacokinetics

Ive been asked what 'Pharmacokinetics' is, so here goes.

The term pharmacokinetics is derived from the Greek words "pharmakon" meaning drug and "kinesis" meaning motion, and can therefore be defined as the science which deals with drug movement in the body. It is concerned with the rate at which drug molecules cross cell membranes to enter, distribute within and leave the body, as well as the chemical changes which they are subject to within it. Pharmacokinetics therefore deals with four vital processes;

- drug absorption,
- distribution,
- metabolism
- and elimination (Cahill, 1994)

Or very loosely "what your body does to the drug itself"!

Photosensitivity of the skin

Short-term damage to the skin from ultraviolet light (i.e. sunlight) can occur from photosensitivity reactions. These are not uncommon and are mostly caused by interaction of the sun with medications some of which have been mentioned already. Many of these reactions, experienced as sunburn-type symptoms, can be avoided by taking extra care to minimise sun exposure.

Safety in the sun should include -

- Wearing protective clothing - loose fitting, tightly woven, dark clothes. Also a hat, preferably with a wide brim, and it has been found that a hat with a 4cm brim will reduce the ultraviolet rays by 50% (Hughes and Van Oulsen, 2001).

- Using a sunscreen with sun protection factor (SPF) of at least 15 indicating UVB protection and 3*** indicating UVA filters (the maximum is four stars). Physical sunscreens usually contain zinc or titanium oxide that reflect the light off the skin. For this reason they are often thick and opaque and are not absorbed into the skin as easily as chemical ones. These absorb the energy of the UV rays before they penetrate and damage the skin. All sunscreens should be applied 15--30 minutes before exposure to the sun to allow time for the chemicals to work. The sunscreen should be applied to clean, dry skin and rubbed in lightly in the direction of hair growth. They should be reapplied every two hours, although more frequently if levels of sweat or water are likely to have washed them off. The quantities suggested on sunscreen containers are often described as generous. This can be subjective and some articles state that less than half the recommended amount of sunscreen is usually applied to achieve the recommended SPF (Neale, G. Williams, and Green, 2002).
- Avoiding the sun, seeking the shade between 11am and 3pm, when the sun is at its highest.
- Avoiding reflective surfaces, such as sand, snow, water and concrete.
- Avoiding sunbeds as these can cause premature ageing, cataracts, sunburn and rashes and may be a risk factor for skin cancer (Diffey, 2003) (Burr and Penzer, 2005).

PMS - Pre-menstrual syndrome

If you find yourself getting particularly weepy (well, weepier than normal) during those ASPCA animal shelter commercials at a certain time of the month, blame it on good ol PMS. According to the American College of Obstetricians and Gynecologists (as reported by womenshealth.gov in 2014), its estimated that 85 percent of menstruating women have at least one PMS symptom as part of their monthly cycle. These symptoms can include acne, tender breasts, bloating or upset stomach, headaches, food cravings, mood swings, anxiety, depression, trouble sleeping or tiredness. Yeah, being a woman is a real treat. But there are a few "quick fixes" you can do to lessen these symptoms. According to Alison M. Leong, M.D., "To combat PMS naturally, try decreasing your sugar, salt, caffeine and alcohol intake." Holding off on these can also help cramps if you additionally suffer from those. "Increase your exercise, calcium and vitamin B to help boost your mood and reduce PMS symptoms like depression and anxiety," she says (livestrong, 2016).

Premarin

This drug is, supposedly (I deliberately phrase this carefully, because I have not seen any of this, but I am aware of the situation), produced from the urine of pregnant mares! They are kept in cruel conditions, which include continual confinement, standing without any option of being able to lie down or even turn around, a restriction of their drinking water (presumably to concentrate their urine), inadequate veterinary overseeing, killing of their newborn or young foals, and then immediate reimpregnation. These pregnancies are continued until the mare becomes infertile or even sick, whereupon she is killed (unknown, 2005). Basically, she is used as a factory on legs!

For this reason some people feel that they are unable to use this drug for their own benefit. The choice is yours.

Prescriptions

Prepaid certificate

If you know you'll have to pay for a lot of NHS prescriptions it may be cheaper to buy a prescription prepayment certificate prescription prepayment certificate (PPC)[139], effectively a prescription 'season ticket'. A PPC covers you for all of your own NHS prescriptions, including dental prescriptions, no matter how many items you need. However, this does not include other health costs, for example the provision of wigs and fabric supports which are only provided through the hospital service.

Currently the prescription charges are UK £8.20 for each item, as from 8th April 2015, so you will see that the costs will very soon mount up, as many people have more that one item prescribed for them that they need to take.

There are two PPC options to choose from -

1. A three month PPC which costs UK £29.10 and will save you money if you need four or more items in the three months.
2. A 12 month PPC costs UK£104.00 and will save you money if you need more than 13 items in a year

How much can I save?

- If you need two items each month you can save around UK £90 with a 12 month PPC,

[139] prescription prepayment certificate

- If you need three items each month you can save around UK £180 with a 12 month PPC,
- If you need four items each month you can save around UK £280 with a 12 month PPC.

There are several payment options available. If you choose the 12 month PPC, you can pay for this by 10 monthly direct debit instalments.

Check the current costs for NHS prescriptions

How to apply for a PPC

Please check if you are entitled to free prescriptions before you apply for your PPC. It's quickest to buy your PPC online. The PPC will start from the day you submit your application, unless you request a different start date. However, the start date must be within one month before or after the date of your application.

If you want to speak to someone about a PPC then you can phone **0300 330 1341** for any queries (NHS, 2014k).

Free prescriptions

You can get free NHS prescriptions if, at the time the prescription is dispensed, you -

- are 60 or over,
- are under 16,
- are 16-18 and in full-time education,
- are pregnant or have had a baby in the previous 12 months and have a valid maternity exemption certificate (MatEx),
- have a specified medical condition and have a valid medical exemption certificate (MedEx),
- have a continuing physical disability that prevents you from going out without help from another person and have a valid MedEx,
- are an NHS inpatient.

You are also entitled to free prescriptions if you or your partner (including civil partners) are named on, or are entitled to, an NHS tax credit exemption certificate or a valid HC2 certificate (full help with health costs), or you receive either -

- Income Support,
- Income-based Jobseeker's Allowance,
- Income-related Employment and Support Allowance, or
- Pension Credit Guarantee Credit,
- Universal Credit

Medical exemptions

People with certain medical conditions can get free NHS prescriptions if -

- they have one of the conditions listed below, and
- they hold a valid medical exemption certificate.

Medical exemption certificates are issued on application to people who have -

- a permanent fistula (for example caecostomy, colostomy, laryngostomy or ileostomy) requiring continuous surgical dressing or requiring an appliance,
- a form of hypoadrenalism (for example Addison's disease) for which specific substitution therapy is essential,
- diabetes insipidus or other forms of hypopituitarism,
- diabetes mellitus, except where treatment is by diet alone,
- hypoparathyroidism,
- myasthenia gravis,
- myxoedema (that is, hypothyroidism requiring thyroid hormone replacement),
- epilepsy requiring continuous anticonvulsive therapy,
- a continuing physical disability which means the person cannot go out without the help of another person. Temporary disabilities do not count even if they last for several months.

Or are undergoing treatment for cancer -

- including the effects of cancer, or
- the effects of current or previous cancer treatment

Also read the medical exemption certificate FAQ

How to apply for a medical exemption certificate

To apply for a medical exemption certificate ask your doctor for an FP92A form. Your GP, hospital or service doctor will sign the form to confirm that your statement is correct. At your GP's discretion, a member of the practice who has access to your medical records can also sign the form.

Your certificate will be valid from one month before the date that the NHS Business Authrority receives the application form.

The MedEx lasts for five years and then needs to be renewed. You may receive a reminder that your certificate needs to be renewed. If you don't receive a reminder, it is your responsibility to ensure that it is renewed.

You can find more information about the application process and refunds on the NHS Business Authority's website (unknown, 2015c).

Prevalence of Transsexualism in the UK

National trends for the UK show -
1/12,000 males, transgender from male to female
1/33,000 females, transgender from female to male

Specific issues around access to services, specific services for men or women, and 'single sex' facilities. In terms of the transgender population, GIRES (Gender Identity Research and Education Society) gives an estimate of 600 per 100,000. If these figures were applied to the Cheshire East community based on the 2005 mid-year estimates, there may be around 2,100 trans people in the area (SIGN, 2002).

Donna Patricia Kelly stated in 2001 *"My calculations therefore indicate that the number of transsexual people in the UK (including post-ops) is at least 1:1000 + or - a third or thereabouts. Or, to put it another way, I would be *very* surprised if it the prevalence were smaller than 1:1400, thus indicating a /minimum/ of about 35,000 trans people in the UK. This number is likely to be substantially higher, perhaps 50,000 or even more. This engineering approach from basic demographics of course completely demolishes previous estimates which were a full order of magnitude smaller. Within the limits of data and the range of assumptions, this is *very* consistent with Lynn Conway's estimate for the US, where she calculates that "The prevalence of MtF transsexualism is thus greater than 1:500 and may be as high as 1:250"* (Conway, 2001).

The Home Office "Report of the interdepartmental working group on transsexual people" (Office, 2000) based on research from the Netherlands and Scotland, estimates that there are between 1,300 and 2,000 male to female and between 250 and 400 female to male transsexual people in the UK. However, Press for Change estimate the figures at around 5,000 post-operative transsexual people. Further, GIRES (GIRES, 2008) claims there are 6,200 people who have transitioned to a new gender role via medical intervention and approximately 2,335 full Gender Recognition Certificates have been issued to February 2009.

The figures are more diverse when looking at the trans community in the UK, where estimates range from 65,000 (Johnson, 2001, p.7) to 300,000 (GIRES, 2008). To put this in context, the former figure is close to the population of Inverness, while the latter is similar to the population of Cardiff (51,000 and 305,000 respectively) (for National Statistics, 2009).

It should be noted with regard to the last two paragraphs, quoted from the "Trans Data Position Paper" by the Office for National Statistics (for National Statistics, 2009), that they have quoted "(Johnson, 2001, p.7)" but don't actually give the reference to this paper, so I have been unable to follow this up.

Prostate cancer

The prostate shrinks considerably when testosterone is removed and oestrogens take it's place. The occurrence of prostate cancer is very rare in transsexuals, but it can occur. This may be due to problems that exist before significant hormone replacement therapy has begun. It is important that transsexuals get their prostate examined, particularly if they start hormone replacement therapy later in life and regardless if they are pre or post op. Having the testicles removed earlier in life helps a lot, but in middle-age M→Fs the protection may not be there. The prostate is not removed in the SRS operation, as it can add to the natural lubrication of the neo-vaginal area, and is also a source of stimulation (unknown, 2005).

Regimes

Male → female

Oestrogen

Use of oral oestrogen, and specifically ethinylestradiol, increases the risk of VTE (venous thromboembolism). Because of this safety concern, ethinylestradiol is not recommended for feminizing hormone therapy. Transdermal oestrogen is recommended for those patients with risks factors for VTE. The risk of adverse events increases with higher doses, particularly doses resulting in supraphysiologic levels. Patients with co-morbid conditions that can be affected by oestrogen should avoid oral oestrogen if possible and be started at lower levels. Some patients may not be able to safely use the levels of oestrogen needed to get the desired results. This possibility needs to be discussed with patients well in advance of starting hormone therapy.

Androgen-reducing medications ("anti-androgens")

A combination of oestrogen and "anti-androgens" is the most commonly studied regimen for feminization. Androgen-reducing medications, from a variety of classes of drugs, have the effect of reducing either endogenous testosterone levels or testosterone activity, and thus diminishing masculine characteristics such as body hair. They minimize the dosage of oestrogen needed to suppress testosterone, thereby reducing the risks associated with high-dose exogenous oestrogen.

Common anti-androgens include the following:

- Spironolactone, an antihypertensive agent, directly inhibits testosterone secretion and androgen binding to the androgen receptor. Blood pressure and electrolytes need to be monitored because of the potential for hyperkalemia. Please see the Spironolactone section.
- Cyproterone acetate is a progestational compound with antiandrogenic properties. This medication is not approved in the United States because of concerns over potential hepatotoxicity, but it is widely used elsewhere. Please see the Cyproterone Acetate section.
- GnRH agonists (e.g., goserelin, triptorelin) are neurohormones that block the gonadtropin-releasing hormone receptor, thus blocking the release of follicle stimulating hormone and luteinizing hormone. This leads to highly effective gonadal blockade. However, these medications are expensive and only available as injectables or implants. Please see the Goserelin section.
- 5-α reductase inhibitors (finasteride and dutasteride) block the conversion of testosterone to the more active agent, 5-α-dihydrotestosterone. These medications have beneficial effects on scalp hair loss, body hair growth, sebaceous glands, and skin consistency. Please see the Finasteride section, and the Dutasteride section.

Cyproterone and spironolactone are the most commonly used antiandrogens and are likely the most cost-effective.

Progestins

With the exception of cyproterone, the inclusion of progestins in feminizing hormone therapy is controversial. Because progestins play a role in mammary development on a cellular level, some clinicians believe that these agents are necessary for full breast development. However, a clinical comparison of feminization regimens with and without progestins found that the addition of progestins neither enhanced breast growth nor lowered serum levels of free testosterone. There are concerns regarding potential adverse effects of progestins, including depression, weight gain, and lipid changes. Progestins (especially medroxyprogesterone acetate) are also suspected to increase breast cancer risk and cardiovascular risk in women. Micronized progesterone may be better tolerated and have a more favourable impact on the lipid profile than medroxyprogesterone acetate does (WPATH, 2012).

Hormone regimes for transgender women (male to women, MTF)

Anti-androgen

Spironolactone = 100–200 mg/day (up to 400 mg)
Cyproterone acetate[140] = 50–100mg/day
GnRH agonists = 3.75 mg subcutaneous monthly

Oral oestrogen

Oral conjugated oestrogens = 2.5–7.5mg/day
Oral 17-β-oestradiol = 2–6mg/day

Parenteral oestrogen

Estradiol valerate = 5–20mg i.m./2 weeks
or cypionate = 2–10mg i.m./week

Transdermal oestrogen

Estradiol patch = 0.1–0.4mg/2X week (unknown, 2014h)

Additional therapies, which may be helpful, include -

cyproterone acetate	oral, tablets	50–100mg daily	it is much less satisfactory than goserelin
Dianette	oral, tablets	1 tablet daily for 21 days; repeat after 7 gap days	contains cypoterone acetate and ethinylestradiol
spironolactone	oral, tablets	100–400mg daily	may be required for additional androgen receptor blockade – long-term use associated with liver dysfunction and possibly hepatoma risk (animal data)
Progesterone is not usually indicated since no biologically significant progesterone receptor sites exist for biological males			
Medroxyprogestero acetate	oral, tablets	100mg twice daily	

[140] Not available in the USA

or Dydrogesterone	oral, tablets	10mg twice daily	
Finasteride	oral, tablets	5mg daily	blocks conversion of testosterone to the more active dihydrotestosterone. Can discourage male pattern hair loss (Psych, 2013).

Table 17.20 – Additional therapies for transwoman in the UK

Testosterone suppression		
goserelin or leuprorelin	intramuscular, depot injections	3.6mg every 4 weeks
		10.8mg every 3 months
Oestrogen replacement		
Oestradiol	oral tablets	1–6mg daily
	transdermal patches	50–150mcg patches 2–3 times a week
(Psych, 2013)	gel	2–4 measures daily

Table 17.21 – Hormone therapy for UK transwoman

	Oestrogen		Anti-androgen	
Chemical	17-β oestradiol		Spironolactone and/or Finasteride	
Brand name	Estradot			
	Estraderm			
	Oesclim	Estrace	Aldactone	Proscar
Taken via	Skin patch	Pill	Pill	Pill
Typical starting dose	start with 0.1 mg patch twice per week; gradually increase up to maximum of 0.4 mg patch twice per week	start with 1–2 mg per day; gradually increase up to maximum 8 mg per day	start with 50–100 mg per day; increase by 50–100 mg each month up to maximum 200–300 mg per day	2.5 mg every other day

Table 17.22 – Regime commonly used by transwomen in British Columbia, Canada

Name	**Dosage**	**When taken**
Cyproterone acetate	100mgs	50mgs morning, 50mgs evening

Name	Dosage	When taken
OR medroxyprogesterone acetate	5–10mgs	split-dosage
OR Spironolactone	up to 100mgs	twice daily, if tolerated
Finasteride	5mgs	once a day
Estradiol valerate	2–4mg	split dosage, morning and evening
OR Transdermal estradiol	100mcg patch	2 times a week (LJ Gooren, Giltay, and Bunck, 2008)

Table 17.23 – Transwomen hormone regime from the Amsterdam Gender Clinic, Holland

Hormone	Dose	Taken when	For how long	Change to
Estradiol Valerate / Progynova / Estrofem	2mgs	morning	1 month	4mgs, 2mgs in morning, and 2mgs in evening
Dutasteride	0.5mg	morning	2 month	Alternate days for 2 months, then once every 3 days
Estradot patches	50mcg	twice a week		
Spironolactone	25mgs	morning	2 months	50mgs for further 2 months
Dutasteride	0.5mg	morning	2 months	Alternate days for 2 months, then once every 3 days
Bicalutamide	50mgs			
Estrofem	4mgs	a day		2mgs in morning, 2mgs in evening
Spironolactone	200mgs	a day		100mgs in morning
Prostap 3	3.75mgs			
Evorel patches	100mcg	twice weekly		
Progynova	2mg	morning		
Estrofem	8mgs	4mgs morning, 4mgs evening		

Hormone	Dose	Taken when	For how long	Change to
Dutasteride	0.5mgs	morning		
Spironolactone	200mgs	morning		
Microgest	200mgs	1st 10 days of the month		
Oestrogen	8mgs	4mgs morning, 4mgs evening		
Progesterone	200mgs	100mgs morning, 100mgs evening		
Spironolactone	200mgs	morning		
Finasteride	1mg	morning		
Oestrogel	0.75mg, 17β oestra-diol	morning & evening		
Progynova	2mgs	3 times daily		
Duphaston	10mgs	morning & evening		
Zumenon	2mgs	3 times daily		
Utrogestan	10mgs	morning & evening		

Table 17.24 – Some self-medding regimes

Female → Male

Hormone regimes for transgender men (female to men, FTM)

Oral

Testosterone undecanoate[141] = 160–240mg/day

[141] Not available in the USA

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Parenterally (i.m. or subcutaneous)

Testosterone enanthate or cypionate = 50–200mg/week or 100–200mg/2 weeks
Testosterone undecanoate - 1000 mg/12 weeks

Transdermal

Testosterone 1% gel = 2.5–10 g/day
Testosterone patch = 2.5–7.5 mg/day (unknown, 2014h)

	Intramuscular injection	
Chemical	Testosterone cypionate	Testosterone enanthate
Brand name	Depo-Testosterone	Delatestryl
Typical starting dose	Typically 50–80mg every two weeks (or 25–40mg every week), gradually increased each month until blood testosterone is within the average "male" range or there are visible changes. Typical maintenance dose is 100–200mg every two weeks (or 50–100mg every week)	
If your ovaries have been removed, your dose will be cut by at least 50%		
Pros	Changes happen more rapidly	
Cons	Fluctuating dose with injection cycle means more extreme side effects at start/end of injection cycle. Risk of injection problems (e.g., abscess)	
	Skin gel	**Skin patch**
Chemical	Dissolved testosterone crystals	
Brand name	AndroGel	Androderm
Typical starting dose	5–10 g per day if no physical or mental health concerns, start with 2.5g per day if there are psychiatric problems or other health concerns	
If your ovaries have been removed, your dose will be cut by at least 50%		
Pros	More stable daily dose - less ups and downs than with injection	
Cons	Changes take longer to happen when first starting	

Table 17.25 – Hormone regime commonly used by transmen in British Columbia, Canada

Oestrogen suppression		
goserelin or leuprorelin	intramuscular, depot injections	3.6mg every 4 weeks
		10.8mg every 3 months

Testosterone replacement		
testosterone enantate or testosterone esters	intramuscular, depot injections	Sustanon 250mg every 2–3 weeks
	intramuscular, depot injections	500mg every 3–6 weeks
testosterone undecanoate	intramuscular, depot injections	Nebido 1g every 3 months
	transdermal gel	5g daily
	transdermal patches	
testosterone undecanoate	oral, tablets	40mg 3 times a day
(Psych, 2013)		up to 80mg 2 times a day

Table 17.26 – Hormone therapy for transmen in the UK

Name	Dosage	When taken
Testosterone injection	200–250mgs	every 2 weeks (LJ Gooren, Giltay, and Bunck, 2008)

Table 17.27 – Transmen hormone regime from the Amsterdam Gender Clinic, Holland

Self-medding

This is when folk get their hormones via internet websites, and take them often without medical supervision and sporadic blood tests. Sometimes this is because they are unable to get their required hormones legitimately possibly because of the political situation in their country. They live under oppressive political regimes with a constant fear of arrest and/or harassment by the governmental authorities. That is at one end of the spectrum, at the other end individuals prefer to manage their own hormonal regimes with very little backup and support from medical doctors. They like to keep things simple and easy to understand.

Safety of HRT

How safe is the HRT we take? Here's the facts -

Stroke

Research suggests that HRT slightly increases the risk of having a stroke. Other things that can increase the risk of stroke include -

- Getting older,
- High blood pressure,
- Smoking,
- Drinking too much alcohol,
- An irregular heartbeat.

How likely is a stroke?

Looking at women in their **50s**, on average, over 5 years -

- In women **not taking HRT - 3 in 1000** would be expected to have a stroke.
- In women **taking HRT - 4 in 1000** would be expected to have a stroke.

Looking at women in their **60s**, on average, over 5 years -

- In women **not taking HRT - 11 in 1000** would be expected to have a stroke.
- In women **taking HRT - 15 in 1000** would be expected to have a stroke.

If you get **migraine-type headaches** which you cannot explain -

- **See a doctor as soon as possible**
- **Do not take any more HRT** until your doctor says you can.

These headaches may be an early warning sign of a stroke (Ltd, 2015).

Blood clots

HRT may increase the risk of blood clots in the veins (also called 'deep vein thrombosis', or DVT), especially during the first year of taking it. See also Deep Vein Thrombosis.

These blood clots are not always serious. However, if a clot travels to the lungs, it can cause chest pain, breathlessness, collapse or even death. This is called 'pulmonary embolism' or PE.

You are more likely to get a blood clot if -

- You are very overweight (BMI above 30kg/m^2),
- You are taking medication containing an oestrogen,
- You are getting older,
- You have cancer,
- You have had a blood clot before,
- Any of your close family have had blood clots,
- You have any blood clotting problem that needs treatment with a medicine such as warfarin,
- You are off your feet for a long time because of major surgery, injury or illness,
- You are going on a long journey and will not be moving about for some time.

How likely is a blood clot?

Looking at women in their **50s**, on average, over 5 years -

- In women **not taking HRT - 3 in 1000** would be expected to get a blood clot.
- In women **taking HRT - 7 in 1000** would be expected to get a blood clot.

Looking at women in their **60s**, on average, over 5 years -

- In women **not taking HRT - 8 in 1000** would be expected to get a blood clot.
- In women **taking HRT - 17 in 1000** would be expected to get a blood clot.

If you get painful swelling in your leg, sudden chest pain or have difficulty breathing -

- **See a doctor as soon as possible**
- **Do not take any more HRT** until your doctor says you can.

These may be signs of a blood clot (Ltd, 2015).

Breast cancer

Your risk of breast cancer is higher if -

- You have a close relative (mother, sister or grandmother) who has had breast cancer,
- You are very overweight.

How likely is breast cancer?

Looking at women aged 50 to 79, on average, over the next five years -

- In women **not taking combined HRT between 9 and 17 in 1,000** will get breast cancer.
- In women **taking oestrogen-progestogen HRT** at age 50 to 79 and take it for **5 years**, between **15 and 21 in 1,000** will get breast cancer (an **extra 4–6 cases**)

if you notice any **changes in your breast**, such as -

- dimpling of the skin,
- changes in the nipple,
- any lumps you can see or feel

Make an appointment to see your doctor as soon as possible.

Dementia

Evorel [estradiol patches] and medicines like it will not stop memory loss (dementia). Women who start using medicines like evorel after the age of 65 may have a small increase in the risk of dementia (Ltd, 2015).

Sexual Health

Men's Health

Issues with sexual health are common for both men and women at any age. Sometimes it's hard to talk about them with friends, partners or health care professionals, but it's important to your well-being to get the information or treatment you need.

Testicular Self Exam

Testicular cancer is the most common type of cancer in men ages 15–34. Beginning at age 15, you should examine your testicles monthly and continue the process through your 30s. A testicular self-examination TSE[142] is important since testicular cancer can often be asymptomatic (there may be no symptoms to indicate a medical problem). However, there may be a dull pain in the lower abdomen and a feeling of heaviness and dragging. A monthly examination will allow you to become familiar with the size and feel of your testicles so any abnormality, such as a lump, can be brought to your doctor's attention. See also Testicular Self Examination.

If detected early, testicular cancer is one of the most easily cured. To show how important TSE is, testicular cancer can double in size every 90 days! That is how important TSE is.

How to do a TSE The best time to check yourself is in the shower or after a warm bath. Fingers glide over soapy skin making it easier to concentrate on the texture underneath. The heat causes the skin to relax, making the exam easier.

1. Examine each testicle gently with both hands. The index and middle fingers should be placed underneath the testicle while the thumbs are placed on the top. Roll the testicle gently between the thumb and fingers. One testicle may be larger than the other. This is normal.

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[142] Testicular self-examination

2 The epididymis is a cord-like structure on the top and back of the testicle that stores and transports the sperm. Do not confuse the epididymis with an abnormal lump. Now repeat the exam on the other side.
3 Feel for any abnormal lumps about the size of a pea on the front or the side of the testicle. These lumps are usually painless.

What are the symptoms of testicular cancer?

In early stages testicular cancer may be symptomless. When symptoms do occur they include -

- Lump on the testicle
- Slight enlargement of one of the testes
- Heavy sensation in testicles or groin

If you find any hard lumps or nodules, please see your doctor promptly. Only a doctor can make a diagnosis (LGBT, 2014c).

Women's Health

Breast Self-Exam

Breast self-examination BSE[143] is one of three ways to detect breast cancer. The best cancer check is a breast x-ray or mammogram. The third best way is a clinical breast exam. See also Breast Self Examination.

BSE is easy to do. Knowing how your breasts look and feel will help you notice any changes. Early detection is the key to successful treatment.

BSE should be done monthly. Check your breasts about one week after your period. If you don't have regular periods, do it at the same time every month.

American Cancer Society Guidelines for Early Detection

Breast Self-Exam Optional, but provides an opportunity to know more about your body and your breasts.

Clinical Exam See a doctor or nurse for a physical breast exam. It should be part of a woman's periodic health examination. A clinical breast exam should occur about every 3 years for women in their 20s & 30s and annually for women over 40.

[143] Breast self-examination

Mammography Women should have a baseline mammogram by age 40 and then once every year.

How to Examine Your Breasts Lie down with a towel under your right shoulder, then raise your right arm above the head. Examine area from -

- underarm to lower bra line,
- across to breast bone,
- up to collar bone,
- back to armpit.

Use the pads of the three middle fingers of the left hand. Hold hand in bowed position. Move fingers in dime-sized circles. Use three levels of pressure -

- light,
- medium,
- firm.

Examine the entire area using a vertical strip pattern.

Now check your left breast with your right hand in the same way. If there are any lumps, knots or changes, tell your doctor right away.

Look for any changes With your hands at your sides. Compare both breasts for symmetry.

Look for changes in -

- shape,
- colour

Check for -

- puckering
- dimpling
- skin changes
- nipple discharge

With your hands over your head. Check the front and side.

Look for -

- symmetry
- puckering
- dimpling

With your hands on your hips, press, down, bend forward.

Check for -

- symmetry
- nipple direction
- general appearance (LGBT, 2014c)

Shared Care

This is where a GP will prescribe medications with a consultant (normally a psychiatrist in our case) taking full clinical responsibility for the treatment. Normally the consultant will/may prescribe the medications, and if he is acting for you in a private capacity, your GP may convert the prescription to a NHS[144] one (which works out cheaper for you at the pharmacists); however, they are under no legal obligation to do so.

Shrinking Testicles!

They'll shrink considerably as the cells die, down to $\frac{1}{4}$ to $\frac{1}{2}$ of their original size.

Although I do not have direct experience of this, I believe that when the testicles start to shrink, that this shrinkage may cause some pain. But not everyone experiences this pain or discomfort, so YMMV.

Sitting down?

Are you sitting down and sitting comfortably? And have you been sitting down for several hours? Well, getting up and walking for 2 minutes every hour could help reverse the negative health effects from prolonged sitting, new research suggests. This research analyzed data from 3,243 people who participated in the U.S. National Health and Nutrition Examination Survey and the participants were followed in this study for three years.

The researchers found that standing more may not be enough to offset the dangers of sitting for too long, but short bursts of light activities, such as walking, cleaning and gardening, can boost the longevity of people who are sedentary for more than half of their day.

Moreover, trading 2 minutes of sitting for 2 minutes of light-intensity activity each hour lowered the risk of premature death by 33%, according to the data.

"Based on these results, we would recommend adding 2 minutes of walking each hour in combination with their normal activities, which should include 2.5 hours of moderate exercise each week," stated Professor Beddhu, the lead researcher (Beddhu et al., 2015).

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[144] The UK-wide National Health Service

Skin care

One of the unfortunate side-effects with us taking HRT is that the skin thins, and tends to lose some of the subcutaneous fat, making it more liable to tear easily. This also happens as we age, and there is no way of reversing this, so we must find some form of skin care that helps our skin, so here it is.

The skin is the largest organ in the human body and one of the beautiful things about it is that it shows what is going on inside. The first thing to do for the skin is to make sure that you eat the right foods, drink a lot of water and also, have a good skincare regimen.

Skin type and treatments

There are five general skin types -

- Oily Skin,
- Dry Skin ,
- Normal Skin,
- Combination Skin, and
- Sensitive Skin.

Sensitive skin may be combined with any one of the aforementioned types. Especially with dry skin so always go for products with the sensitive label.

Dry Skin

If your skin tends to have an old appearance, looks ashy or feels tight, then it is considered dry. In more extreme cases, dry skin lacks elasticity and can be extremely sensitive to the sun, wind, and cold temperatures. Since you have dry skin, you have to make sure that you do not expose your skin to extreme weather for long periods of time and always moisturise.

Treatment

Find a moisturising bath soap or body wash with natural oils like almond, coconut or olive oil. Any other oil of your choice is ok if you have preference.

Weekly treatments are recommended for your skin. Fill a tub with honey, milk and half a cup of any nourishing oil and add boiling hot water to the mix. Wait for it is cool to your desired temperature then soak for as long as you want; the longer the better. For ladies, make sure to exfoliate every other day and always wash your makeup off. Since you have dry skin, exfoliate gently and every two days and moisturize every morning and night before bed. For makeup, make sure to use only the ones with natural products.

Oily Skin

If your sebaceous glands are always on the fritz and your face looks as though you swam across the Olive Oil Ocean, then you have oily skin. Chances are, you tend to break out easily into spots. Whenever you do, do not prick your pimples or blackheads.

Treatment

Your skin tends to attract more dirt than dry skin, so wash your face twice a day with a good oil eliminating face scrub and warm water.

Normal Skin

Some consider normal skin to be combination skin, but it is not. If your skin is oily in the "T zone" and your nose while dry and taut on the cheeks, it is considered normal. It's also considered normal if it changes with seasons (dryer in winter, oilier in summer). Normal skins can also be 'Normal-To's' as in normal to oily or normal to dry.

Treatment

Wash your face with cleansers that are designed for your normal/normal-to skin type. Wipe an alcohol free, hydrating toner all over the face. Apply moisturiser more frequently to dry skin.

Combination Skin

Combination skin is comprised of two extreme skin types on one face. These situations occur when there is acne and a lot of oil in one area when the rest of the skin is generally dry (no oil).

Two common examples are dry skin with papular and pustular acne on the cheeks or a normal skin with inflamed papular and pustular acne in the chin and mouth area.

Treatment

Tend to each area appropriately as described above. If the acne is severe, consult a dermatologist.

Sensitive Skin

Please note that you may have sensitive skin and normal, oily, or dry. If your skin has allergic reactions to beauty products and is usually sensitive to the sun, wind, and cold weather, it is sensitive. Sensitivity can show up in rash, redness, inflammation, acne, and dilated capillaries.

Treatment

Look for cleansers, toners, makeup, and moisturisers that are fragrance-free and hypoallergenic. Cleanse, tone and moisturise with gentle products everyday. The idea for your skin is to always choose products with a soothing benefit. Some common ingredients to look for are: chamomile, azulene, bisabolol, allantoin, lavender, camphor, calamine, rosemary, thyme, aloe vera, coconut oil etc.

General skin care for all skin types

Prevent sun damage

Sunscreen is the real fountain of youth. Get into the habit of applying sunscreen or a lotion with minimum SPF 15 to 30 protection daily. Remember that the sun's rays can still be damaging in winter months as it reflects off snow. If you don't like taking the time to put on both moisturiser and sunscreen, buy a moisturiser with sunscreen.

Wash your face in the morning and in the evening

This is a vital step and you must remember to do this. Use a facial cleanser to wash your face with and a flannel or a sponge. Washing your face with a cleanser helps you get rid of any spots.

Exfoliate

Never use walnut shells as they will cause micro tears. Avoid plastic microbeads as they pollute the environment and bioaccumulate up the food chain to fish. Experiment to discover what works for you.

Live a healthy lifestyle

Quit smoking. Few common items age the skin as effectively as tobacco. Eat a healthy diet which includes many fruits and vegetables. Reduce stress when possible.Use a moisturiser. Using one will replace the moisture and natural minerals that you have washed away when washing your face.

Drink plenty of water

This will keep you hydrated. If you don't, your body will suck out the moisture from your skin and give it to your body. This will dry out your skin and may cause spots and encourage outbreaks of pimples.

Eat plenty of vitamin C enriched foods

For example, strawberries, bananas, and other common fruits are high in vitamins E, D and C.

Make sure you get a lot of exercise in the week

Make sure you break out into a sweat every now and then.

Get enough sleep

Teenagers need around 8–10 hours and adults usually need around 8 hours of sleep. Not getting enough sleep will make you feel tired throughout the day and will also give you bags under your eyes which won't make it a healthy looking skin.

Reconsider your makeup routine

Although it looks as if your skin is healthy, makeup can give you spots and can encourage a load of outbreaks of pimples. Make sure the make-up you use is formulated to avoid clogging pores.

Remove makeup before you go to bed

Sleeping with your makeup still on leads to bacteria build up, breakouts, and enlarged pores (Chan, 2015). If you are feeling lazy, makeup removal wipes will do the job just fine.

- Have a bag of makeup removal wipes on your bed table if you feel like you are going to forget.

Sanitise your tools

Wash your makeup brushes daily with lukewarm water and baby shampoo and softly towel dry with a clean piece of cloth. You can also sanitise afterwards by spraying methylated spirits on your clean brushes.

- You can find empty small spray bottles at the poundstore.

DIY Skin Care Remedies

Some cheap home remedies

Masks work wonders! 20 minutes a day of full fat Greek style yogurt on your face will BEGIN to clear up dark spots and pimples within a week for most people. After about a month, you will have glowing skin. Bonus, put the mask on your lips as well and it will get rid of flaky skin there. Just make sure you stick to it daily, and be sure to moisturise afterwards.

Wash your face with oatmeal

Oatmeal is a great way to combat acne, rashes, and flakiness. Any brand of plain oatmeal will do, just take a fistful and hold it under warm water for two or three minutes, then massage into wet skin for about a minute and rinse off. The oatmeal should not feel rough like you're scrubbing your skin.

Make a honey face mask

Honey is also a great mask. A thin layer left on the face for 20 minutes will add glow and moisture, and is also good against acne.

Skip the shower, take a bath

If you can take a bath, that's a great way to provide skin care as well. Try exfoliating in the shower and then sitting in the tub, as any treatment you do will sink in better. Cold water tightens your skin.

Try some whole milk to remove dead skin

Whole milk is really great at removing old skin because of the lactic acid. Pour it directly into a hot bath. It is a bit drying, so don't stay more than 20 minutes and be sure to moisturise afterwards.

Use coconut milk in your bath

Coconut milk is really soothing on sunburn and a great moisturiser.

Use oils to moisturise your skin

Moisturising your skin is very important, and a number of natural oils mimic the proteins and fats in your body so they are particularly good. Some of the best are: vitamin E oil (read the label to make sure you're getting as pure oil as possible, as some brands mix it with other oils), jojoba oil (safe for face as well!), coconut oil, and shea butter. Olive oil (yes, the stuff for cooking) is great for some skin, but actually causes flaking for other people, so just pay attention to what your body does if you try it. If you live in a really wintry place, petroleum jelly is good to seal in moisture, but not as a moisturiser itself.

Try a spa day

Most spas will let you use their facilities without getting a pricey treatment, so if you want to occasionally try a hot tub or steam room, or even go Eastern European style with a cold plunge and then a sauna to invigorate your skin, sweat out toxins, and improve circulation, it's totally doable and you might like it!

Tips

- Avoid stretching or pulling on the delicate skin near your eyes when putting on creams or cosmetics. This delicate area shows age markings like wrinkles much sooner than it should when subjected to too much rough handling.
- You may be able to improve your skin by taking care of your body such as with good hygiene, nutrition and exercise. Practice good hygiene such as taking showers with mild soap to reduce microbe count on skin. Occasionally use a strong bar soap strong enough the get rid of most microbes and rinse off soap well. Use exercise such as walking to reduce cellulite and improve muscle tone.
- Carefully choose your facial scrub to match your pore size. The type and size of the grains in the face scrub can actually make the difference between exfoliated and irritated skin. Larger grains are more abrasive while tinier beads are more gentle.
- Wash all cosmetics off as soon as you know you will not be going out again and avoid wearing cosmetics whenever possible to give your skin a rest.
- Avoid touching your skin with high force or avoid scratching your skin as much as possible.

- Lemon juice works well for reducing scars and making them lighter.
- Make sure you are getting a lot of vitamins, and eating healthy foods. Water is really effective too for skin.
- Make sure you drink a lot of water so your skin won't look dry.
- Vitamins are essential for healthy skin, especially vitamins A, B,and C. Vitamin E helps to improve the complexion when applied externally.
- Washing your face with mild soap during the day cleans your skin from the dirt that causes black heads and pimples, although washing a lot may cause dryness. Note that you should visit a dermatologist to check your face if mild soap can be applicable to your skin.
- Never pick at a blemish. Many poor results come of picking at breakouts, such as scarring, infection, or permanent enlargement of the pore. You are also more likely to get another breakout in the same place over time.
- Clean your mobile and any other device that may come in contact with your skin.
- Make sure to clean your face daily for oily skin. If after using facial cleanser and it feels tight, then you're using something too strong.
- Change the applicators and clean the brushes you use to apply make-up on a consistent basis. Bacteria and oils can build up in these places and then be spread back on the skin each time make-up is applied.
- Never coat your entire face in foundation. Chances are, you only need a little bit in areas you are most self-conscious in.
- Oil blotting sheets can help absorb oil through the day so you are not tempted to re-apply powder or foundation, or over wash your face.
- If you're sunburned, apply some plain yogurt mixed with aloe vera gel on your skin. That will smooth the irritated skin.
- Washing your face with a mixture of brown sugar and a few drops of milk (enough to form a mud-like consistency) washes away dirt and excess oil, leaving your skin feeling smooth and refreshed. This scrub can be left on your face for as long as you like.
- Never go to bed while wearing makeup. Clean it with wipes or just wash your face with water.
- Do not try chemical products unnecessarily because they can be harmful.
- Use homemade masks to moisturise your skin. They're easy to make, and they really work! For instance, a mixture of grapes, lemon and egg white is very helpful for oily skin and honey promotes the healing of ulcers and burns. Fresh herbs ground into a paste and applied to problem skin may also help reduce skin problems.
- Wash your pillowcase often and avoid wearing hair products to bed. The combination of hair products and facial oils on the pillowcase can cause blemishes.
- If your skin gets a little stressed though e.g. due to plenty of sun, try Aloe Vera Gel with at least 90% pure aloe barbadensis leaf juice in it. Aloe vera is known for healing properties and can do wonders for the skin.

- As good as a hot shower or bath feels, it can remove natural oils from your skin cause it to be dry and glow less. Instead, take a lukewarm bath or shower and before exiting stand under cold water for 5-10 seconds. This will leave your skin glowing and the natural oils and vitamins in your skin will stay.
- Use a good moisturiser right after a shower if you have dry skin. Drink loads of water.
- Wash your face every day and night, also make sure you get the make up off your face. Especially under your eyes.

Warnings

- Never allow anyone to 'pop' or otherwise break open a blemish, not even your mum! This is a very unsafe practice as bacteria and germs can enter through the broken skin. And if you do 'pop' a blemish add alcohol to reduce the chance of infection.
- Over washing skin can make it red and sore. It can also damage the skin.
- Use caution when using any product containing acids or peroxides such as acne creams and fade creams. These increase the skins' sensitivity to sun and may cause redness and peeling.
- Toner can dry out skin if used too often.
- Choose a sunblock specifically meant for your face as some sunblocks can cause breakouts on some skin types.

Sleep

Sleep is very important for us as it helps our bodies cope with the stresses and strains of daily life, which are increased when we take exogenous hormones, i.e. hormones that are not produced by our bodies. But, unfortunately, we live in the country with the highest prevalence of non-restorative sleep[145] in Europe. The UK has the highest prevalence, followed by Germany, and with Spain in the lowest place.

The most important factors positively associated with non-restorative sleep were younger age, dissatisfaction with sleep, difficulty getting started in the morning, stressful life, presence of anxiety, bipolar or depressive disorder, and having a physical disease (any of these sound familiar? :) When compared with those who had difficulty in initiating or maintaining sleep, but without non-restorative sleep, those with non-restorative sleep

[145] sleep which does not leave you feeling refreshed

more often reported a variety of daytime impairments, such as irritability, physical and mental fatigue. Those with non-restorative sleep consulted a doctor twice as frequently for their sleeping difficulties than did those with insomnia (Ohayon, 2005).

Sleep is defined as a state of unconsciousness from which a person can be aroused. In this state, the brain is relatively more responsive to internal stimuli than external stimuli. Sleep should be distinguished from coma. Coma is an unconscious state from which a person cannot be aroused. Sleep is essential for the normal, healthy functioning of the human body. It is a complicated physiological phenomenon that scientists do not fully understand.

Historically, sleep was thought to be a passive state. However, sleep is now known to be a dynamic process and our brains are active during sleep. Sleep affects our physical and mental health and is essential for the normal functioning of all the systems of our body, including the immune system. The effect of sleep on the immune system affects one's ability to fight disease and endure sickness.

States of brain activity during sleep and wakefulness result from different activating and inhibiting forces that are generated within the brain. Neurotransmitters (chemicals involved in nerve signaling) control whether one is asleep or awake by acting on nerve cells (neurons) in different parts of the brain. Neurons located in the brainstem actively cause sleep by inhibiting other parts of the brain that keep a person awake.

Sleep is prompted by natural cycles of activity in the brain and consists of two basic states: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep, which includes Stages 1 through 4.

During sleep, the body cycles between non-REM and REM sleep. Typically, people begin the sleep cycle with a period of non-REM sleep followed by a very short period of REM sleep. Dreams generally occur in the REM stage of sleep.

Sleep problems can affect women at different times, but are especially common in perimenopausal women and increase after age 40. Not being able to sleep or insomnia can be associated with a variety of factors including stress, mental health problems, disease, increased use of medications and hormone imbalances. A good nights sleep can help you maintain energy, rebalance hormones and ward off infections and illness (womeninbalance.org, 2016a).

What to do?

Keep good sleep hygiene - or sleep habits - at night. These include -

- Set a bedtime and wake up time,
- Avoid caffeine and alcohol before bed,
- Avoid naps longer than 30 min during the day,

- Establish a pre-sleep ritual,
- Avoid stimulation or bright lights right before bed,
- Exercise regularly (womeninbalance.org, 2016a).

Importance of sleep

Animal studies have shown that sleep is necessary for survival. The normal life span of rats is 2 to 3 years. However, rats deprived of sleep live for only about 3 weeks. They also develop abnormally low body temperatures and sores on their tails and paws. The sores probably develop because of impairment of the rats' immune systems.

In humans, it has been demonstrated that the metabolic activity of the brain decreases significantly after 24 hours of sustained wakefulness. Sleep deprivation results in a decrease in body temperature, a decrease in immune system function as measured by white blood cell count (the soldiers of the body), and a decrease in the release of growth hormone. Sleep deprivation can also cause increased heart rate variability.

For our nervous systems to work properly, sleep is needed. Sleep deprivation makes a person drowsy and unable to concentrate the next day. It also leads to impairment of memory and physical performance and reduced ability to carry out mathematical calculations. If sleep deprivation continues, hallucinations and mood swings may develop.

Release of growth hormone in children and young adults takes place during deep sleep. Most cells of the body show increased production and reduced breakdown of proteins during deep sleep. Sleep helps humans maintain optimal emotional and social functioning while we are awake by giving rest during sleep to the parts of the brain that control emotions and social interactions.

Stages of Sleep

As mentioned earlier, sleep is a dynamic process. There are two distinct states that alternate in cycles and reflect differing levels of neuronal activity. Each state is characterized by a different type of brain wave (electrical activity that is recorded with the help of electrodes placed on the skull) activity. Sleep consists of nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM is further subdivided into the following four stages:

- Stage I (light sleep)
- Stage II
- Stage III & IV (deep sleep)

The stages of NREM sleep and REM sleep cycle over and over again during a night's sleep. Stages I, II, III, and IV are followed by REM sleep. A complete sleep cycle, from the beginning of stage I to the end of REM sleep, usually takes about one and a half hours.

For the purpose of analysis, a night's sleep is divided into three equal time periods: Sleep in the first third of the night, which comprises the highest percentage of NREM; sleep in the middle third of the night; and sleep in the last third of the night, the majority of which is REM. Awakening after a full night's sleep is usually from REM sleep.

NREM Sleep

Stage I is a stage of light sleep and is considered a transition between wakefulness and sleep. During this stage, the muscles begin to relax. It occurs upon falling asleep and during brief arousal periods within sleep, and usually accounts for 5% to 10% of total sleep time. An individual can be easily awakened during this stage.

Stage II occurs throughout the sleep period and represents 40% to 50% of the total sleep time. During stage II, brain waves slow down with occasional bursts of rapid waves. Eye movement stops during this stage.

In stage III, extremely slow brain waves called delta waves begin to appear. They are interspersed with smaller, faster waves. In stage IV, delta waves are the primary waves recorded from the brain. These two stages are distinguished from each other only by the percentage of delta activity. Together they represent up to 20% of total sleep time. Stages III and IV are called deep sleep, during which all eye and muscle movement ceases. It is difficult to wake up someone during these two stages. If someone is awakened during deep sleep, he does not adjust immediately and often feels groggy and disoriented for several minutes after waking up. Some children experience bedwetting, night terrors, or sleepwalking during deep sleep.

REM Sleep

REM sleep represents 20% to 25% of the total sleep time. REM sleep follows NREM sleep and occurs four to five times during a normal 8 to 9-hour sleep period. The first REM period of the night may be less than 10 minutes in duration, while the last may exceed 60 minutes. In a normal nights sleep, bouts of REM occur every 90 minutes.

When the person is extremely sleepy, the duration of each bout of REM sleep is very short or it may even be absent. REM sleep is usually associated with dreaming. During REM sleep, the eyeballs move rapidly, the heart rate and breathing become rapid and irregular, and the blood pressure rises.

The muscles of the body are virtually paralyzed. The brain is highly active during REM sleep, and the overall brain metabolism may be increased by as much as 20%. The electrical activity recorded in the brain during REM sleep is similar to that which is recorded during wakefulness.

Sleep at Different Stages of Life

Infancy

Infants have an overall greater total sleep time than any other age group. Their sleep time can be divided into multiple periods. In newborns, the total sleep duration in a day can be 14 to 16 hours. Over the first several months of life, sleep time decreases; by age 5 to 6 months, sleep consolidates into an overnight period with at least one nap during the day.

REM sleep in infants represents a larger percentage of the total sleep at the expense of stages III and IV. Until age 3 to 4 months, newborns transition from wakefulness into REM sleep. Thereafter, wakefulness begins to transition directly into NREM sleep.

Adulthood

In adults, sleep of 8 to 8.4 hours is considered fully restorative. In some cultures, total sleep is often divided into an overnight sleep period of 6 to 7 hours and a nap of 1 to 2 hours.

Some people may need as little as 5 hours or as much as 10 hours of sleep every day. The period of time a person sleeps depends also on the fact whether he or she has been deprived of sleep in previous days. Sleeping too little creates a "sleep debt." This debt needs to be adjusted by sleeping for longer periods over the next few days. People who sleep less have an impairment of judgment and reaction time.

Old age

People tend to sleep more lightly and for shorter periods as they get older. In elderly persons, the time spent in stages III and IV decreases by 10% to 15%, and the time in stage II increases by 5% compared to young adults, representing an overall decrease in total sleep duration.

Time taken to fall asleep and the number and duration of overnight arousal periods increase. Thus, to have a fully restorative sleep, the total time in bed must increase. If the elderly person does not increase the total time in bed, complaints of insomnia and chronic sleepiness may occur.

Sleep fragmentation results from the increase in overnight arousals and may be exacerbated by the increasing number of medical conditions related to old age, including sleep apnoea (interrupted breathing during sleep), musculoskeletal disorders, and cardiopulmonary disease.

Circadian Rhythms That Influence Sleep

Biological variations that occur in the course of 24 hours are called circadian rhythms. Circadian rhythms are controlled by the body's biological clock. Many bodily functions follow the biologic clock, but sleep and wakefulness comprise the most important circadian rhythm. Circadian sleep rhythm is one of the several body rhythms modulated by the hypothalamus (a part of the brain).

Light directly affects the circadian sleep rhythm. Light is called a "zeitgeber", a German word meaning time-giver, because it sets the biological clock. A practical purpose has been proposed for the circadian rhythm, using the analogy of the brain being somewhat like a battery charging during sleep and discharging during wakefulness.

Body temperature cycles are also under control of the hypothalamus. An increase in body temperature is seen during the course of the day and a decrease is observed during the night. The temperature peaks and troughs are thought to mirror the sleep rhythm. People who are alert late in the evening (evening types) have body temperature peaks late in the evening, while those who find themselves most alert early in the morning (morning types) have body temperature peaks early in the evening.

Melatonin (a chemical produced by the pineal gland in the brain) has been implicated as a modulator of light entrainment. It is secreted maximally during the night. Prolactin, testosterone, and growth hormone also demonstrate circadian rhythms, with maximal secretion during the night.

Circadian rhythms can be affected to a certain degree by almost any kind of external stimulus, for example, the beeping of the alarm clock or the timing of meals. When we cross time zones, our circadian rhythms get disrupted leading to jet lag. It usually takes several days for our body rhythms to adjust to the new time.

Symptoms similar to those seen in people with jet lag are common in people who work during nights or work in shifts. Because these people's wake time conflicts with powerful sleep-regulating cues like sunlight, they often become uncontrollably drowsy during work or may have difficulty falling asleep during their off time. Their biological clock wants to do one thing while they are doing something entirely different. People working in shifts have an increased risk of heart, gastrointestinal, emotional, and mental problems. All these problems may be related to the disruption of the circadian sleep rhythm.

Substances That Alter Sleep

Sleep and wakefulness are influenced by different neurotransmitters in the brain. Some substances can change the balance of these neurotransmitters and affect our sleep and wakefulness. Caffeinated drinks (for example, coffee) and medicines (for example, diet pills) stimulate some parts of the brain and can cause difficulty in falling asleep. Many drugs prescribed for the treatment of depression suppress REM sleep.

People who smoke heavily often sleep very lightly and have reduced duration of REM sleep. Heavy smokers tend to wake up after 3 or 4 hours of sleep due to nicotine withdrawal. Some people who have insomnia may use alcohol. Even though alcohol may help people to fall into light sleep, it deprives them of REM sleep and the deeper and more restorative stages of sleep. Instead, it keeps them in the lighter stages of sleep from which they can be awakened easily.

During REM sleep, we lose some of our ability to regulate our body temperature. Therefore, abnormally hot or cold temperatures can disrupt our REM sleep. If our REM sleep is disturbed, the normal sleep cycle progression is affected during the next sleeping time and there is a possibility of slipping directly into REM sleep and going through long periods of REM sleep until the duration of REM sleep that is lost is caught up.

Sleep Deprivation

Because the function of sleep has not been fully determined, the exact number of hours that a person should sleep is unknown. Some people claim to work optimally with only 3 to 5 hours of sleep per night, while some admit needing at least 8 hours of sleep per night (or more) to perform effectively. Therefore, sleep deprivation is best defined by group means and in terms of the tasks impaired.

In tasks requiring judgment, increasingly risky behaviours emerge as the total sleep duration is limited to 5 hours per night. The high cost of an action is seemingly ignored as the sleep-deprived person focuses on limited benefits. These findings can be explained by the fact that metabolism in the prefrontal and parietal associational areas of the brain decrease in individuals deprived of sleep for 24 hours. These areas of the brain are important for judgment, impulse control, attention, and visual association.

Sleep deprivation is a relative concept. Small amounts of sleep loss (for example, 1 hour per night over many nights) produce subtle cognitive impairment, which may go unrecognized. More severe restriction of sleep for a week leads to profound cognitive deficits, which may also go unrecognized by the individual. If you feel drowsy during the day, fall asleep for very short periods of time (5 minutes or so), or regularly fall asleep immediately after lying down, you are probably sleep-deprived.

Many studies have made it clear that sleep deprivation is dangerous. With decreased sleep, higher-order cognitive tasks are impaired early and disproportionately. On tasks used for testing coordination, sleep-deprived people perform as poorly as or worse than people who are intoxicated. Total sleep duration of 7 hours per night over 1 week has resulted in decreased speed in tasks of both simple reaction time and more demanding computer-generated mathematical problem solving. Total sleep duration of 5 hours per night over 1 week shows both a decrease in speed and the beginning of accuracy failure.

Total sleep duration of 7 hours per night over 1 week leads to impairment of cognitive work requiring simultaneous focus on several tasks. In driving simulations, for example, accidents increase progressively as total sleep duration is decreased to 7, 5, and 3 hours per night over 1 week. Driver fatigue is responsible for an estimated 100,000 motor vehicle crashes and 1,500 deaths each year, according to the National Highway Traffic Safety Administration.

Since drowsiness occurs just before falling asleep, driving while drowsy often leads to disaster.

According to the National Sleep Foundation *"If you have trouble keeping your eyes focused, if you can't stop yawning, or if you can't remember driving the last few miles, you are probably too drowsy to drive safely."* It is important to know that caffeine and other stimulants cannot overcome the effects of severe sleep deprivation. Therefore, if you find yourself driving in a sleep-deprived state, it is imperative that you find a safe place to stop and catch up on your sleep before continuing safely on your way (Russo and Shaikh, 2014).

It seems therefore that at times of growth or restoration, for example, starting taking hormones for the first time, or post-operatively, our bodies need more time for S-sleep and also for D-sleep, and we should therefore listen to our bodies and get more sleep. Sounds obvious doesnt it, but I hope that this helps to explain why.

Smoking and taking hormones

In 2005 it was stated *"it has been proven that, depending on the type, duration and intensity of nicotine consumption, smoking can reduce or completely cancel the efficacy of orally administered oestrogens. Not only does smoking diminish the otherwise well-established beneficial effects of oestrogen on hot flashes and urogenital symptoms and its positive effects on lipid metabolism, i.e. by reducing cholesterol, but smoking also specifically reduces oestrogens ability to prevent osteoporosis"* (A. Mueck and H Seeger, 2005).

By giving up smoking you also reduce the risk of respiratory, cardiovascular and gastrointestinal disorders (Haslett, 1996), and although the risks of smoking are now well known, if we are taking hormones and smoking, we are increasing the chances of us having problems. Would it not be better to either cut down our smoking, or better still, give up? Only you can decide.

Sperm banking

Some transwomen may decide to bank their sperm before they start oestrogen treatment, and they become infertile. So you may find that you have to pay a private company to do this. Prices can vary, but on average it will cost £200 - £400 to have your sperm extracted and frozen, plus a further £125 a year to store the sperm (NHS, 2014m).

You need to be aware that the legal maximum age a man can donate or bank his sperm is 41, this was laid down by the Human Fertilisation and Embryology Authority (HFEA) in 2012. This was apparently as beyond age 41 the sperm quality tends to decrease and diminish.

According to Dr. Silber, of St Luke's Infertility Hospital in the US, "Men experience an age-related decrease in testicular size and in sperm production. In some men, there is a decline in testosterone production and a decreased ability of the body to produce and mature sperm cells, which becomes noticeable after the age of 40"

It is also known that as men age, sperm cells can accumulate mutations that are passed to offspring. Regardless of age, sperm continues to reproduce through division. If a sperm becomes altered or mutates, any other sperm that is produced by the natural division will also be altered or mutated. Each successive division introduces a slight risk of error in the genetic material of the new sperm, which is passed on to the children (LSB, 2014).

Stopping hormones prior to surgery

Much discussion occurs in various forums about the discontinuing of hormone therapy prior to SRS surgery. Doctor Eugene Schrang of Neenah, Wisconsin, USA., says that when the genetic female undergoes routine surgery, nature has provided protective mechanisms (which are not yet properly understood) against the formation of thrombotic emboli (which can cause DVT's and/or pulmonary emboli) that are not present in the genetic male taking female hormones. Therefore, even though the

likelihood of this eventuality is remote, he recommends, that you stop taking hormones three weeks prior to and three weeks after any surgery! Withdrawal symptoms may be uncomfortable, but temporary, and are preferable to dying.

Most surgeons have a similar policy but with slightly differing time-scales.

Also, at some stage surgery will be required, whether its SRS, breast augmentation, or some gender unrelated surgery. The current medical trend by the surgeons in the UK seems to be to stop all hormonal intake 6 weeks prior to surgery. However, the doctors own drug reference book suggests *"Oestrogen-containing oral contraceptives should preferably be discontinued 4 weeks before major elective surgery and all surgery to the legs"* (BNF, 2016a).

But the East Cheshire NHS Trust have gone one step further and seem to be more enlightened, by saying *"For minor surgery or those which will not immobilise the patient post-op, for surgery which has had a high thrombotic risk e.g. major joint surgery/prev VTE or any surgical procedure which will immobilise patients - to stop Combined Oral Contraceptive one day pre-op"* (Debray, Razzaq-Sheikh, and Littlewood, 2014)

They go on to say *"Oral progestogen-only contraceptives (Femulen, Micronor, Microval, Neogest, Norgeston, and Noriday) may be continued as there is no increased risk of thromboembolism. This also applies to the progestogen-only depot contraceptives (Depo-Provera, Noristerat). Stopping the combined oral contraceptive (COC) before major surgery is a controversial issue. The risk of postoperative VTE increases from 0.5–1% for pill users versus non users. This small excess risk in COC must be balanced against the risks of stopping the pill 4-6 weeks prior to surgery, including unwanted pregnancy, the effects of surgery and anaesthesia on a pregnancy, and the risk of a subsequent termination.(SIGN, 2002) Therefore in East Cheshire based on specialist opinion it is advised that for minor procedures where mobility will not be an issue to continue. However for surgery which has had a high thrombotic risk e.g. major joint surgery/prev VTE or any surgical procedure which will immobilise patients it is advised to stop the combined oral contraceptive pill one day pre-op and to restart on discharge ensuring patient takes extra contraceptive precautions as per British National Formulary (BNF)*[146] *recommendations"* (SIGN, 2002).

If you have been prescribed aspirin then this may be of interest for you. According to an Irish study, aspirin should be stopped five days before elective surgery (Redmond, 2005).

[146] British National Formulary

Hormone Replacement Therapy

Taking HRT[147] is likely to increase the risk of post-operative venous thromboembolism but this risk has not been well quantified. Current advice regarding continuing or stopping HRT is conflicting, with the BNF advising stopping HRT (Sridhar and Grigg, 2000) and specialist groups advising continuing (Kearon and Hirsh, 1997). Most women on HRT are likely to have additional risk factors for thromboembolism which in themselves necessitate use of peri-operative thromboprophylaxis. New guidance from Royal College of Obstetricians (RCOG, 2011) recommends stopping HRT pre-op (SIGN, 2002).

Peri-operative drug management

Evidence collected by the National Confidential Enquiry into Peri-operative Deaths (NCEPOD) suggests that peri-operative drug management is not currently optimal and omission of important medication may contribute to post operative mortality. Omission of regular drug therapy may cause exacerbation of the underlying pathology or withdrawal symptoms which may compromise patient outcome. NCEPOD suggests that patients do not receive essential medication pre-op owing to staff misinterpreting the term "nil by mouth" (NBM) (Phillips, Hutchinson, and T. Davidson, 1993) (SIGN, 2002).

What does NBM mean?

"NBM" is medico-nursing terminology for "nil-by-mouth", meaning no solid food or liquids to be eaten or drunk for a period of time. This time in the UK is summarised here -

Clear fluids (water/squash) - none in the 2 hours prior to surgery (except for 30mL to administer medication.

Food (includes milk) - none in the 6 hours prior to surgery.

Medicines - regular medication should be administered up to 1 hour prior to surgery with 30mls of water unless they need to be withheld (SIGN, 2002).

[147] Hormone Replacement Therapy

Stress management

There are many articles in magazines and newspapers about 'Stress Management'. There are many books, CD's, DVD's, websites, seminars, all about 'Stress Management'. In fact, 'Stress Management' is a major industry in the 21st Century!

So let's break it down into its component parts, and find out how we can do it easily, and cheaply. It doesn't need to have lots of time and money thrown at it, it just needs a bit of fore-thought and care to establish a routine that will help us in 'Stress Management', and make it take a back-seat in our lives, and to be able to deal with it without it needing to be capitalised. It's just something we do that helps us to manage our daily stress levels.

In looking at the causes of stress, remember that your brain comes hard-wired with an alarm system for your protection. When your brain perceives a threat, it signals your body to release a burst of hormones to fuel your capacity for a response. This has been labeled the "fight-or-flight" response.

Once the threat is gone, your body is meant to return to a normal relaxed state. Unfortunately, the nonstop stress of modern life means that your alarm system rarely shuts off.

That's why stress management is so important. Stress management gives you a range of tools to reset your alarm system.

Without stress management, all too often your body is always on high alert. Over time, high levels of stress lead to serious health problems. Don't wait until stress has a negative impact on your health, relationships or quality of life. Start practicing a range of stress management techniques today.

Evaluate how you react to stress

Stress management skills often don't come naturally. You can learn new stress management skills or modify your existing stress management skills to help you cope better, though.

First, take a look at how you react to stress. Some people seem to take everything in stride. Their naturally laid-back attitudes shine through, even in stressful situations. Another deadline? Bring it on. The dishwasher is leaking? No problem, it'll be a simple repair. Others get anxious at the first sign of a stressful situation. Running late for a meeting? Time to panic! Stuck in a traffic jam? Let the cursing begin!

Here are some common but unhealthy reactions to stress. Do any of these describe your reactions? If you're not sure, consider keeping a daily journal for a week or so to monitor your reactions to stressful situations (mayoclinic, 2013d).

Pain - You may unconsciously clench your jaws or fists or develop muscle tension, especially in your neck and shoulders, all of which can lead to unexplained physical pain. Stress also may cause a variety of other health ailments, including upset stomach, shortness of breath, back pain, headaches and insomnia.

Overeating - Stress may trigger you to eat even when you're not hungry, or you may skip exercise. In contrast, you may eat less, actually losing weight when under more stress.

Anger - Stress may leave you with a short fuse. When you're under pressure, you may find yourself arguing with co-workers, friends or loved ones sometimes with little provocation or about things that have nothing to do with your stressful situation.

Crying - Stress may trigger crying bouts, sometimes seemingly without warning. Little things unrelated to your stress may leave you in tears. You also may feel lonely or isolated.

Depression - Sometimes stress may be too much to take. You might avoid the problem, call in sick to work, feel hopeless or simply give up. Chronic stress can be a factor in the development of depression or anxiety disorders.

Negativity - When you don't cope well with stress, you may automatically expect the worst or magnify the negative aspects of any undesirable situation.

Smoking - Even if you quit smoking long ago, a cigarette may seem like an easy way to relax when you're under pressure. In fact, stress is a leading cause of having a smoking relapse. You may also find yourself turning to alcohol or drugs to numb the effects of stress (mayoclinic, 2013d).

Two main types of stress

Stress is your body's reaction to the demands of the world. Stressors are events or conditions in your surroundings that may trigger stress. Your body responds to stressors differently depending on whether the stressor is new - acute stress - or whether the stressor has been around for a longer time - chronic stress (mayoclinic, 2013f).

Acute stress

Also known as the fight-or-flight response, acute stress is your body's immediate reaction to a perceived threat, challenge or scare. The acute-stress response is immediate and intense, and in certain circumstances it can be thrilling. Examples of acute stressors include having a job interview or getting a speeding ticket.

A single episode of acute stress generally doesn't cause problems for healthy people. However, severe acute stress can cause mental health problems, such as post-traumatic stress disorder, and even physical difficulties such as a heart attack (mayoclinic, 2013f).

Chronic stress

Mild acute stress can actually be beneficial - it can spur you into action, motivate and energise you. The problem occurs when stressors pile up and stick around. This persistent stress can lead to health problems, such as headaches and insomnia. The chronic-stress response is more subtle than is the acute-stress response, but the effects may be longer lasting and more problematic. See also Chronic stress.

Effective stress management involves identifying and managing both acute and chronic stress (mayoclinic, 2013f).

Know your stressors

Effective stress management starts with identifying your sources of stress and developing strategies to manage them. One way to do this is to make a list of the situations, concerns or challenges that trigger your stress response. You'll notice that some of your stressors are events that happen to you while others seem to originate from within (mayoclinic, 2013f).

External exasperations

External stressors are events and situations that happen to you. Some examples of external stressors include -

Major life changes - These changes can be positive - a new marriage, a planned pregnancy, a promotion or a new house. Or they can be negative - the death of a loved one or a divorce.

Environment - The input from the world around us can be a source of stress. Consider how you react to noises, such as a barking dog, or to too much or too little light in a room.

Unpredictable events - Out of the blue, uninvited houseguests arrive. Or you discover your rent has gone up or that your pay has been cut.

Workplace - Common stressors at work include an impossible workload, endless emails, urgent deadlines and a demanding boss.

Social - Meeting new people can be stressful. Just think about going on a blind date and you probably start to sweat. Relationships with family often spawn stress as well. Just think back to your last argument with your partner or child (mayoclinic, 2013f).

Strategies to manage external stressors include lifestyle factors such as eating a healthy diet, being physically active and getting enough sleep which help boost your resiliency. Other helpful steps include asking for help from others, using humour, learning to be assertive, and practicing problem-solving and time management.

Internal irritations

Not all stress stems from things that happen to you. Much of our stress response is self-induced. Those feelings and thoughts that pop into your head and cause you unrest are known as internal stressors. Examples of internal stressors include -

Fears - Common ones include fear of failure, fear of public speaking and fear of flying.

Uncertainty and lack of control - Few people enjoy not knowing or not being able to control what might happen. Think about how you might react when waiting for the results of a medical test.

Beliefs - These might be attitudes, opinions or expectations. You may not even think about how your beliefs shape your experience, but these preset thoughts often set us up for stress. Consider the expectations you put on yourself to create a perfect holiday celebration or advance up the career ladder (mayoclinic, 2013f).

The good news is that we have the ability to control our thoughts. The bad news is that our fears, attitudes and expectations have been our companions for a long time and it often takes some effort to change them. Strategies to manage internal stressors include reframing your thoughts, challenging negative thoughts, using relaxation techniques, and talking with a trusted friend or counselor (mayoclinic, 2013f).

Techniques

Once you've identified the unhealthy reactions you may be having to uncontrolled stress, you can begin to improve your stress management skills. Stress management techniques abound, including -

Scale back - Cut back on your obligations when possible. While it may seem easier said than done, take a close look at your daily, weekly and monthly schedule and find meetings, activities, dinners or chores that you can cut back on or delegate to someone else.

Prepare - Stay ahead of stress by preparing for meetings or trips, scheduling your time better, and setting realistic goals for tasks both big and small. Stress mounts when you run out of time because something comes up that you didn't account for - build in time for traffic jams, for example.

Reach out - Make or renew connections with others. Surrounding yourself with supportive family, friends, co-workers, or clergy and spiritual leaders can have a positive effect on your mental well-being and your ability to cope with stress. Volunteer in your community.

Take up a hobby - It may seem cliche, but when you engage in something enjoyable, it can soothe and calm your restless mind. Try reading, gardening, crafts, tinkering with electronics, fishing, carpentry, music things that you don't get competitive or more stressed out about.

Relax - Physical activity, meditation, yoga, massage and other relaxation techniques can help you manage stress. It doesn't matter which relaxation technique you choose. What matters is refocusing your attention to something calming and increasing awareness of your body.

Get enough sleep - Lack of sufficient sleep affects your immune system and your judgment and makes you more likely to snap over minor irritations. Most people need seven to eight hours of sleep a day.

Get professional help - If your stress management efforts aren't helpful enough, see your doctor. Chronic, uncontrolled stress can lead to a variety of potentially serious health problems, including depression and pain (mayoclinic, 2013d).

Stress usually doesn't just magically get better on its own. You may have to actively work on getting control of the stress in your life so that it doesn't control you. When you first identify how you react to stressful situations, you then can put yourself in a better position to manage the stress, even if you can't eliminate it. And if your current efforts at stress management aren't working, try something new (mayoclinic, 2013d).

Chronic stress

Your body is hard-wired to react to stress in ways meant to protect you against threats from predators and other aggressors. Such threats are rare today, but that doesn't mean that life is free of stress.

On the contrary, you undoubtedly face multiple demands each day, such as shouldering a huge workload, making ends meet and taking care of your family. Your body treats these so-called minor hassles as threats. As a result you may feel as if you're constantly under assault. But you can fight back. You don't have to let stress control your life.

Understanding the natural stress response

When you encounter a perceived threat - a large dog barks at you during your morning walk, for instance your hypothalamus, a tiny region at the base of your brain, sets off an alarm system in your body. Through a combination of nerve and hormonal signals, this system prompts your adrenal glands, located atop your kidneys, to release a surge of hormones, including adrenaline and cortisol.

Adrenaline increases your heart rate, elevates your blood pressure and boosts energy supplies. Cortisol, the primary stress hormone, increases sugars (glucose) in the bloodstream, enhances your brain's use of glucose and increases the availability of substances that repair tissues.

Cortisol also curbs functions that would be nonessential or detrimental in a fight-or-flight situation. It alters immune system responses and suppresses the digestive system, the reproductive system and growth processes. This complex natural alarm system also communicates with regions of your brain that control mood, motivation and fear.

When the natural stress response goes haywire

The body's stress-response system is usually self-limiting. Once a perceived threat has passed, hormone levels return to normal. As adrenaline and cortisol levels drop, your heart rate and blood pressure return to baseline levels, and other systems resume their regular activities.

But when stressors are always present and you constantly feel under attack, that fight-or-flight reaction stays turned on.

The long-term activation of the stress-response system - and the subsequent overexposure to cortisol and other stress hormones - can disrupt almost all your body's processes. This puts you at increased risk of numerous health problems, including -

- Anxiety,
- Depression,
- Digestive problems,
- Heart disease,
- Sleep problems,
- Weight gain,
- Memory and concentration impairment (mayoclinic, 2013b).

That's why it's so important to learn healthy ways to cope with the stressors in your life (mayoclinic, 2013b).

Why you react to life stressors the way you do

Your reaction to a potentially stressful event is different from anyone else's. How you react to stressors in your life is affected by such factors as -

Genetics - The genes that control the stress response keep most people on a fairly even keel, only occasionally priming the body for fight or flight. Overactive or underactive stress responses may stem from slight differences in these genes.

Life experiences - Strong stress reactions sometimes can be traced to traumatic events. People who suffered neglect or abuse as children tend to be particularly vulnerable to stress. The same is true of victims of violent crime, airplane crash survivors, military personnel, police officers and firefighters.

You may have some friends who seem laid-back about almost everything and others who react strongly at the slightest stress. Most reactions to life stressors fall somewhere between those extremes (mayoclinic, 2013b).

Learning to react to life stressors in a healthy way

Stressful events are a fact of life. And you may not be able to change your current situation. But you can take steps to manage the impact these events have on you.

You can learn to identify what stresses you and how to take care of yourself physically and emotionally in the face of stressful situations.

Stress management strategies include -

- Eating a healthy diet and getting regular exercise and plenty of sleep,
- Practicing relaxation techniques or learning to meditate,
- Fostering healthy friendships,
- Having a sense of humour,
- Seeking professional counselling when needed (mayoclinic, 2013b).

The payoff for learning to manage stress is peace of mind and - perhaps - a longer, healthier life.

Help relieving stress

Stress. We all deal with it. Whether it arises from our jobs, family life, drama with friends, a relationship problem, or finances, stress is there. While a little stress is good for you, allowing you to grow physically and mentally, excessive and chronic stress is harmful. Prolonged stress can even lead to tension headaches and other health problems that limit your functioning

at work, at school and in your relationships (mayoclinic, 2014c) Rather than letting your stress take over your life, try some methods of stress-management that you can apply to prevent and deal with stress before it jeopardises your health.

Reframing Stressful Thoughts

Be aware that stress begins with our perceptions

Your body has a very efficient reaction to dangerous events that pumps up your "fight-or-flight" response, allowing you to jump out of the way of an oncoming car and save your life (harvard, 2011). This reaction causes your heart to pound, your pulse to quicken, and your muscles to tense. But you may also unconsciously perceive that this reaction is necessary for non life-threatening situations, such as traffic jams, looming deadlines, or family issues (harvard, 2011). You must learn ways to counter your body's stress response so that you can "put the brakes" on and allow your body to relax (harvard, 2011).

Identify types of thinking that lead to stress

You may be experiencing unproductive, negative thoughts that lead to worrying, which can trigger the release of stress hormones (harvard, 2011). This is a response that is appropriate if, say, you run into a stressful situation like a bear in your path, but may not be appropriate when traffic is making you late to work. Identify common stressful thoughts by noticing if they fall into these categories (helpguide, 2016a) -

"Should" or "Must" statements - You have a strict list of things you "should," "must," or "should not" do, and feel stressed out or anxious when you do not follow these rules (helpguide, 2016a).

Catastrophizing - You expect the worst-case scenario or blow things out of proportion. Even small problems are "horrible" or a "disaster" (cci health, 2008).

All-or-nothing thinking - You see things only in black or white, as good or bad. Instead of acknowledging the complexities (or "gray areas") of being human, things are either wrong or right and there is no in between (cci health, 2008).

"What if"ing - You find yourself having an internal conversation about things you fear, such as "What if my child is hurt?" "What if I fail?" "What if I'm late?" and so on (cci health, 2015b).

Reframe your thoughts

Sometimes, a stressful situation is just a matter of perspective. Pessimism, for example, is an excellent example of avoidable stress we put ourselves through. Instead of focusing on the negatives and the problems that are causing you anxiety, concentrate on the positives (usc, 2016), (usc, 2016).

- Negative thoughts lead to a negative mood state and positive thoughts lead to a positive mood state. When you feel down, pay attention to your thoughts. What have you been telling yourself? Try to spin negative thoughts into positives.
- For example, you may think to yourself "I'll never finish all my work." Change this thought by spinning it: "If I work at a steady pace and take regular breaks, I can knock this work out in xxx hours."
- When you change your viewpoint, you can change your level of stress altogether. Do your best to see things in a positive light, and avoid cynicism at all costs (wikihow, 2016).

Challenge your negative thoughts

Another way to combat stressful thoughts is to ask yourself whether there's really any truth to them. Disputing and disproving your thoughts can help you view your thoughts objectively instead of immediately accepting them as truth (cci health, 2015a).

Try writing down two categories of information

Make a column for evidence of/for the stressful thought and another for evidence against it (cci health, 2015a). Or, if you don't have paper or time, try to do this exercise mentally.

- Write the evidence in the appropriate column. So if you're catastrophizing because you're been running late (and you are thinking "I'm going to be fired"), your "for" column might look like: "I was late twice last week and they're not going to tolerate me being late again;" while your "against" column might look like: "My boss said he understands that I have to drop my son off at preschool before I can drive to work," "We have a time and attendance policy that allows me to be late a certain number of times, and I'm nowhere near that point," and so on.

Keep a diary

Although keeping a diary, also known as a 'journal', may seem strange or tedious, writing down your thoughts on a regular basis can help keep you stress-free. When you feel bogged down with some emotional or mental stressor, write about it in your journal. Getting it out on paper will give you a sense of relief you might not otherwise find (psychologytoday, 2013).

- Write honestly and without fear. Your journal is only for you: no one else needs to read it or see what is stressing you out. It is a safe, judgement-free place to get out all your worries, emotions, thoughts, and feelings (psychologytoday, 2013). Once your thoughts are down on paper, they will no longer be taking up space in your brain.
- Journaling can help you experience clarity and see the source of your stress.
- Write out your problems to organize your thoughts. When your thoughts are not organized, you can't think clearly, which leads to confusion and stress. If you have a problem and can't decide between two solutions, make a two column pros and cons list (for and against), such as dividing a sheet of paper down the center to compare two ways to handle that situation.

Avoiding Unnecessary Stress

Accept that stress is unavoidable

You can take steps to reduce your stress and learn how to cope with stress, but you will never be completely rid of stress (mayoclinic, 2014a). Stress serves a purpose as a healthy response to overwhelming stimuli or perceived threats, and it can be dealt with in an equally healthy fashion (mayoclinic, 2014a).

- Stressors that may be unavoidable include school work and exams, busy days at work, new babies, getting married, or moving. Some of these are actually good things, but can still be a source of stress in your life.
- Learning healthy stress management techniques can help you "turn off" your stress alarm system so that you are not in a constant state of stress as you move through life (mayoclinic, 2014a).

Avoid stress when you can

Seems obvious, right? Sometimes staying away from what is stressing you out is harder than it sounds. If you know particular person or activity is the origin of your stress, cut them or it out of your life, or limit your exposure as much as possible. There are at least seven culprits of unnecessary stress; beware of falling prey to these issues (healthline, 2014).

- Stressing about money you have spent (e.g. overspending whilst out shopping, lending money to family or friends, etc.),
- Having clutter in your home or office space,
- Being pessimistic,
- Being late,
- Spending too much time comparing your life to others' on social media,
- Waiting until the last minute to complete a task,
- Ruminating about past events (wikihow, 2016).

Be better organised

Oftentimes, stress arises from feeling overwhelmed. Use a planner to keep track of your "to-do lists". Clean your desk and visit Pinterest to find useful ways to manage your paperwork and household chores. Being organised and getting your priorities straight can help you break responsibilities down into manageable pieces and focus on the things that really matter to you (american, 2016).

Learn to say "no"

You cannot do everything you are asked, so why keep pretending that you can? Indeed, the more you promise and don't deliver, the less people will perceive you as being reliable. Instead, be assertive and learn to say "no" politely, but firmly. Keep track of your schedule to clearly acknowledge when you do not have the time or resources to take on extra tasks.

- Assertive people maintain eye contact, speak in a clear and non-threatening tone while standing up for themselves. If you know that you are already overbooked, say so. It's okay to say "no" when you do it in a way that also respects others.
- Some people take on too much out of fear of missing out on new and exciting opportunities. Yet, they end up not performing as well as they would because they are dividing their energies between so many different tasks or activities. Carefully weigh the pros and cons of new obligations, and decide if the effort will be worth it considering your current workload (honorsblog, 2013).

Learn how to delegate

As with trying to do everything, never delegating is about you trying to have control and not trusting that others can do their job as well as you can. Learn to let go by giving more credence to the abilities of others. Giving up tasks may seem stressful in theory, but will free you up for more personal time. Find reliable people in your life that you can trust with tasks that you are too stressed or anxious to manage (helpguide, 2016b), (uoregon, 2016).

Making Environmental Changes

Clean up a bit

Even the most steadfast of souls will waver in an ever-messy environment. If your home, office, car, or work space is overly messy or dirty, it is certainly having an effect on your mental well-being. Take a few minutes to clean up your most unorganised areas, and your mind will breathe a sigh of relief. Tips for reducing clutter are as follows (psychologytoday, 2012b) -

- Throw away items that are rarely used and have no value rather than stockpiling them.
- Gather as a team (i.e. spouses, families, or roommates) and take on cleaning together. Group effort makes the process go by quicker and with more fun.
- Sort through papers and mail and toss or file as needed. Develop a regular schedule of doing this to prevent papers from piling up.
- Designate places to store frequently used items so they can be easily retrieved when you need them.
- Clean your work space after each work session to prevent clutter from getting out of hand (wikihow, 2016).

Take a few minutes to get ready

It's hard to feel prepared for the day when you haven't taken time to get yourself ready. Spend a few extra minutes in the morning to prepare yourself for the day's events. Take an extra long shower, put on your favorite outfit, and go into the day ready to take on anything (wikihow, 2016).

Listen to some music

Music has shown to have a very strong effect on mood and mental state. Calm yourself down by listening to your favorite soothing music. Although you may prefer heavy metal or rap, try listening to something a bit softer and slower for the best effects. Keeping music playing in the background while you work, study, or just go about your daily activities is a great way to subconsciously alter your stress levels.

- Researchers have found that music can change brain functioning in similar ways as medication. So, regular music really can help to "cure" stress and anxiety (unr, 2016).

Try aromatherapy

That's right, what you smell can actually alter your stress levels. Scientific studies have linked the scent of lavender and oranges to reduced stress and anxiety levels (umm, 2015). Use a lavender scented air freshener in your home, office, or car, or spritz a bit of the essential oil onto your hair and skin before you head out the door in the morning. You can also dab a bit of the essential oil onto your temples to relieve a stress-induced headache (abcnews, 2016).

Change your environment

If making little changes isnt enough to cheer you up, try moving to a completely new place for a bit. If work or studying is too difficult in your office or at home, relocate to a cozy coffee shop or a park. Having a new environment will help you to move your thoughts away from your stressors, and give you a chance to breathe and recover from your anxiety (pbs, 2010).

Talk to new people

It's possible the people you talk to are stressors. Don't completely take them out of your life, but try meeting some different folks. They can offer a new perspective on things you never even thought about, or get you involved in new stress-reducing activities (mayoclinic, 2013e).

Relaxing Activities to Try Out

Take a bath

Some people are bath people while others are shower people. No matter which you are, it is hard to deny the comfort of a warm bubble bath with a cozy drink and a good book. If you're stressed out, try curling up in your bathtub for a while. The warmth will relax your muscles, and help to soothe away your stress.

Maintain a favourite hobby

When we get stressed and anxious, it's easy to push hobbies to the side and focus on 'priorities.' However, by leaving out any free time for yourself, you may be making yourself more stressed. Return to a lost hobby by playing your favourite sport, picking up your art journal, or heading out for a hike. You'll feel refreshed and better able to deal with your stressors when you've given yourself time to do something you love (Zawadzki, Smyth, and Costigan, 2015).

Try out a new activity

If you don't have any old hobbies that you want to continue, or you never had any in the first place, try out a new activity you've been interested in. It's never too late to learn a new trade. Try auditing a class at a local community college, or find other classes in your area. Better yet, teach yourself something new, such as a language or crafting skill, and practice to get better. Learning a new activity forces your mind off of your stressors, making it easier for you to relax.

Head outside

Sunlight is a natural cure for depression, which is tied to stress and anxiety (globalhealingcenter, 2013). Even if you aren't able to get sunlight, mother nature provides excellent stress relief via the great outdoors. Walk through a park, hike up to a mountain, go for a fishing trip - whatever interests you. It's hard to be stressed when you're witnessing the beauty of the natural world, while putting your body to work at the same time (takingcharge, 2010).

Laugh it out

Laughter is the best medicine, so they say. Laughing may seem difficult if you're stressed and anxious, but incorporating it into your life will make a marked difference. Turn on your favourite sitcom, look at funny YouTube videos, or get together with a funny friend. Smiling and laughing release stress-relieving hormones in your brain which will have you feeling better in no time (mayoclinic, 2014b).

Drink a cup of tea

Tea-drinkers have shown to be less stressed over time than non-tea drinkers, making this a great activity for reducing stress. Grab a cup of black tea for the best results, but any tea will do. Having the warm cup to hold onto will help you to relax, while the flavour will give you something sweet to focus on.

Get a massage

Massages aren't just great for your body, they actually release feel-good hormones in your brain as well. The next time you're feeling stressed, call up your favourite masseuse and schedule an appointment. Getting your tension worked out of your muscles will help to work the tension out of

your mind as well. Better yet? Have a loved one give the massage for you. The combination of your partner or spouse giving you the massage will release extra hormones, practically demolishing whatever stress you had (WebMD, 2016a).

Practice yoga regularly

You can practice any of the different forms of Yoga for stress relief. Try Hatha yoga, which combines stretching, breathing techniques, and meditation. It soothes your distressed mind, refreshes your thoughts, tones body muscles and generates new awareness like never before (cnn, 2014).

- You can make the benefits of yoga last longer when you practice it regularly. Early morning is the perfect time, but you can practice it whenever you feel stressed out. If you are pressed on time, combine it with an exercise routine you are already following as your warm up or cool down practice.

Do guided meditation

Practicing meditation has proven to relieve stress remarkably. Various meditation patterns can help you get rid of stress and calm your mind for better focus and clear thinking. You can practice either of meditation such as Zen, Tibetan, Transcendental Meditation (TM) irrespective of your religious affiliation (yogajournal, 2015).

- If you are a beginner it's best to take on a guided meditation program under an expert. You can get a hold of good books and videos on meditation for regular practice.

Adopting a Stress-Fighting Lifestyle

Eat healthy foods

Few would be surprised to hear that among the myriad benefits healthy eating provides, stress relief is one of them. Don't let junk food and sugary sweets bog you down and increase your anxiety hormones. Instead, incorporate healthy grains, fruits, and vegetables into your daily diet, and your body will compensate by creating more stress-fighting hormones (WebMD, 2016b).

Get daily exercise

The infamous 'runners high' isn't a phenomenon isolated solely to runners; exerting yourself physically releases endorphins that make you happy. That means that if you're stressed, you can cheer yourself up and throw your anxiety out the window just by making your heart work a bit harder. Head for a bike ride or swim, pick up some weights, or play your favourite sport to gain both physical and mental health (adaa, 2016).

Focus on your sleep

When people get stressed and overwhelmed with a million and one things to do, often one of the first things to be sacrificed is sleep. However, this is one of the biggest health mistakes you can make. Getting adequate sleep allows your body to recharge and refresh, leaving you with a clean slate in the morning (sleepfoundation, 2016).

- If you don't get enough sleep, your body can't get rid of the excess hormones and toxins that have built up and cause stress, making your stress a never-ending cycle. Try to get 7–9 hours of sleep on a nightly basis.

Cuddle up more often

If you are in a healthy relationship, try going to your partner for a bit of physical touch. Studies have shown that regular cuddling, kissing, and sex all release oxytocin - a hormone that produces happiness and reduces stress (psychologytoday, 2012a). That's right - some of your favourite activities actually improve your mental well-being. Do these on a regular basis to keep your hormone levels up in general, making it less likely that youll get stressed out in the first place.

Practice your spirituality

A top reason many people participate in religious practices – to find relief of stress and anxiety. If you are already a part of a religious group, try turning towards it more during your times of stress for its peaceful benefits. It is likely you will find relief with the support of your faith community, while growing stronger spiritually simultaneously (greatist, 2013).

- If you suffer from chronic stress, consider joining a religious group, and see what inner guidance and comfort it has to offer.

Maintain healthy relationships

It's easy to get stressed when the people you surround yourself with are unhealthy and co-dependent. Rather than maintaining negative relationships with people that annoy you or cause anxiety, begin to nurture relationships that support you and make you feel better. You'll feel better in the long run, even if it's difficult in the short run, to seek and keep happier, healthier friendships in your life.

Tips

- Note that not all stress reducing activities will work for all people. Experiment with different techniques to see what works for you.
- Think of the positives in your life and think of a special moment that has happened today. Do this everyday.
- Read a good book when you feel stressed.
- Drink tea with no caffeine, as caffeine can make it harder to cope with stress. Go with decaf.

Warnings

- Contact a therapist for continuing mental pain, just as you would for a physical ailment. A therapist is a professionally trained problem solver, a person who can bring to bear all the insights of psychology to point out choices that you are not aware of.
- If you are feeling suicidal or feel like you might hurt yourself, get help immediately! Call your local suicide prevention hotline, or the psychiatric hotline of a hospital in your area. If you do not know where to call, your local police department will be able to provide you with assistance.
- Your doctor may be able to prescribe medication to control anxiety and depression.

Stretch marks

Stretch marks are red spoke-like lines that appear on the skin during times of rapid physical growth (such as puberty or pregnancy). During puberty, stretch marks on the breasts are very common and completely normal. Other common places for stretch marks are on the hips and thighs. Over time, the stretch marks will fade to match your normal skin colour.

Sunshine protection

Limit your time in the sun and use an effective sun cream to protect your skin. Sun creams are graded by a sun protection factor SPF[148]. This is related to the length of protection they give against sunburn. A higher SPF offers longer protection. Sun creams are made from chemicals that absorb UV light. Titanium and zinc oxide are sunblocks that provide a physical barrier against UV rays.

Sun creams do not give 100% protection, so it is very important not to spend a long time in the sun, whatever your skin tone. Having fair skin increases your risk of skin cancer. However, having darker skin does not mean there is no risk. Bob Marley, the Jamaican reggae star, died of skin cancer at the age of 36.

Protect your skin

- Avoid going outside when the sun is at its highest point (10am to 3pm).
- Try not to spend a lot of time in the sun.
- Sunbeds are NEVER recommended.
- Always use a high SPF sun-cream which blocks UVA and UVB radiation - even on cloudy days and if you are skiing or taking part in winter sports.
- Use the right amount of sun cream: at least 2 tablespoons for an average adult every time. Apply 30 minutes before going outside and re-apply every two hours, after swimming, sweating a lot or exercising.
- Cover up close knit clothes and wide brimmed hats offer the best protection.

Protect your eyes

- Sunlight can cause eye problems, including cataracts and cancer.
- Dont stare directly at the sun.
- Wear sunglasses, ideally wrap-arounds.
- Badly fitting glasses offer poor protection.
- Buy sunglasses that block out 100% of UVA/UVB rays - look for a British Standard mark or UV 400 label (MIMS, 2016b).

[148] sun protection factor

Supplies

In the UK

Nu-Care Products Limited

Unit 21 Broadmead Business Park,
Broadmead Road,
Stewartby,
Bedfordshire, MK43 9NX
For BD Blunt Fill and Filter Needles
Not for injections, BD Blunt FILL needles are for use with vials, BD Blunt FILTER needles are for use with ampoules.

Oncall medical supplies

http://www.oncallmedicalsupplies.co.uk/
For needles, syringes, sharps bins, skin swabs, and other requisites.

Testosterone

Recent research on testosterone is showing that subcutaneous testosterone is a very efficient delivery mechanism in young transmen, and perhaps it could also be used for older transmen? (Olson et al., 2014)

But there are possible black clouds on the horizon, with a FDA Advisory Panel stating in September 2014 *"There is little evidence that testosterone replacement therapy effectively treats normally sagging levels of the hormone in aging American males"*. This panel overwhelmingly voted, 20-1, to tighten use of the popular drugs and require drug makers to conduct tests assessing the drugs' risk of heart attack and stroke (drugs.com, 2014b)

The FDA is not required to follow the recommendations of its expert panels, but usually does.

Along with sharply curtailing how many men might be prescribed testosterone supplements, insurance companies could also limit coverage for their use if the FDA follows its panel's advice, experts stated.

In what has become known as the "Low-T" fad, Baby Boom generation men have turned to testosterone replacement therapy in response to the sagging muscles, lower energy levels and sexual problems that often accompany natural ageing, the FDA noted in a review provided to committee members in advance of the meeting.

"There's a large group of men out there who are getting older, and they are looking for ways to evade the consequences of aging," Dr. Bradley Anawalt, an endocrinologist from the University of Washington in Seattle, said ahead of the meeting.

The FDA review pointed out there's no clear scientific evidence showing testosterone replacement can reverse some of the effects of aging. Yet the "Low-T" craze has been aided by consumer advertising for remedies that promise renewed vitality and strength for ageing men, the report said. It also noted that there's growing evidence many men who are receiving testosterone replacement therapy do not need it.

One recent study found a 30% increased risk of stroke or heart attack in a group of men recently prescribed testosterone therapy, the FDA said. Another found that men 65 and older experienced a two-fold increase in heart attack risk within the first three months of receiving a testosterone prescription, according to the agency.

In June 2014, the FDA announced that testosterone supplement products must now carry a warning label on the general risk of blood clots in the veins.

It has been stated that doctors, who aren't hormone experts, are performing testosterone level tests at the wrong time of the day, which can lead to overdiagnosis of low levels.

Testosterone levels are at their peak early in the morning and decline naturally throughout the day, but some doctors have been performing hormone tests at all times of the day, diagnosing some men as having low testosterone when in fact their levels are normal (drugs.com, 2014b).

Testosterone replacement therapy, menopause and libido: the facts

Menopause can affect female sexuality and relationships by various means, and sexual problems often occur both during menopause, and with ageing. Sexual problems are estimated to occur in 5% of sexually active women in middle age, yet many women do not disclose the problem.

Despite our society being much more open in discussing sensitive issues, many women are still too embarrassed to seek help when things are not quite right. Although some women do not feel that an active sex life is vital, often quoting that they'd rather have a cup of tea, 84% of women in a recent survey feel that it is important to continue an active sex life into older age.

Sexual problems can occur from lack of interest or desire, decreased arousal, and discomfort. Changes associated with menopause, and changes associated with the ageing process itself rather than hormone changes can all play a part in sexual difficulties. Factors that particularly

affect menopausal women include sleep disturbance leading to tiredness, nuisance of heavy and irregular periods, tensions with their partner (which then leads to reduced sexual activity often causing more tension), stress over other life events (which often happen around the time of the menopause, such as problems with teenage children, children leaving home, elderly parents, work pressures), menopausal symptoms signifying the ageing process and the need to come to terms with this, and hormonal changes.

Hormones and libido

The hormones oestrogen, progesterone and androgens, are all important in sexual desire and response: both oestrogen and progesterone levels fall during menopause, whilst androgens fall with age, declining particularly after the age of 40 years. The fall in oestrogen may also cause vaginal dryness and discomfort, and this can affect sexual desire. Because of the role of these hormones, some women do benefit from hormone therapy but, for women especially, the other personal and relationship factors are as, if not more, important.

Continued communication with your partner is vital to work through this and find out what is the best option for you. Many women do benefit from some help at this stage, whether it is advice or specific therapy but, with guidance, there is no reason why women can't continue to enjoy an active sex life well into old age.

Understanding oestrogen

The lack of oestrogen causes vaginal dryness and discomfort, due to vaginal tissues becoming thin, less elastic, less well supported and fragile. This is a frequent menopausal problem, yet women often don't report it. A previous Menopause Matters survey showed that more than half (51%) of menopausal and postmenopausal women suffer from bothersome vaginal symptoms, yet the majority of them (79%) had not discussed their symptoms with a healthcare professional.

Almost half of these women (47%) said symptoms were so severe that they affected their sex lives. One quarter even said that they make excuses to avoid having sex with their partner. A more recent survey showed that of women who had noticed reduced libido associated with menopause, more than 8% believed that the vaginal dryness and discomfort was a significant contributory factor.

Treating vaginal dryness

For vaginal dryness, there are treatments available such as vaginal lubricants and moisturisers that can be purchased from pharmacies, and available on prescription. To treat the underlying problem of the effects of lack of oestrogen on the vagina (vaginal atrophy), vaginal oestrogen in the form of a small tablet, cream or vaginal ring is also effective.

Because the oestrogen is given in a small dose and is concentrated in the vaginal tissues, very little, if any, gets into the rest of your body, and so is not likely to be associated with the risks and side effects of HRT. Vaginal oestrogen therefore can be used even if you cannot or are advised not to take HRT, which circulates throughout your body (systemic HRT).

In some women, control of menopausal symptoms by systemic HRT can improve sleep pattern, increase energy levels and reduce distress: changes that can lead to an improvement in libido both directly and indirectly, simply by restoring oestrogen levels. However, some types of HRT can cause the body to produce less testosterone, which is important for libido, mood and energy levels. The tablet form of HRT can have this effect, as can the oral contraceptive pill and thyroxine. One type of tablet HRT that does not have this effect is tibolone, and in fact tibolone may increase testosterone-like activity production.

Tibolone can be considered if your periods have stopped, since it is a period-free preparation. Also, a non-tablet form of HRT, such as a patch or gel, has a lesser effect in reducing testosterone, compared with tablet HRT.

Testosterone replacement therapy

Since testosterone (one of a group of hormones known as androgens, produced both from the adrenal gland and the ovaries) is thought to play an important part in sexual interest and response, some women may benefit from testosterone replacement therapy. There is a gradual decline in androgen production from the age of 40, so by the time you reach 70, your androgen levels are 7% - 8% less than in earlier years. A 50% reduction in testosterone levels is also seen following removal of the ovaries. Symptoms of androgen deficiency include persistent fatigue and low mood, as well as the low libido. Testosterone replacement may be considered in women who have had their ovaries removed, and women on tablet HRT who have symptoms suggestive of testosterone insufficiency and may wish to try a different route, or type of HRT.

Apart from the HRT preparation tibolone, the only other currently available licensed way for women to take testosterone in the UK is by an implant.

The implant is a small pellet placed under the skin of the abdomen every six months. Its use in the UK is currently limited, and only available in a small number of NHS clinics and some private clinics.

A study showed that testosterone gel improved frequency of sexual activity and sexual interest in postmenopausal women taking HRT, but the appropriate dose for women is yet to be determined. Currently there are no licensed testosterone gel preparations in the UK, but testosterone gel licensed for use in men is used for some women under specialist supervision.

Although a change in the type of HRT or, for some women, a form of testosterone along with HRT is worth considering, the other factors affecting libido should not be ignored.

Other factors

Women need to feel secure, loved, wanted, and emotionally close to their partner to be able to fully enjoy sexual relations.

The menopausal changes of weight gain, skin changes, and impact of loss of fertility can all affect self-confidence in a woman, influencing how she feels about herself, her relationship and her sexuality. On the other hand, she may find that menopause has a positive effect on sexual response by signaling the end of heavy and often painful periods, negating the need for contraception and allowing more freedom and time with her partner, especially if children have left home.

Sexual difficulties can also be due to medical problems and medications. Sexual problems affect about 3% of men, with erectile dysfunction (impotence) being the most common problem. Men are often even more reluctant than women to report problems and seek treatment. As difficulties continue, tension builds up, and the problem escalates. Effective treatment is available however, and medical help should be sought sooner rather than later (Currie, 2016).

The real side effects of testosterone replacement therapy for men

As men go through male menopause, or 'andropause', they can experience both physical and emotional changes that vary dramatically in severity between men. This period can last for decades, and usually occurs very gradually. It is associated with a reduction in testosterone, which is why testosterone replacement therapy is prescribed in some cases, particularly when symptoms are having a negative impact on a man's life. However, there are some concerns over the safety of testosterone replacement therapy, and here, well examine these potential side effects and safety risks, and dispel the myths most commonly believed.

What happens during male menopause?

Menopause in men is difficult to diagnose, given that it happens gradually over decades, and lacks the defining moment that women experience when their periods stop. A man's testosterone levels reduce by around 1% per year from the age of thirty, and research shows (Feldman, 2014) that by the age of 60, a man has on average around 20% less testosterone than he had at puberty, and by the age of 80, around 50% less.

The symptoms commonly associated with male menopause include a loss of lean muscle mass and tendency to put on weight, low libido, difficulty maintaining an erection, depression, loss of vitality and physical strength, sleep disturbances, reduced cognitive function, and hot flushes. The main reason these symptoms occur is due to a reduction of free testosterone in a mans body, the active form of male sex hormone. Alongside this, an increase in sex hormone binding globulin is seen, which binds to testosterone and prevents it being usable by the body. We may also see a change in the testosterone to oestrogen balance around this time, due to an increase in the enzyme aromatase, which converts more testosterone to oestrogen. This enzyme is found in your fat cells, as well as your adrenal glands, which is why those medically classed as obese are more likely to experience these symptoms.

What is testosterone replacement therapy?

Testosterone replacement therapy is designed to raise testosterone levels, to help prevent symptoms associated with its deficiency. It is available in a variety of formats, including gels which are rubbed onto the skin, oral tablets, injections, and patches. A number of studies have been done to assess which is most effective, however it has not yet been proven which type of preparation raises testosterone levels most efficiently.

The benefits found in research (Huanguang et al., 2015) from taking testosterone replacement therapy include a minor to moderate improvement in lean body mass and muscle strength, increased bone mineral density, a modest enhancement in sexual function, a reduction in body fat, and a reduction in depressive symptoms.

Who requires testosterone replacement therapy?

It is difficult to assess which men should be given testosterone replacement therapy, because there are a lack of established reference ranges for 'normal' testosterone. Testosterone levels vary greatly between individuals, and if a man has always had fairly high testosterone levels and these drop to normal ranges, he may experience the same symptoms as a man whose levels have dropped from normal to low. Generally, the prescription of testosterone is assessed based on hormone levels, as well as symptom analysis.

Are all the symptoms of male menopause due to low testosterone?

Another issue with the therapy is that it is not entirely clear whether the symptoms associated with male menopause are purely down to a reduction in testosterone levels. Research studies have failed to clearly attribute this link. The symptoms experienced around this time could also be due to other health problems that tend to develop with age, such as cardiovascular disease, and side effects from the medication used. However some studies show (Behre et al., 1997) that a low level of testosterone may actually increase the risk of heart disease and brittle bones, suggesting that testosterone indeed has a role to play.

What are the potential side effects of testosterone replacement therapy?

There have been limited studies looking at the potential benefits and health risks of testosterone replacement therapy, and it is difficult to make a clear conclusion on these risks. This is because studies vary widely in terms of the type of testosterone replacement therapy used, dose, duration of treatment, and age group or health status of men analysed. Findings are inconsistent, and what is required are a number of placebo-controlled research trials on a large group of men. The results of these trials also need to be compared to the health risks of having low testosterone, which can include an increased risk of heart disease and osteoporosis.

There are three key areas of concern when it comes to the use of testosterone replacement therapy, based on a number of studies, notably, those by Calof OM et al (Calof et al., 2005), Fernández-Balsells et al (Fernández-Balsells et al., 2010), and Haddad RM et al (Haddad et al., 2007).

Raised red blood cell count (polycythaemia) - This could potentially increase the risk of thrombosis or a stroke, due to alterations in the thickness of the blood. However, research has not clearly proven an increased risk of these events from taking testosterone.

An increased risk of cardiovascular disease - Research into testosterone replacement therapy and cardiovascular risk has produced many conflicting results. Despite research suggesting a link between an increased risk of cardiovascular problems in those with low testosterone, some research has suggested that testosterone replacement therapy may increase the risk of heart attack and stroke. A large review of the data (Finkle et al., 2014) in over 55,000 patients showed twice the risk of heart attack in those who received testosterone replacement therapy, including in younger men with a pre-existing heart condition. However this review did not analyse the effect of different types of testosterone prescription. In 2014, a different study (Borst et al., 2014) found that oral testosterone replacement therapy produces a significant increase in the risk of cardiovascular disease, but this

was not seen when given via injections, or through the skin. Furthermore, a more recent review of the data (Corona et al., 2014) revealed that no link was established between a higher risk of cardiovascular problems and the therapy.

Prostate problems - The area of greatest concern is the data suggesting an increased risk of prostate cancer or noncancerous enlargement of the prostate. This was first analysed in research (Kang and H. J. Li, 2015) which showed that testosterone replacement therapy increases the levels of prostate-specific antigen, a marker used in the detection of prostate cancer. However, not a single study has yet shown a clear correlation between testosterone replacement therapy and actual prostate cancer diagnosis. It is not fully clear the role testosterone plays in prostate cancer risk, especially given that most men are diagnosed as they age, when testosterone levels are naturally declining.

What is clear from the data is that more research is required. For those considering testosterone replacement therapy, its vital that you are properly screened for prostate cancer, both with a digital rectal examination and blood test. Alongside this, cardiovascular health should be assessed before making a decision as to whether the therapy is appropriate. It has been recommended (Isidori et al., 2015) that anyone who has pre-existing prostate problems or prostate cancer should avoid taking the therapy, and those who are deemed appropriate for starting testosterone replacement therapy should be regularly reviewed, re-examined and have their blood analysed to ensure their risk of developing health problems has not increased. There are of course many natural agents which may help to support testosterone levels without the need for hormone replacement therapy, including zinc, vitamin E and various herbal preparations (Jeans, 2016).

The risks of breast cancer

There is a possible side-effect of some drugs, that there is an increased risk of breast cancer. The risks to us are negligible, but, it could happen. So here are some articles which seem relevant. The last article is very interesting, a very large sample, over an extended period, and some unfortunate folk did get breast cancer.

The increased risk of breast cancer due to use of oestrogens is controversial. Several studies have suggested that long-term oestrogen therapy may be associated with a slightly increased risk of breast cancer. Meta analysis of 51 studies (epidemiological data) supports a modest risk increase associated with long-term hormone replacement therapy (HRT) (Kaufman, Palmer, and Mouzon, 1991).

One study of Swedish women has reported that a 10% increase in the relative risk of breast cancer may occur and that the risk is related to increasing duration of oestrogen therapy. In that study, women with more than nine years of oestrogen use had a 70% greater relative risk of breast cancer than controls. That study, however, examined use of a variety of oestrogen preparations of which estradiol was the most frequently prescribed. In addition, women who took progestins did not demonstrate a decreased risk of breast cancer and may even have been at higher risk (unknown, 2003).

The Toronto Breast Cancer Study has reported that women who receive unopposed conjugated estrogens for less than 15 years are not at increased risk of breast cancer. In that study, an increase in the risk of breast cancer for women who used conjugated estrogens for more than 15 years was not ruled out (Palmer, Rosenberg, and Clarke, 1991).

The Case-Control Surveillance Study has reported that there is *"no evidence that the use of unopposed conjugated estrogens increases the risk of breast cancer, even after long duration of use or long latent intervals, but the possibility of a modest increase (less than a doubling) could not be excluded."* (drugs.com, 2014c).

This study took details from the "Women's Health Initiative" study and investigated coronary heart disease (CHD), invasive breast cancer, stroke, pulmonary embolism, colorectal cancer, endometrial cancer, hip fracture, and death. Their results were summarized as *"findings from the intervention and extended postintervention follow-up of the 2 WHI hormone therapy trials do not support use of this therapy for chronic disease prevention, although it is appropriate for symptom management in some women"* (J. Manson et al., 2013).

A very recent study, Incidence of breast cancer in a cohort of 5,135 transgender veterans published in "Breast Cancer Research and Treatment", of November 2014 investigated 5,135 transgendered individuals in the United States from 1996 to 2013. Ten breast cancer cases were confirmed from this large sample. Seven were in female-to-male patients, two in male-to-female patients, and one in a natal male with transvestic fetishism. They concluded *"Although definitive conclusions cannot be made regarding breast cancer incidence in transgender transgender (TG)*[149] *veterans who did or did not receive Veterans Administration Cross-Sex Hormones Cross-Sex Hormones (CSH)*[150] *due to the sample size and duration of observation, it appears that TG veterans do not display an increase in breast cancer incidence. This is consistent with European studies of longer duration that conclude that CSH treatment in gender dysphoric patients of either birth sex does not result in a greater incidence than the general population"* (Brown and Jones, 2014).

What it essentially is saying that our risk of breast cancer is not increased by the hormone treatments that we receive.

[149] transgender

[150] Cross-Sex Hormones

The risks of smoking

Around 114,000 smokers in the UK die every year from smoking-related diseases. It is estimated that in England one in five deaths in men and women aged 35 or over can be attributed to smoking.

In 2006/7 in England there were 1.4 million hospital admissions for adults aged 35 and over with a primary diagnosis of a disease that can be caused by smoking. Smoking was implicated in around 18% of all deaths in England in 2007.

Approximately one third of all deaths from cancer can be attributed to smoking and around 82% of deaths from lung cancer.

Heart disease is the leading cause of death in the UK and smoking is thought to be responsible for around 17% of these deaths. Smokers under the age of 40 are five times more likely than non-smokers to have a heart attack. For smokers who have other prime risk factors for developing heart disease, namely high blood pressure and high cholesterol, the chance of having a heart attack may be up to eight times greater than for a non-smoker (MIMS, 2016b).

Smoking is the primary cause of preventable illness and premature death, accounting for approximately 100,000 deaths a year in the United Kingdom (hscic.gov.uk, 2012). Smoking harms nearly every organ of the body and dramatically reduces both quality of life and life expectancy. Smoking causes lung cancer, respiratory disease and heart disease as well as numerous cancers in other organs including lip, mouth, throat, bladder, kidney, stomach, liver and cervix. The 2010 US Surgeon General report, "How Tobacco Smoke Causes Disease", concludes that *"there is no risk-free level of exposure to tobacco smoke, and there is no safe tobacco product"* (General, 2010). In 2011 among adults aged 35 and over, around 79,100 deaths (18% of all deaths of adults aged 35 and over) were estimated to be caused by smoking (hscic.gov.uk, 2012). Smoking kills 500 out of every 1,000 people who continue the habit, so smokers have a one in two chance of dying prematurely (Doll, 1994). This is despite research dating back 60 years which first proved the link between smoking and lung cancer (Doll and Hill, 1954).

The usage of Aspirin

Many people use a low-dose of aspirin prophylactically for the prevention of strokes and heart attacks, and it is known to work well. But some people have started using this without medical supervision and they may not fare so well. Recently, the US Food and Drug Administration has concluded that aspirin should not be routinely used for the primary prevention of heart attack or stroke in patients with no history of cardiovascular disease.

"The FDA has reviewed the available data and does not believe the evidence supports the general use of aspirin for primary prevention of a heart attack or stroke," it recently said. *"In fact, there are serious risks associated with the use of aspirin, including increased risk of bleeding in the stomach and brain, in situations where the benefit of aspirin for primary prevention has not been established,"* the FDA added.

The agency did, however, endorse the use of aspirin for secondary prevention in patients with known cardiovascular disease or who have had a stroke or heart attack.

US doctors often recommend daily aspirin in low doses, 75-100mg, to asymptomatic adults for the primarily prevention of heart attack and stroke. And the American Heart Association recommends daily low dose aspirin for primary prevention in people at high risk of myocardial infarction and ischemic stroke but only after consultation with a healthcare provider, said Richard Stein, a cardiologist and professor of medicine at New York University School of Medicine and a spokesman for the association.

Taking aspirin for a few days to treat aches and pains is associated with very few adverse event reports, Stein said, *"but once you start giving people 81 mg [a commonly available low dose aspirin] a day, every day, you are significantly reducing the activity of their platelets."*

This can be very beneficial if you rupture a plaque, he noted, but can also increase the risk of gastrointestinal bleeding, an intracranial hemorrhage, or some other serious hemorrhagic complication (unknown, 2014c).

Thrush

Thrush is caused by *"Candida Albicans"*, a yeast that lives on the skin and in the mouth, throat, vagina and intestinal tract, usually without any problems. Occasionally conditions change and it multiplies rapidly causing symptoms (Greer, 1998). This is known as clinical thrush or candidiasis (Weston, 2000). It can affect the mouth, under the foreskin, and the vagina, and in the last two can result in a smelly discharge (the smell has been likened to that of yeast). Oral thrush looks very similar to small pieces of white fish left in the mouth after eating fish and chips, before having a drink! The other non-oral thrush is a small irritating whiteish layer which on occasion itches maddingly!

Oral thrush can be eradicated by the use of nystatin (prescribed by your doctor), and the other can be eradicated by the use of Canesten Cream, topically applied, but both (in the case of resistant infection) can be eradicated by oral Fluconazole. All of these can be obtained under

prescription from your GP, however it may be cheaper to buy the Canesten over the counter at the pharmacy than by paying the prescription charge. Depending on the severity of the condition, Canesten can eradicate the infection in two to three days if applied three times a day.

If you have thrush then you should refrain from oral or penetrative sex until you are clear of the infection for at least five days. This will help to ensure that you do not pass it on to your sexual partner.

Alternative therapies for thrush

- Live yogurt, which contains Lactobacillus acidophilus, can be eaten regularly.
- Garlic is a powerful natural antibiotic and garlic supplements can be taken orally.
- Add eight to ten drops of tea tree essential oil, which is antifungal, to a warm bath to ease the symptoms.
- Certain foods encourage the growth of yeast, so people prone to recurrent thrush could consider changing their diet. Wine, beer, vinegar, coffee, cheese, cakes, white bread, sausages, smoked fish, sugar and foods that contain monosodium glutamate should be avoided (Weston, 2000).

Transdermal medication.

How many times have you rubbed a dock leave on yourself when stung by a stinging nettle? For centuries, the skin has been a popular, but not very effective, route for drug delivery, and these drugs have been applied topically as rubs, liniments and ointments, usually with the aim of providing a localised effect but also, on occasion, to gain systemic effects. These systemic effects can now be delivered in a way that is more practical and reliable i.e. transdermal drug delivery, sometimes known as "patch therapy".

This form of medication has many advantages over the oral route -

1. It avoids the hostile environment of the gastrointestinal tract, with its changing PH, foods, digestive enzymes and variable motilities and transit times.
2. Allows constant and prolonged plasma drug levels to be maintained.
3. Avoids first-pass elimination by the liver, and
4. Increases compliance as you only need to apply a new patch every other day, or whenever, instead of orally several times a day.

However, it does have some disadvantages -

1. It can't be used for drugs that require high blood levels, due to poor absorption by the skin.
2. The adhesive doesn't stick to all skin types.
3. The drug may cause skin irritation or sensitisation, and
4. Some people find them uncomfortable to wear.

Estradiol can be given via a patch because when given orally, Estradiol and conjugated oestrogens are substantially metabolised on the first pass through the liver to oestrone or conjugates, while simultaneously modifying hepatic function. Continuous rate-controlled transdermal administration, however, allows appropriate Estradiol plasma levels to be achieved with much lower doses of Estradiol than required orally. Also the appropriate oestrone/Estradiol ratios can be maintained because of the avoidance of the first pass through the liver.

The patch should be applied to a fatty area below the waist (usually buttock or thigh) and renews twice weekly, although a seven-day patch is currently being developed (Haslett, 1996). I have been using patches for a couple of years now and have had no problems with their stickiness, but then I am sticking the patches to my stomach! There is some space between the slacks waistband and the base of my bra, and that's where I'm sticking them. The advantages are that there is little movement of the stomach wall as there is with the thigh or buttock, so it sticks and stays far better.

However, clinical trials with Estraderm TTS which delivers Estradiol for $3\frac{1}{2}$ days, demonstrated that the patch did not act as an osteoporosis prophylaxis (Kelly, 1994). Also, where oral conjugated equine oestrogens (like Premarin) have been demonstrated to favourably affect the patients lipid profile, offering protection from cardiovascular disease, lipoprotein levels do not appear to be altered to the same degree with the usage of transdermal oestrogens (Kelly, 1994).

Transgender Definitions

I have included this section just to try to achieve some consistency in gender terms that we use to describe ourselves, or others. I now do not consider myself as a "transsexual", I have completed my transition and am now a woman, but if pushed I would consider "transwoman" as useful.

Acquired Gender

The "gender" (when opposite to the sex assigned at birth) in which a person lives (LGBT, 2014c).

Androgynous

A person who does not fit clearly into the typical gender roles of their society. Androgynous people may identify as beyond gender, between genders, moving across genders, entirely genderless, or any or all of these. Androgyne identities include pan-gender, bi-gender, ambi-gender, non-gendered, a-gender, gender-fluid or intergender (LGBT, 2014c).

Androgynes, Gender Queer, Gender Bender, and Gender Blender

These are some terms used for people who merge the characteristics of men and women in various ways which are sometimes subtle and sometimes shocking. They may consider themselves outside of the male-female two-gender model and identify as "Third Gender" or "Two Spirit" (for National Statistics, 2009).

Assexual

A person who does not desire physical/sexual relationships with other people (LGBT, 2014c).

Bisexuals

People who are physically and/or romantically attracted to other-and same-gender individuals. This does not mean that bisexuals must have relationships with more than one gender or that they are equally attracted to all genders, but simply that the potential exists to be attracted to more than one gender (LGBT, 2014c).

Coming Out

The process of a queer person becoming aware of his/her sexual orientation, gender identity, and/or intersex identity, and of letting other people know. This is a life-long, continual process because we live in a hetero-normative, gender-normative society. It is not uncommon for non-heterosexual people to be "out" to some people (e.g., certain friends, family) and not "out" to others (e.g., a boss, work colleagues). The decision to disclose one's sexual orientation or gender identity should always be a personal decision – you should never out another person (LGBT, 2014c).

Cross Dressers

Wear clothing usually associated with the gender "opposite" to their anatomical sex. Cross dressing may be done full- or part-time in the privacy of the person's own home or in public. Cross-dressers' gender identity remains the same as their anatomical sex, and they typically do not seek medical treatment. Erotic pleasure is sometimes the motivation for cross dressing, especially in younger people. Cross-dressers can be attracted to either same-sex or opposite-sex partners, or both (LGBT, 2014c).

Drag

A term applied to individuals who cross dress often for entertainment purposes (LGBT, 2014c).

Drag Kings and Drag Queens

Present larger than life images of men and women, exaggerating gender stereotypes for entertainment, attention, or self-gratification (for National Statistics, 2009).

Gay Men

Men who form their primary loving and sexual relationships with other men (LGBT, 2014c).

Fag(got), Queen, Fairy

These are typically considered to be derogatory terms for gay men. Some gay men have chosen to reclaim these words and use them to have positive meanings, especially when using them in the company of other gay men and/or lesbians (LGBT, 2014c).

Gender reassignment

The process by which an individual reassigns their gendered appearance (LGBT, 2014c).

Gender recognition

The legal recognition of an individual's acquired gender as the opposite of the sex assigned at birth.

Usually once a person has begun the process of transitioning, pronouns that are appropriate to the gender towards which he or she is transitioning should be used (for National Statistics, 2009).

Gender Variance

A persons feelings about his or her gender identity that do not conform to the stereotypical boy/man or girl/woman category as assigned at birth. This variance is increasingly understood to derive from sex differentiation in the structure and working of the brain, which may be inconsistent with the other physical sex characteristics (LGBT, 2014c).

Heterosexuals/Straight People

People who are physically attracted to individuals of the "opposite" gender (LGBT, 2014c).

Homosexuals

Men and women who form their primary loving relationships with people of the same gender. Many gay people prefer that the terms "gay men and lesbians" or "gay people" be used to describe homosexuals as a group rather than the term "homosexuals" (LGBT, 2014c).

Intersex

This is a general term used for a variety of conditions in which a person is born with chromosomal, hormonal, and/or anatomical attributes that do not fit the "typical" definitions for female or male. Many intersex people are surgically "corrected" in infancy, and some grow up to feel like they have had an essential part of themselves taken away without their consent (for National Statistics, 2009).

Lesbians

Women who form their primary loving and sexual relationships with other women. Some lesbians prefer to call themselves "lesbians" and use the term "gay" to refer to gay men. Others use the term "gay" to refer to all homosexuals (LGBT, 2014c).

Dyke

This is typically considered to be a derogatory term for lesbians. Some lesbians have chosen to reclaim this word to have a positive meaning, especially when using it in the company of other lesbians and/or gay men (LGBT, 2014c).

Omnisexual/pansexual

A person who is physically and/or romantically attracted to all or many gender expressions. Ominsexual attraction typically is more focused on individuals not conforming to a certain gender identity (LGBT, 2014c).

Queer

An umbrella term which embraces a matrix of sexual orientations and behaviors of the not-exclusively-heterosexual majority. Queer is a reclaimed word that was formerly used solely as a slur but that has been semantically overturned by members of the maligned group, who use it as a term of defiant pride. It is important to note that today, even those for whom the term mighty apply, some still see the word as a hateful insult (LGBT, 2014c).

Trans

Trans is an umbrella term used to describe people whose lives appear to conflict with the gender norms of society. Whether this is in their clothing, in presenting themselves or undergoing hormone treatment and surgery.

Being trans does not imply any specific sexual orientation (LGBT, 2014c).

Transgender

This is an umbrella term that applies to anyone who does not feel that their gender identity (e.g., identifying as male, female, or other) matches their anatomical/biological sex (for National Statistics, 2009).

Transitioning

There is a spectrum of what transitioning looks like for different people. It can range from simply socially presenting (clothes, hair, mannerisms, overall gender expression) as the gender with which they identify, to use of hormones, to surgical procedures to modify the physical body (for National Statistics, 2009).

Transman

A female-to-male (FTM) transsexual man (transman) is someone who was labelled female at birth but has a male gender identity and therefore transitions to live completely and permanently as a man (LGBT, 2014b).

Female-to-male transsexual men can be described as straight if they are attracted to women, gay if they are attracted to men or bisexual if they are attracted to both men and women (LGBT, 2014b).

Transsexual

This is typically used to describe people who identify as transgender who are transitioning toward the gender with which they identify. This may include socially presenting (e.g., clothing, hair, mannerisms, overall gender expression) as the gender with which they identify, or it may include more extensive changes like taking hormones and/or surgical procedures to modify their body (for National Statistics, 2009).

Transsexualism

This term is used to describe a person who has "transitioned", or is in the process of "transitioning", or intends to transition from male to female or female to male. For a transsexual person, the process of "transitioning", may involve a variety of treatments including: hormone therapy, surgery and hair removal. People who have transitioned do not necessarily identify as trans any longer; they may identify as simply a man or a woman. Some transsexual people may not transition due to family or other social constraints (LGBT, 2014c) (for National Statistics, 2009).

When people complete their transition, they may no longer regard themselves as part of the trans umbrella. They might consider having been transsexual to just be an aspect of their medical history which has now been resolved and so is no longer an issue in their life. In such cases, they simply describe themselves as men or as women and it is most disrespectful to insist on calling them trans, transgender or transsexual against their wishes (LGBT, 2014b).

Transvestite

A transvestite individual feels compelled to wear clothing normally associated with the opposite sex, but does not desire to live permanently as a member of the opposite sex (LGBT, 2014c).

Transwoman

A male-to-female (MTF) transsexual woman (transwoman) is someone who was labelled male at birth but has a female gender identity, and therefore transitions to live completely and permanently as a woman (LGBT, 2014b).

Male-to-female transsexual women can be described as straight if they are attracted to men, lesbian if they are attracted to women or bisexual if they are attracted to both men and women (LGBT, 2014b).

Transphobia

Examples of Transphobic Crime -

- A 16 year old trans girl, on her way to school, regularly experienced people shouting insults from their cars like, "Girl with a cock", "There's the he/she/it", "Tranny boy" and other names.
- An 18 year old received 84 abusive and threatening text messages within three days after she told her former school class that she had transitioned.
- An older boy pulled up the skirt of a 12 year old trans girl to look at her genitals.
- A trans women was discovered at a bus station by another woman who then engaged in yelling abuse, spitting, punching, kicking and trying to scratch the trans woman's face.
- A trans police officer was outed by the press under the headline "Lady Boy in Blue". She was then threatened by a group of young men, near her home; her car was vandalised.
- An elderly trans man was surrounded by a teen-age gang who shouted insults and poked him with sticks.
- A 15 year old trans girl was beaten up on her way home.
- A trans woman was raped at knife-point on her way home.
- An assailant approached a trans woman, after realising she was transsexual, punched her to the ground, undid his trousers and forced her to perform an act of oral sex on him.
- A son murdered his father on discovering he was a transsexual person (GIRES, 2010).

The following are a few examples of transphobic attitudes -

- The belief/insistence that trans women are not "real women",
- The belief/insistence that trans men are not "real" men,
- The belief/insistence that non-binary genders are invalid. You are either 'male' or 'female', there are no other options available.
- The belief/insistence that transsexual people are gay people in denial and wish to have sex reassignment surgery to attempt to restore 'heteronormativity',

- The refusal to acknowledge a trans persons true gender,
- Refusal to use the correct name for a trans person,
- Repeated and deliberate mis-gendering of trans people,
- Exclusion of trans people from activities, services or conversations (LGBT+, 2016).

Transphobia has been defined by the UK Crown Prosecution Service as -

> "The fear of or a dislike directed towards trans people, or a fear of or dislike directed towards their perceived lifestyle, culture or characteristics, whether or not any specific trans person has that lifestyle or characteristic. The dislike does not have to be so severe as hatred. It is enough that people do something or abstain from doing something because they do not like trans people."

Transphobia and prejudice against trans people are sadly all too common in our society and trans people often meet with discrimination and prejudice when they're trying to get on with their lives and perform everyday activities (LGBT+, 2016).

Transphobia is fear, discrimination or hatred against transgender people or people of non-binary gender.

Transphobia is often closely connected with homophobia and is justified for the same reasons that homophobes use to justify their hatred of gays (religion, prescriptive gender norms, etc.). Indeed, many clueless homophobes conflate homosexual people with transgender people and cross-dressers. Transphobia also manifests itself in some schools of radical feminist thought, as some feminists resent the idea that people who aren't "really" women might make claims as women.

On a societal scale, it can manifest itself in any number of ways, from systemic discrimination against transgender people in housing, healthcare, and employment, to a relatively high murder rate, to a series of demeaning depictions in the mass media.

Media and police

Transgender people are regularly discriminated against by the media and police. Both the media and police when involving a transgender person invariably use the descriptor "transsexual" or "transvestite" (with its associated archaic psychiatric baggage) in place of transgender. Transgender people face high rates of rape and deaths in custody while in prison. The media, in going for sensationalised stories, typically publish the transgender person's previous name without permission even if they have legally changed their name and that name change is protected by privacy laws. An individual's gender identity is suggested in these stories to be fake or a fraud by connotation, with the intention to deceive.

When referring to trans women, the use of recycling exaggerated stereotypes such as "long and leggy", "tall physique", "fierce looking", "muscular", etc. combined with negative notions that transgender individuals are perverted or depraved is all-too common in the media. Such stereotypical imagery is imposed on other media such as film and television, where trans women are mostly portrayed in acting roles as sick, twisted, prostitutes or "stranger danger" serial killers.

On 9 May 2014, the UK Press Complaints Commission ruled in Dr Kate Stone v Daily Mirror, that the publication of a person's transgender status is not relevant and that the disclosure of a person's previous name without consent was an unjustified intrusion into their privacy (PCC, 2014). Newspapers named in the original complaint complied with the ruling and removed reference to Dr. Stone's birth name and transgender status on-line. The media covering the PCC case, not involved in the original complaint, ignored the ruling, such as The Guardian with a piece written by feminist journalist Yvonne Roberts, who referred to Dr. Stone as "Transgender Kate Stone" before amending their story caption to "Scientist Kate Stone" six hours after publication, following complaints by readers (the story url however remains unchanged and visible as "transgender-kate-stone-press-complaints-commission-ruling") (TheGuardian, 2014).

Among fundamentalist Christians

Fundamentalist Christians do not, as a rule, (Roberts, 2008) think highly of transgender people. This opinion is generally based upon a handful of biblical verses, such as Genesis 1:26: "And God created man in His image, in His likeness; male and female He created them... and it was very good." From this, through a generous bit of interpolation, conservative Christians conclude that transgender people (like gays) are either actively rebelling against God (Wright, 2010) or have been socialized into it by bad parenting, the liberal media, and other such machinations of Satan (Bohlin, 2001).

Some fundamentalists, such as Pastor Sean Harris of Berean Baptist Church in Fayetteville, North Carolina, have advocated beating children at the first sign of "gender-inappropriate" behaviour; for example, says the pastor, when a four-year-old boy lets his wrist go limp, his father needs to paste him one in the jaw, and if his daughter starts acting too butch, he needs to demand that she make herself attractive (Murdock, 2012).

I'd like to conclude this small section with a scripture from Galatians 3:28 which reads, "There is neither Jew nor Greek, neither slave nor free, neither male nor female; for you are all one in Christ Jesus."

In the UK ...

In the UK, homophobic and transphobic hate crime is still a serious issue. In 2013, one in eight lesbian, gay and bisexual people were the target of verbal abuse, physical assaults and harassment. What's more, some reports suggest that as many as 75% of transgender people are victims of hate crime every year. In the UK, a hundred lesbian, gay, bisexual and transgender (Lesbian, Gay, Bisexual and Transsexuals (LGBT)) hate crimes are reported to the police weekly, but estimates from LGBT organisations suggest a far higher incident rate. Many individuals receive so much abuse that they don't see the point in reporting every incident, while others don't trust the police system to act. There are even more worrying statistics about homophobic abuse online, which is almost never reported. In 2013 the word 'faggot' was tweeted a staggering 13 million times.

Hate crimes and incidents are any crime or incident which is targeted at a victim because of the offender's hostility or prejudice against an identifiable group of people.

So any incident or crime, which is perceived to be motivated because of a person's sexual orientation or transgender identity - either their actual sexual orientation or gender identity or as perceived by the offender - will be recorded as such. Hate crimes can be committed against a person or property.

A homophobic hate crime is -

> "Any criminal offence which is perceived, by the victim or any other person, to be motivated by a hostility or prejudice based on a persons sexual orientation or perceived sexual orientation."

A transphobic hate crime is -

> "Any criminal offence which is perceived, by the victim or any other person, to be motivated by a hostility or prejudice against a person who is transgender or perceived to be transgender" (Vision, 2016).

What type of incidents can be a homophobic or transphobic hate incident?

Homophobic and transphobic hate incidents can take many forms including -

- verbal and physical abuse,
- physical violence,
- teasing,
- bullying,
- threatening behaviour,

- online abuse,
- damage to property,

It can be a one-off incident or part of an ongoing campaign of harassment or intimidation.

Hate incidents are not only carried out by strangers. It could be carried out by a carer, a neighbour, a teacher or someone you consider a friend (CAB, 2015).

Treatment aims

For a long time I have wondered exactly what are the aims of my medical treatment? Is it good breast development? Is it gaining social acceptance in the community in which I live? Is it having a good sex life? Or is it some combination of all of these things? Well, those are my aims, but the doctors think in terms of numbers, thinking if we can't measure it then its not important! Although that last bit may not be quite true :)

Breast growth, easy, that's the Tanner Scale (wikipedia, 2016). Social acceptance? That's harder to measure, although there are probably psychological tests which can 'supposedly' measure that! A good sex life? Ditto!

But the numbers really come to the fore with blood results of the various hormones that we take. The generally stated medical aims are *"The aim of therapy is to achieve a plasma estradiol level in the upper follicular range (400–600 pmol/litre) (Seal et al., 2012) and testosterone level in the normal female range (0–2.8 nmol/litre) (H. Turner and WJA, 2009)"*.

However, in 2013, the Royal College of Psychiatrists downgraded this to *"a representative range for the upper half of the follicular range is 300–400 pmol/l or 80–140 pg/ml"* (Psych, 2013).

They then go on to say *"Levels higher than this **may** be associated with the established side-effects of excessive oestrogen, particularly thromboembolism, hypertension and myocardial infarction. Physiological levels should be able to produce the desired phenotypic changes, particularly if the circulating androgen levels and their effects are suppressed"* (Psych, 2013). I have highlighted the word "may", as it is not an absolute, definite fact, just something that might happen, and again might not happen!

Understanding "Enteric Coating"

There isn't just one enteric coating that is used industry-wide. There are many different formulations that are used for different applications (i.e., one for gelcaps, one for granules, another for tablets, etc.). Here's a link to one company that makes the coatings for pharmaceutical companies: www.idealcures.com/enteric-coating.html (where it says "weight gain" in their table, don't worry, they're talking about how much weight it adds to the pills coated with it). The entire purpose of these coatings is to allow them to survive through stomach acids - saliva isn't going to dissolve the coating, so for those who've planned to dissolve such pills under your tongue (sublingual administration), enteric coated pills won't work for that. You'd have to "breach the barrier" to absorb the medication sublingually (i.e., puncture the gelcap or crush the tablet). Some will invariably go down your throat and into your stomach - and these coatings are usually added for a limited number of reasons. Either -

1. because the medication is likely to make your stomach upset if dissolved there.
2. to time-release the medication instead of all at once.
3. to target the medication to the small intestine.

Coated medicines are usually labeled as being "Enteric Coated" or "Time Release" or "Targeted Medication" (or words to that effect). Some people are allergic to the coatings themselves and labeling regulations therefore require that the packaging information indicates that such coatings are present.

See also Methods of Delivery or Administration, and also How to Take Your Tablets.

Units of measurement

International Unit (IU)

This is a standard measure of the biological activity (biological effect) of manufactured medicinal drugs and vitamins. For every substance to which this unit is assigned, there is an internationally accepted biological effect expected with a dose of 1 IU. Other quantities of the standard preparation of the substance are expressed in multiples of this dose and may be converted into mass units. For example, 1IU is equivalent to 45.5 microgram (0.0455 milligram) of insulin, 0.6 microgram (0.0006 milligram) of penicillin, 0.3 microgram (0.0003 milligram) of vitamin-A, 50 micrograms (0.050 milligram) of vitamin-C, or 25 nanograms (0.000025 milligram) of vitamin-D (businessdictionary.com, 2014).

Unit	microgram	milligram

1 IU	45.5 microgram of insulin	0.0455 milligram of insulin
	0.6 microgram of penicillin	0.0006 milligram of penicillin
	0.3 microgram of Vitamin A	0.0003 milligram of Vitamin A
	50 micrograms of Vitamin C	0.050 milligram of Vitamin C
	25 nanograms of Vitamin D	0.000025 milligram of Vitamin D

Table 17.28 – Equivalents of 1 IU

Urinary Tract Infections

Urinary tract infections (UTI's) are common in adults, with the greatest prevalence in women. One-half of all women will develop a UTI at some point. Recurrent UTIs also may be an issue for women. Sexual intercourse is a major risk factor, and postcoital prophylactic antibiotic treatment has been shown to be effective. Immediate antibiotic treatment of UTI symptoms also has shown efficacy. Although cranberry supplements or juice may be effective, the benefit of other commonly recommended treatments, such as frequent or postcoital voiding, increased fluid consumption, and avoiding bubble baths, has not been shown (Fiore and Fox, 2014).

Urinary tract infections are one of the most common bacterial infections, and over 50% of women will have a UTI during their lifetimes. Antibiotics are used for prophylaxis of recurrent UTIs but can lead to emergence of drug-resistant bacteria. Therefore, it is reasonable to investigate nutritional strategies for prevention of UTI's. Cranberry juices and supplements have been used for UTI prophylaxis, but with variable efficacy. Because dried cranberries may contain a different spectrum of polyphenolics than juice, consuming berries may or may not be more beneficial than juice in decreasing the incidence of UTI's in susceptible women. The primary objectives of this study were to determine if consumption of sweetened, dried cranberries (SDC) decreases recurrent UTI's and whether this intervention would alter the heterogeneity, virulence factor (VF) profiles, or numbers of intestinal E. coli (Burleigh et al., 2013).

Cranberry juice is a popular beverage with many health benefits. It has anthocyanins to supplement dietary needs. Based on in-vitro evidence cranberry juice is an inhibitor of CYP enzymes and at higher amounts as potent as ketoconazole (CYP3A) and fluconazole (CYP2C9). There is, however, a discrepancy between in-vitro and in-vivo observations with respect to a number of substrates (cyclosporine, warfarin, flurbiprofen, tizanidine, diclofenac, amoxicillin, ceflacor); with the exception of a single report on midazolam, where there was a moderate increase in the AUC.

Vaginal Itching and Discharge

Vaginal itching (pruritus), discharge, or both result from infectious or noninfectious inflammation of the vaginal mucosa (vaginitis), often with inflammation of the vulva (vulvovaginitis). Symptoms may also include irritation, burning, erythema, and sometimes dysuria and dyspareunia. Symptoms of vaginitis are one of the most common gynecologic complaints.

Pathophysiology

Some vaginal discharge is normal, particularly when oestrogen levels are high a few days before ovulation. Oestrogen levels are also high during the first 2 weeks of life (because maternal oestrogens are transferred before birth), during the few months before menarche and during pregnancy (when oestrogen production increases), and with use of drugs that contain oestrogen or that increase oestrogen production (eg, some fertility drugs). However, irritation, burning, and pruritus are never normal.

Normally in women of reproductive age, Lactobacillus sp is the predominant constituent of normal vaginal flora. Colonization by these bacteria keeps vaginal pH in the normal range (3.8 to 4.2), thereby preventing overgrowth of pathogenic bacteria. Also, high oestrogen levels maintain vaginal thickness, bolstering local defenses.

Factors that predispose to overgrowth of bacterial vaginal pathogens include -

- Use of antibiotics (which may decrease lactobacilli),
- Alkaline vaginal pH due to menstrual blood, semen, or a decrease in lactobacilli,
- Poor hygiene,
- Frequent douching,
- Pregnancy,
- Diabetes mellitus.

Etiology

The most common causes vary by patient age.

Children

Vaginitis usually involves infection with gastrointestinal tract flora (nonspecific vulvovaginitis). A common contributing factor in girls aged 2 to 6 years old is poor perineal hygiene (eg, wiping from back to front after bowel movements, not washing their hands after bowel movements). Chemicals in bubble baths or soaps may cause inflammation and pruritus of the vulva, which often recur. Foreign bodies may cause nonspecific vaginitis, often with a scant bloody discharge.

Women of reproductive age

Vaginitis is usually infectious. The most common types are -

- Bacterial vaginosis,
- Candidal vaginitis,
- Trichomonal vaginitis (usually sexually transmitted).

Vitality

Vitality is the juice of life. Some days it can be difficult to come by if you are stressed out, living with a chronic disease, overworked or just plain worn out. People at midlife have so many responsibilities, from work to caring for elderly parents to caring for friends in need. Transition itself is very stressful. Many times it is difficult - if not virtually impossible - to make yourself a priority.

What to do?

Take a breath and give yourself permission to not be perfect - If you are seeking to regain vitality begin with carving out some time just for you. This will help you think about what you need most. Perhaps call it "Me time"?

Re-charge your energy - Do this by prioritising and doing those things that help you increase your energy. It may be spending time with a dear friend, reading, taking a nap, or reconnecting to nature.

Listen to your body talk - Vitality begins inside. Is your body talk negative? Or, is it positive? Is the way you think about yourself sapping your creativity? Gently make a deal with yourself to only give yourself loving thoughts.

Release the guilt of "not being everything to everyone" - Those that you love in your life will not collapse if you move to nurture yourself. In the end they will thank you, as it is impossible to give to others from a place of imbalance and exhaustion.

Find something to laugh about - Lighten the moment by laughing at yourself (many things in life are truly funny!). Smiles, energy and attitude will give you the capacity to once again be on the path of full personal vitality (womeninbalance.org, 2016c).

Vitamins

There is some anecdotal evidence that taking a daily vitamin and mineral supplement will assist our bodies cope with the usage of the hormones. Lowering androgen and increasing oestrogen levels tends to decrease the available skin oil to the skin, and they can also cause brittle hair and nails, and a thinning of the skin may well occur, then supplements may help. There is also a case for the usage of some form of oil supplementation to the fingernails, perhaps in the form of some brand of hand cream, but whichever works best for you. But we also need to consider the timing of taking the tablets as, vitamin C reputedly increases the therapeutic effectiveness of oral contraceptives, possibly by, in the case of ethinylestradiol, competing for sulphation in the gastrointestinal mucosa, thus increasing the plasma concentration of the oestrogen. In other words, Vitamin C should not be taken at the same time as any oestrogen tablets, it is better to take them 12 hours apart to get the most benefit out of both tablets.

A large study in 2011 showed that in women who were 60 years old or older, that their use of the most common dietary supplements (i.e., multivitamins, vitamin B6, folic acid, iron, magnesium, and zinc) showed an increased risk of mortality, except for the usage of calcium which showed a reduced risk of mortality in older women

Common vitamins

Age	**Folate µg**	**Niacin mg**	**Riboflavin mg**	**Thiamin mg**	**Vit A µg**
Males					
19–70	400	16	1.3	1.2	900
>70	400	16	1.3	1.2	900
Females					
19–70	400	14	1.1	1.1	700
≥70	400	14	1.1	1.1	700
Age	**Vit B12 µg**	**Vit C mg**	**Vit D IU**	**Vit E mg**	**Vit K µg**
Males					
19–70	1.3	90	600	15	120
>70	2.4	90	800	15	120

Age	Folate µg	Niacin mg	Riboflavin mg	Thiamin mg	Vit A µg
Females					
19–70	2.4	75	600	15	90
≥70	2.4	75	800	15	90 (L. Johnson, 2014)

Table 17.29 – Recommended Daily Intakes for Vitamins

Vitamin A

Vitamin A helps form and maintain healthy teeth, bones, soft tissue, mucus membranes, and skin. Half to 65% of the adult RDA for vitamin A is easily obtained simply by eating the recommended five servings of fruits and vegetables per day.

Gender	Age range	RDA or AI
Females	19 years and over	770 mcg/day (2,565 IU/-day)
Males	14 years and up	900 mcg/day (3,000 IU/-day)

Table 17.30 – Recommended Dietary Allowance (RDA) in micrograms (mcg) of Retinol Activity Equivalents (RAE)

Upper tolerable limit (UL) = 19 years and up, 3,000 mcg/day (10,000 IU/day)

The tolerable upper intake levels of a supplement are the highest amount that most people can take safely. Higher doses might be used to treat vitamin A deficiencies.

Food Sources - Dark-coloured fruit, dark leafy vegetables, egg yolk, fortified milk and dairy products (cheese, yogurt, butter, and cream), liver, beef, and fish (Unknown, 2014).

Deficiencies - Vitamin A deficiency can result from inadequate intake, fat malabsorption, or liver disorders. Deficiency impairs immunity and hematopoiesis[151] and causes rashes and typical ocular effects (eg, impaired night vision) (L. Johnson, 2014).

[151] This is a process of blood cell production and maturation in the bone marrow (AB, 2011)

Vitamin C

Vitamin C, also called ascorbic acid, is an antioxidant that promotes healthy teeth and gums. It helps the body absorb iron and maintain healthy tissue. It also promotes wound healing.

Age & Gender	RDA or AI
Females 19 years and up	75 mg/day
Males 19 years and up	90 mg/day

Table 17.31 – Recommended Dietary Allowance (RDA) of Vitamin C

Upper tolerable limit (UL) = 2,000 mg/day

Food Sources - Broccoli, brussels sprouts, cabbage, cauliflower, citrus fruits, potatoes, spinach, strawberries, tomato juice, tomatoes (Unknown, 2014).

Deficiencies - In developed countries, vitamin C deficiency can occur as part of general undernutrition, but severe deficiency (causing scurvy) is uncommon. Symptoms include fatigue, depression, and connective tissue defects (eg, gingivitis, petechiae, rash, internal bleeding, impaired wound healing) (L. Johnson, 2014).

Vitamin D

Vitamin D is also known as the "sunshine vitamin," since it is made by the body after being in the sun. Ten to 15 minutes of sunshine three times a week is enough to produce the body's requirement of vitamin D. People who do not live in sunny places may not make enough vitamin D. It is very difficult to get enough vitamin D from food sources alone. Vitamin D helps the body absorb calcium, which you need for normal development and maintenance of healthy teeth and bones. It also helps maintain proper blood levels of calcium and phosphorus. See also Further discussion of Vitamin D.

Age & Gender	RDA or AI
Age 1–70	600 IU / 15 mcg/day
Age 70 and older	800 IU / 20 mcg/day

Table 17.32 – Recommended Dietary Allowance (RDA) or Adequate Intake (AI) of Vitamin D

Upper tolerable limit (UL) = 4,000 IU or 100 mcg/day

Food Sources - Fish (fatty fish such as salmon, mackerel, herring, and orange roughy), fish liver oils (cod's liver oil), fortified cereals, fortified milk and dairy products (cheese, yoghurt, butter, and cream) (Unknown, 2014).

Deficiencies - Inadequate exposure to sunlight predisposes to vitamin D deficiency. Deficiency impairs bone mineralization[152] , causing rickets in children and osteomalacia[153] in adults and possibly contributing to osteoporosis (L. Johnson, 2014).

Vitamin E

Vitamin E is an antioxidant also known as tocopherol. It plays a role in the formation of red blood cells and helps the body use vitamin K.

Category	RDA or AI
Adults	15 mg/day (22.4 IU)

Table 17.33 – Recommended Dietary Allowance (RDA) in milligrams (mg) and International Units (IU) of Vitamin E

Upper tolerable limit (UL) = 1,000 mg/day (1,500 IU)

Food Sources - Avocado, dark green vegetables (spinach, broccoli, asparagus, turnips) margarine (made from safflower, corn, and sunflower oil) oils (safflower, corn, and sunflower), papaya and mango, seeds and nuts, wheat germ and wheat germ oil (Unknown, 2014).
Because vitamin E is fat-soluble, supplements are best absorbed with food.

Deficiencies - Dietary vitamin E deficiency is common in developing countries; deficiency among adults in developed countries is uncommon and usually due to fat malabsorption. The main symptoms are haemolytic anemia and neurologic deficits (L. Johnson, 2014).

Vitamin K

Vitamin K is not listed among the essential vitamins, but without it blood would not coagulate. Some studies suggest that it is important for promoting bone health.

Vitamin K is actually a group of compounds. The most important of these compounds appears to be vitamin K1 and vitamin K2.

Vitamin K1 is obtained from leafy greens and some other vegetables.

Vitamin K2 is a group of compounds largely obtained from meats, cheeses, and eggs, and synthesized by bacteria.

[152]This is the deposition of calcium hydroxyl apatite salts converting osteoid to rigid bone; dependent on mineral availability (calcium, phosphate and hydrogen ions), enzyme action (alkaline phosphatase), osteocyte activity (osteoblasts and osteoclasts), hormones (parathyroid hormone, thyroid calcitonin) and vitamin D (Mooney, 2009)

[153]Osteomalacia refers to a softening of your bones, which are more likely to bow and fracture than are harder, healthy bones (M. C. Staff, 2014a)

Gender	RDA or AI
Adult females	90 micrograms/day
Adult males	120 micrograms/day

Table 17.34 – Recommended Dietary Allowance (RDA) or Adequate Intake (AI) of Vitamin K

Vitamin K is well-tolerated even at high doses. Researchers have not set a maximum safe dose.

Food Sources - Cabbage, cauliflower, cereals, dark green vegetables (broccoli, Brussels sprouts, asparagus), dark leafy vegetables (spinach, kale, collards, turnip greens), fish, liver, beef, eggs (Unknown, 2014).

Deficiencies - Vitamin K deficiency results from extremely inadequate intake, fat malabsorption, or use of coumarin anticoagulants. It decreases levels of prothrombin and other vitamin Kdependent coagulation factors, causing defective coagulation and, potentially, bleeding (L. Johnson, 2014).

Vitamin B1

Thiamine (vitamin B1) helps the body cells change carbohydrates into energy. Getting plenty of carbohydrates is very important during pregnancy and breast-feeding. It is also essential for heart function and healthy nerve cells.

Age & Gender	RDA
Adult males	1.2 mg/day
Adult females	1.1 mg/day (medscape, 2014e)

Table 17.35 – Recommended Dietary Allowance (RDA) of Vitamin B1

Food Sources - Dried milk, egg, enriched bread and flour, lean meats, legumes (dried beans), nuts and seeds, organ meats, peas, whole grains (Unknown, 2014).

Deficiencies - Thiamin deficiency (causing beriberi) is most common among people subsisting on white rice or highly refined carbohydrates in developing countries and among alcoholics. It also develops when intake of other nutrients is inadequate, as may occur in young adults with severe anorexia; it often occurs with other B vitamin deficiencies (L. Johnson, 2014).

Vitamin B2

Riboflavin (vitamin B2) works with the other B vitamins. It is important for body growth and the production of red blood cells.

Recommended Dietary Allowance (RDA) of Vitamin B2 is 1-1.6 mg for adults.

Food Sources - Dairy products, eggs, green leafy vegetables, lean meats, legumes, milk, nuts (Unknown, 2014).

Deficiencies - Riboflavin deficiency usually occurs with other B vitamin deficiencies.

- - **Primary deficiency** - results from inadequate intake of fortified cereals, milk, and other animal products.
- - **Secondary deficiency** - is most commonly caused by chronic diarrhoea, malabsorption syndromes, liver disorders, haemodialysis, peritoneal dialysis, long-term use of barbiturates, and chronic alcoholism (L. Johnson, 2014).

Vitamin B3

Niacin is a B vitamin that helps maintain healthy skin and nerves. It is also has cholesterol-lowering effects.

Gender	RDA or AI
Males	16 mg/day
Females	14 mg/day

Table 17.36 – Recommended Dietary Allowance (RDA) or Adequate Intake (AI) of Vitamin B3

Upper tolerable limit (UL) = 35 mg/day for (adults of all ages)

Food Sources - Avocado, eggs, enriched breads and fortified cereals, fish (tuna and salt-water fish), lean meats, legumes, nuts, potato, poultry (Unknown, 2014).

Deficiencies -

- - **Primary deficiency** - results from extremely inadequate intake of both niacin and tryptophan, which usually occurs in areas where maize (Indian corn) constitutes a substantial part of the diet. Deficiencies of protein and many B vitamins commonly accompany primary niacin deficiency.
- - **Secondary deficiency** - may be due to diarrhoea, cirrhosis, or alcoholism (L. Johnson, 2014).

Vitamin B5

Pantothenic acid is essential for the metabolism of food. It is also plays a role in the production of hormones and cholesterol.

Age & Gender	RDA
Adult Males & Females	5 mg/day (medscape, 2014d)

Age & Gender	RDA

Table 17.37 – Recommended Dietary Allowance (RDA) of Vitamin B5

Food Sources - Avocado, broccoli, kale, and other vegetables in the cabbage family, eggs, legumes and lentils, milk, mushroom, organ meats, poultry, white and sweet potatoes, whole-grain cereals (Unknown, 2014).

Deficiencies - Isolated deficiency of pantothenic acid virtually never occurs (L. Johnson, 2014).

Vitamin H

Biotin is essential for the metabolism of proteins and carbohydrates, and in the production of hormones and cholesterol.

Age & Gender	RDA
Male & Female	30 mcg/day (medscape, 2014a)

Table 17.38 – Recommended Dietary Allowance (RDA) of Vitamin H

Food Sources - Chocolate, cereal, egg yolk, legumes, milk, nuts, organ meats (liver, kidney), pork, yeast (Unknown, 2014).

Deficiencies -Isolated deficiency of biotin virtually never occurs (L. Johnson, 2014).

Vitamin B6

Vitamin B6 is also called pyridoxine. Vitamin B6 helps form red blood cells and maintain brain function. This vitamin also plays an important role in the proteins that are part of many chemical reactions in the body. Eating larger amounts of protein may reduce vitamin B6 levels in the body.

Age & Gender	RDA
Males <50 years old	1.3 mg/day
>50 years old	1.7 mg/day
Females <50 years old	1.3 mg/day
>50 years old	1.5 mg/day (Reddy, 2014)

Table 17.39 – Recommended Dietary Allowance (RDA) of Vitamin B6

Deficiency usually occurs in conjunction with inadequate intake of other B vitamins due to poor diet or malabsorption states (medscape, 2014f).

Food Sources - Avocado, banana, legumes (dried beans), meat, nuts, poultry, whole grains (milling and processing removes a lot of this vitamin) (Unknown, 2014).

Deficiencies - Because vitamin B6 is present in most foods, dietary deficiency is rare. Secondary deficiency may result from various conditions (L. Johnson, 2014).

Vitamin B12

Vitamin B12, like the other B vitamins, is important for metabolism. It also helps form red blood cells and maintain the central nervous system.

Gender & Age	Adequate Intake (AI)
14 years and up	2.4 mcg/day

Table 17.40 – Recommended Dietary Allowance (RDA) in micrograms (mcg) of Vitamin B12

Even at high doses, vitamin B12 seems fairly safe. Experts have not found a specific dose of vitamin B12 that's dangerous. No tolerable upper intake levels have been set.

Food Sources - Meat, eggs, fortified foods such as soymilk, milk and milk products, organ meats (liver and kidney), poultry, shellfish (Unknown, 2014).

Deficiencies - Dietary vitamin B12 deficiency usually results from inadequate absorption, but deficiency can develop in vegans who do not take vitamin supplements. Deficiency causes megaloblastic anemia, damage to the white matter of the spinal cord and brain, and peripheral neuropathy (L. Johnson, 2014).

Vitamin B9

Folate works with vitamin B12 to help form red blood cells. It is needed for the production of DNA, which controls tissue growth and cell function. Any woman who is pregnant should be sure to get enough folate. Low levels of folate are linked to birth defects such as spina bifida. Many foods are now fortified with folic acid.

Gender	RDA
Male & Female	about 200–400 µg/day (Ghadban, 2014)

Table 17.41 – Recommended Dietary Allowance (RDA) of Vitamin B9

Healthy individuals have about 500–20000 µg of folate stored, mainly in the liver.

Food Sources - Asparagus and broccoli, beets, brewer's yeast, dried beans (cooked pinto, navy, kidney, and lima), fortified cereals, green, leafy vegetables (spinach and romaine lettuce), lentils, oranges and orange juice, peanut butter, wheat germ (Unknown, 2014).

Deficiencies - Folate deficiency is common. It may result from inadequate intake, malabsorption, or use of various drugs. Deficiency causes megaloblastic anaemia (indistinguishable from that due to vitamin B12 deficiency) (L. Johnson, 2014).

Water

Water is essential for life. Water is a component of blood; many nutrients are dissolved in water so they can be absorbed effectively in the digestive tract. Cells need to be bathed in water. Water carries waste from our body, and water absorbs and transports heat so that our skin, muscles and vital organs maintain the proper temperature. Drinking enough water is essential for elimination and preventing constipation.

You need to hydrate. Water is essential to maintaining stamina. Even getting mildly dehydrated can compromise normal physiology. Did you know that sometimes we may think we are hungry when we are really thirsty? Of course then, drinking water can help in weight management. Water can help keep your skin clear and glowing too!

What to do?

Drink at least 2 pints of water a day. Remember - once you are thirsty, you are already dehydrated! So drink enough water before you reach that point. Be sure to drink water that is at room temperature. Ice cold water restricts the digestive tract. Get in the habit of carrying water with you all day. Start with a glass of water in the morning, have water in your car, at your desk and in your bag or briefcase (womeninbalance.org, 2016b).

What is a hormone?

Mention has been made of hormones and anti-androgens, and I've been asked what the difference is. Therefore, a hormone[154] is *"A substance, usually a peptide or steroid, produced by one tissue and conveyed by the bloodstream to another to effect physiological activity, such as growth or metabolism"* (medical-dictionary, 2014), or more simply *"a chemical substance produced in the body*

[154] a chemical substance produced in the body which has a specific regulatory effect on the activity of certain cells or a certain organ or organs (medical-dictionary, 2014)

that controls and regulates the activity of certain cells or organs. Hormones are essential for every activity of life, including the processes of digestion, metabolism, growth, reproduction, and mood control. Many hormones, such as neurotransmitters, are active in more than one physical process" (medicinenet, 2012). As androgens are hormones manufactured by the testes and adrenal cortex (testosterone being well-known), an anti-androgen drug is something that minimises the amount of androgens being produced by the male body, thereby allowing other hormones to have a greater effect than otherwise.

What is a 'vitamin'?

Any of a group of organic substances essential in small quantities to normal metabolism, found in minute amounts in natural foodstuffs or sometimes produced synthetically (Dictionary.com, 2014).

Why we forget and how to remember

Unless you have a photographic memory, you likely find it hard to remember everything you learn, even an hour or two after you learn it. Why? Research about how we remember and forget gives us a clue.

How quickly we forget

19th century psychologist Hermann Ebbinghaus created the "Forgetting Curve" after studying how quickly he learned, then forgot, a series of three-letter trigrams. Here's what he discovered -

In the time it takes to make and drink a cup of coffee, you'll forget 42% of what you learned.

In about the time it takes to watch your favourite TV show, you'll forget 56% of what you learned.

During the course of a normal workday, you'll forget 64% of what you learned.

In less than a week, you'll only remember 25% of what you learned.

Why we forget

Our brains are hardwired to recall important facts. The process that determines what you remember and what you forget makes recalling every single detail nearly impossible.

Memory decay - When you learn something, a new memory "trace" is created. But if you don't rehearse and repeat what you've learned, memories decay and fade.

Interference - Old memories and new information compete with and distort the formation of new memories, making it difficult to remember what's new.

Failure to store - Some information is never transferred from short-term memory to long-term memory - especially details that are likely to be unimportant.

Memory repression - Memories of traumatic or disturbing events can be suppressed as a means of coping with difficult situations.

How to remember

In the century since Ebbinghaus discovered the Forgetting Curve, scientists have suggested several things you can do to reverse its effects -

Sleep - During slow-wave and REM sleep, memories are transferred from temporary storage in the hippocampus to more permanent memory around the cortex.

Novelty - Learning in creative or unfamiliar circumstances, or in new ways, is more memorable because it triggers additional activity in the hippocampus.

Stress - Like novelty, stressful or dangerous situations can make events more memorable. Stress helps imprint these "flashbulb memories" into our minds for easy recall.

Spaced repetition - best method - Reviewing what you learn strengthens the memory of it. Every additional review renews the learning, slows the forgetting curve, and makes the information more permanent in your memory.

How to take advantage of spaced repetition

It was Ebbinghaus who first identified the phenomenon of spaced repetition for improving memory. Since then, numerous studies have affirmed its powerful effects. Here's how to use spaced repetition to improve your learning -

Quick review - Within a few hours of first learning something new, read your notes, adding thoughts or summaries of the notes every few lines. If you don't have notes, reread the text or, if you're learning online vs. a classroom, re-watch portions of the course, taking notes this time.

Skip a day - While it may be tempting to repeat the process as soon as you can, an important part of spaced repetition is the spacing. The first review should be quick. Each subsequent review should take place at a longer interval than the previous one.

Review the material again - Review everything you've learned, not just what you've forgotten. For example, if you learned a new skill from online training, watch the course again, adding to your notes to make them more complete.

Take a test - Testing your memory improves retention by 20–50%. If your learning platform offers assessments or quizzes, take them to test your memory and make note of what youve missed for further review.

Repeat several times - The next review should take place 3–5 days later. Then review again roughly 6–10 days after that. Add another test for better retention. After 5–6 reviews at longer intervals, what you've learned will be a permanent part of your memory (pluralsight, 2016).

Zoff

If you use any sort of patches, or even elastoplasts, when you remove them or change them you tend to be left with a slightly-sticky grey residue around the edge of where the patch/elastoplast was. This can be laboriously scraped away with your fingernail, but at the risk of tearing the skin and starting to bleed. But a far more effective method of removal is "Zoff", a product made by Smith+Nephew which removes it very easily. It can be bought over the counter at your pharmacists and comes as little wipes, although I have used it in a liquid form on the ward whilst working in a hospital. It does have one downside though, it stinks, it really does smell and stink horrible, without being too fussy about it, although the smell does soon go. Having used it on numerous occasions and in different circumstances, I can thoroughly recommend it.

Chapter 18

Other resources

Books

Here are some books that you might find useful and interesting, again, this list is not exhaustive, just some that I've heard of.

Alice in Genderland: A Crossdresser Comes of Age
Richard J. Novic M.D.

Becoming a Visible Man
Jamison Green

Butch Is a Noun
S. Bear Bergman

Conundrum
Jan Morris

Finding the Real Me: True Tales of Sex and Gender Diversity
Tracie O'Keefe; Katrina Fox;

From The Inside Out: Radical Gender Transformation, FTM and Beyond
Morty Diamond

The Gender Frontier
Mariette Pathy Allen

Gender Outlaw: On Men, Women, and the Rest of Us
Kate Bornstein

How Sex Changed: A History of Transsexuality in the United States
Joanne Meyerowitz

Just Add Hormones: An Insider's Guide to the Transsexual Experience
Matt Kailey

The Last Time I Wore a Dress
Daphne Scholinski; Jane Meredith Adams;

Made In God's Image: A Resource for Dialogue About the Church and Gender Difference
Cook, Ann Thompson.

My Gender Workbook: How to Become a Real Man, a Real Woman, the Real You, or Something Else Entirely
Kate Bornstein

My Husband Betty: Love, Sex, and Life With a Crossdresser
Helen Boyd

Nobody Passes: Rejecting the Rules of Gender and Conformity
Matt Bernstein Sycamore

The Riddle of Gender: Science, Activism, And Transgender Rights
Deborah Rudacille

Self Made Men: Identity, Embodiment and Recognition Among Transsexual Men
Henry Rubin

Sex Changes: The Politics of Transgenderism
Pat Califia

Sexing the Body: Gender Politics and the Construction of Sexuality
Anne Fausto-Sterling

Stone Butch Blues
Leslie Feinberg

Toward a Recognition of Androgyny
Carolyn G. Heilbrun

Trans Liberation: Beyond Pink or Blue
Leslie Feinberg

Trans-Sister Radio: A Novel
Chris A. Bohjalian

Transgender Emergence: Therapeutic Guidelines for Working With Gender-Variant People and Their Families
Arlene Istar Lev

Transmen and FTMs: Identities, Bodies, Genders, and Sexualities
Jason Cromwell

Transparent: Love, Family, and Living the T with Transgender Teenagers
Cris Beam

True Selves: Understanding Transsexualism-For Families, Friends, Coworkers, and Helping Professionals
Mildred L. Brown; Chloe Ann Rounsley

Whipping Girl: A Transsexual Woman on Sexism and the Scapegoating of Femininity
Julia Serano

TransForming Families: Real Stories of Transgendered Loved Ones
Mary Boenke, Walter Trook Publishing, 1999.

Shes Not There: A Life in Two Genders
Jennifer Finney Boylan, Doubleday/Broadway, 2003.

Email

Sooner or later you will need some support, either face-to-face, or by a forum or email. Here are some email lists suggestions for you, but this is not an exhaustive list, you can easily search for more -

Crone

Go to CRONE portal is the place for those wishing to join the 500+ member **CRONE** hormones list to apply for an invitation.

CRONE is an international list for information about proper uses of female hormones and related products. A searchable archive of over 12,500 postings is available to members, along with many collected files and selected links. The title infers accumulated wisdom rather than age.

The list is designed for, and membership is limited to, those who are currently, or will in the near future be benefitting from female hormone therapy, and selected prescribers and researchers seeking to keep abreast of developments in the field.

CRONE is a list where the moderators keep the discussion on-topic. Those needing support in other aspects of their lives should have access to that elsewhere. But discussion on anything related to hormone therapy can take place in a safe, helpful, well-informed and "low noise" environment.

The pharmaceutical companies and their products, the research, the learned journals and professional conferences are all international. The chemical substances, and the responses and needs of the human body have no regard for national or continental borders. To limit the search for knowledge to one country is to create a dangerous vulnerability to the effects of the historical prejudices, the commercial interests, the myths, the unquestioned traditions that too often flourish. Members of **CRONE** have found that discussion in an international forum is the most effective way to avoid those dangers.

TS-DIY

Ts Do It Yourself Hormones

This site is strictly for MTF-FTM transsexuals who are already on hormones without a prescription or may be considering starting hormones on their own and are not sure how to go about it. This group can also be used as a guide for obtaining hormones from a doctor.

This group is for informational purposes only and is not intended to be a substitute for a doctors care or advice and is only a source of opinionated information. HORMONES ARE DANGEROUS! Do not substitute what is said here over what a doctor might tell you.

TS-OVER-40

TS-Over-40

This is a support group for Transsexuals 40 and up at any stage of transition. We are here to help resolve any problems that may occur, which can be from advice to real life experience.

Transsexual-UK

Transsexual-UK

A fast growing group with a variety of discussion, "Transsexual-UK" is a light hearted group with like minded members who share ideas and information, support one another, debate issues and often use the group as a social outlet. Whilst you are free to lurk, members are encouraged to ask questions and seek advice from the group, use the information resources, or simply just to enjoy a little social banter and a giggle.

Other groups

These are other groups that I have heard of, but have no knowledge of.

Facial Feminization Surgery
FTM Phalloplasty Info
FTM Surgery Financial Planning
FTM Surgery Info
FTM Medoidioplasty
MTF Surgery Info
Phalloplasty Info
The Art of Tucking
The Deciding Line (FTM Lower Surgeries)
Voice TS Group
Transsexual voice for the tone deaf

Films

Here are some films that you might find useful and entertaining, again, this list is not exhaustive, just some that I know of.

The Aggressives, 2005.
The Aggressives: young, hot, male-identified lesbians who don't call themselves men but pass nonetheless. This documentary follows five members of a New York City butch subculture: army recruit Marquise; runway model Kisha; pretty boy Rjai; Tiffany; club kid Octavia; and Flo.

Boys Dont Cry, 1999.
The story of the life of Brandon Teena, a transgender teen in Nebraska. Based on a true story.

Iron Ladies, 2001.
A volleyball team composed mostly of gay men and one transsexual athlete competes in the 1996 Thailand national championships. Based on a true story.

Ma Vie En Rose, 1997.
Seven-year-old Ludovic (Georges Du Fresne) is convinced he's a girl trapped in a boy's body in this Belgian film. His expressions of sexual identity, which include wearing dresses and starring in a classroom performance of "Snow White," put a strain on his family and elicit teasing and intolerance from his schoolmates and neighbours.

Normal, 2003.
After being married to Irma for 25 years, Roy decides the stress of being a woman in a man's body has grown intolerable. Roy's decision to pursue a sex confirmation operation is greeted with intolerance and disgust by some of his co-workers and members of his church. Irma eventually comes to some understanding, and supports Roy through his journey to becoming Ruth.

Southern Comfort, 2001.
Documents the last year of Robert Eads life before his death from cervical cancer. Portrays Robert and his adopted family of transsexuals living in the depths of Georgia, including his vivacious male-to-female transsexual girlfriend, Lola.

TransAmerica, 2005.
Bree (Felicity Huffman) gets the shock of her life when she discovers a son she didn't know she had, just a week before her final sex confirmation surgery. After bailing him out of jail, the two set out on a cross-country journey riddled with road bumps.

Transgeneration, 2005.
A year-in-the-life documentary series that follows four college students– Gabbie, Lucas, Raci, and T.S. –who are juggling the challenges of academia with their commitment to transition from their birth sex.

Some web sites

All links are in alphabetical order, not in order of relevance. I make no recommendations, if youre interested, then have a look on that particular site.

The Beaumont Society

The Beaumont Society

The Beaumont Society is a national self help body run by and for those who cross-dress or are trans-sexual. We welcome all transgender people and their partners, regardless of gender, sexual orientation, race, creed or colour, and all varieties from nervous new transgender people to those who are experienced and confident in their second gender.

Depend

Depend

An organisation offering free, confidential and non-judgemental advice, information and support to all family members, spouses, partners and friends of transsexual people in the UK

GIRES

GIRES (Gender Identity Research and Education Society)

Information for trans people, their families and the professionals who care for them.

Mermaids

Mermaids

Mermaids is probably the most recognised UK support organisation and offers information, support, friendship and the opportunity for children to share experiences. Additionally, they can also support, where possible, to help their families understand and accept their childs gender identity issue.

Press for Change

Press for Change

Press for Change is a political lobbying and educational organisation, which campaigns to achieve equal civil rights and liberties for all transgender people in the United Kingdom, through legislation and social change.

TGmeds

Tgmeds

My website where this ebook is hosted. Online since December 2000, hosting articles, abstracts, and research from 1988, mostly related to transsexuals.

Surgeons

Here is a list of surgeons that may be useful for you.

TGSurgeons List

Chapter 19

Appendix 1

American vs British Drug names

US name	UK name
Epinephrine	Adrenaline
Norepinephrine	Noradrenaline
Acetaminophen	Paracetamol
Albuterol	Salbutamol
Anthralin	Dithranol
Apazone	Azapropazone
Cosyntropin	Tetracosactide (tetracosactrin)
Cromolyn sodium	Sodium cromoglicate
Deferoxamine	Desferrioxamine
Dextroamphetamine	Dexamfetamine
Ergonovine	Ergometrine
Floxacillin	Flucloxacillin
Glutaral	Glutaraldehyde
Glyburide	Glibenclamide
Gold sodium thiomalate	Sodium aurothiomalate
Isoproterenol	Isoprenaline
Leucovorin	Leucovorin calcium
Folinic acid	Calcium folinate
Mechlorethamine	Chlormethine (mustine)
Meperidine	Pethidine
Metaproterenol	Orciprenaline
Mineral oil	Liquid paraffin
Nafronyl	Naftidrofuryl
Niacin	Nicotinic acid
Niacinamide	Nicotinamide
Norethindrone	Norethisterone
Penicillin G	Benzylpenicillin
Phytonadione	Phytomenadione

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Pizotyline	Pizotifen
Propoxyphene	Dextropropoxyphene
Quinacrine	Mepacrine
Rifampin	Rifampicin
Scopolamine	Hyoscine
Succinylcholine	Suxamethonium
Sulfamethazine	Sulfadimidine

Table 19.1 – American vs British Drug names

American vs British Lab values

Test	Conventional	SI Units
Albumin	3.9–5.0 g/dL	35–50 g/L
Alkaline phosphatase	44–147 units/L	40–120 units/L
ALT	6–59 units/L	20–65 units/L
AST	10–34 units/L	15–45 units/L
BUN	7–20 mg/dl	2.9–8.9 mmol/L
Bilirubin, direct	0.0–0.3 mg/dL	0–8 mmol/L
Bilirubin, total	0.2–1.9 mg/dL	0–20 umol/L
Calcium	8.5–10.9 mg/dL	2.15–2.5 mmol/L
Chloride	101–111 mmol/L	98–106 mmol/L
Cholesterol, total	100–240 mg/dL	2-5–19 mmol/L
CO2	20–29 mEq/L	20–29 mmol/L
Creatinine	0.8–1.4 mg/dL	70–120 mmol/L
Gamma-GT	0–51 units/L	10–58 units/L
Glucose	64–128 mg/dL	3.3–11 mmol/L
LDH	105–333 units/L	300–600 mmol/L
Magnesium	1.5–2 mEq/L	0.7–1.05 mmol/L
Phosphorus	2.4–4.1 mg/dL	0.8–1.4 mmol/L
Potassium	3.5–5 mEq/L	3.5–5 mmol/L
Protein, total	6.3–7.9 g/dL	60–80 g/L
Sodium	136–144 mEq/L	136–144 mmol

Table 19.2 – American vs British Lab values

Conversion table

Component	Conventional Unit	Conversion Factor	SI Unit
Estradiol	pg/mL	3.671	pmol/L
Estriol	ng/mL	3.467	nmol/L

Estrone	ng/dL	37	pmol/L
Progesterone	ng/mL	3.18	nmol/L
Testosterone	ng/dL	0.0347	nmol/L

Table 19.4 – Conversion factors between the US and European SI units

This table provides the conversion factors between the units used in the US and by the Endocrine Society and the SI units commonly used elsewhere such as the NHS.

Metric weights and Liquid measures

Metric system	
Metric weight	**Metric liquid measure**
1 femtogram (fg) = 0.001pg	1 femtoliter (fL) = 0.001pL
1 picogram (pg) = 0.001ng	1 picoliter (pL) = 0.001nL
1 nanogram (ng) = 0.001µg	1 nanoliter (nL) = 0.001µL
1 microgram (µg) = 0.001mg	1 microliter (µL) = 0.001mL
1 milligram (mg) = 0.001g	1 milliliter (mL) = 0.001L
1 centigram (cg) = 0.01g	1 centiliter (cL) = 0.01L (10 mL)
1 decigram (dg) = 0.1g	1 deciliter (dL) = 0.1L (100 mL)
1 gram (g) = 1g	1 liter (L) = 1L (1000 mL)
1 dekagram (dag) = 10g	1 dekaliter (daL) = 10L
1 hectogram (hg) = 100g	1 hectoliter (hL) = 100L
1 kilogram (kg) = 1000g	1 kiloliter (kL) = 1000L

Table 19.5 – Metric weights and Liquid measures

How to evaluate health information on the internet

I thought that this was extremely good when I found it, worthy of repeating it.

Millions of people are using the internet to get health information. And thousands of websites are offering health information. Some of those sites are reliable and up-to-date; some are not. How can you tell the good from the bad?

First, it's important to carefully consider the source of information and then to discuss the information you find with your health care professional. These questions and answers can help you determine whether the health information you find on the internet or receive by email from a website is likely to be reliable.

Qs & As: Evaluating internet health information

Who runs the website?

Any good health website should make it easy to learn who is responsible for the site and its information. On the U.S. Food and Drug Administration's (FDA) website, for example, the FDA is clearly noted on every major page, along with a link to the site's home (main) page, www.fda.gov.

Information about who runs the site can often be found in an "About Us" or "About this website" section, and there's usually a link to that section on the site's home page.

What is the purpose of the website?

Is the purpose of the site to inform? Is it to sell a product? Is it to raise money? If you can tell who runs and pays for the site, this will help you evaluate its purpose. Be cautious about sites trying to sell a product or service.

Quackery abounds on the web. Look for these warning signs and remember the adage "If it sounds too good to be true, it probably is."

- Does the site promise quick, dramatic, miraculous results? Is this the only site making these claims?
- Beware of claims that one remedy will cure a variety of illnesses, that it is a "breakthrough," or that it relies on a "secret ingredient."
- Use caution if the site uses a sensational writing style (lots of exclamation points, for example.)
- A health website for consumers should use simple language, not technical jargon. Get a second opinion. Check more than one site.

What is the original source of the information on the website?

Always pay close attention to where the information on the site comes from. Many health and medical websites post information collected from other websites or sources. If the person or organization in charge of the site did not write the material, the original source should be clearly identified. Be careful of sites that don't say where the information comes from.

Good sources of health information include -

- Sites that end in ".gov," sponsored by the federal government, like the U.S. Department of Health and Human Services (www.hhs.gov), the FDA (www.fda.gov), the National Institutes of Health (www.nih.gov), the Centers for Disease Control and Prevention (www.cdc.gov), and the National Library of Medicine (www.nlm.nih.gov).
- .edu sites, which are run by universities or medical schools, such as Johns Hopkins University School of Medicine and the University of California at Berkeley Hospital, health system, and other health care facility sites, like the Mayo Clinic and Cleveland Clinic.
- .org sites maintained by not-for-profit groups whose focus is research and teaching the public about specific diseases or conditions, such as the American Diabetes Association, the American Cancer Society, and the American Heart Association.
- Medical and scientific journals, such as The New England Journal of Medicine and the Journal of the American Medical Association, although these aren't written for consumers and could be hard to understand.
- Sites whose addresses end in .com are usually commercial sites and are often selling products.

How is the information on the website documented?

In addition to identifying the original source of the material, the site should identify the evidence on which the material is based. Medical facts and figures should have references (such as citations of articles in medical journals). Also, opinions or advice should be clearly set apart from information that is "evidence-based" (that is, based on research results).

How is information reviewed before it is posted on the website?

Health-related websites should give information about the medical credentials of the people who prepare or review the material on the website.

How current is the information on the website?

Websites should be reviewed and updated on a regular basis. It is particularly important that medical information be current, and that the most recent update or review date be clearly posted. These dates are usually found at the bottom of the page. Even if the information has not changed, it is helpful to know that the site owners have reviewed it recently to ensure that the information is still valid. Click on a few links on the site. If there are a lot of broken links, the site may not be kept up-to-date.

How does the website choose links to other sites?

Reliable websites usually have a policy about how they establish links to other sites. Some medical websites take a conservative approach and do not link to any other sites; some link to any site that asks or pays for a link; others link only to sites that have met certain criteria. Look for the website's linking policy, often found in a section titled "About This Web Site."

What information about its visitors does the website collect, and why?

Websites routinely track the path visitors take through their sites to determine what pages are being used. However, many health-related websites ask the visitor to "subscribe" or "become a member." In some cases, this may be done so they can collect a fee or select relevant information for the visitor. In all cases, the subscription or membership will allow the website owners to collect personal information about their visitors.

Many commercial sites sell "aggregate" data about their visitors to other companies - what percent are women with breast cancer, for example. In some cases, they may collect and reuse information that is personally identifiable, such as a visitor's ZIP code, gender, and birth date.

Any website asking users for personal information should explain exactly what the site will and will not do with the information. The FDA website, for example, spells this out in its Privacy Statement. Be sure to read and understand any privacy policy or similar language on the site, and don't sign up for anything you don't fully understand.

How does the website manage interactions with visitors?

There should always be a way for visitors to contact the website owners with problems, feedback, and questions. The FDA's website provides contact information on its Contact Us page.

If the site hosts a chat room or other online discussion areas, it should tell its visitors about the terms of using the service. Is the service moderated? If so, by whom, and why? It is always a good idea to spend time reading the discussion without joining in, to feel comfortable with the environment, before becoming a participant.

Can the accuracy of information received in an email be verified?

Carefully evaluate email messages. Consider the origin of the message and its purpose. Some companies or organizations use email to advertise products or attract people to their websites. The accuracy of health information may be influenced by the desire to promote a product or service.

Is the information that's discussed in chat rooms accurate?

Assessing the reliability of health information that you come across in web discussion groups or chat rooms is at least as important as it is for websites. Although these groups can sometimes provide good information about specific diseases or disorders, they can also perpetuate misinformation. Most internet service providers don't verify what is discussed in these groups, and you have no way of knowing the qualifications or credentials of the other people online. Sometimes people use these groups to promote products without letting on that they have a financial stake in the business. It's best to discuss anything you learn from these groups with your health care professional.

Related Resources

Healthfinder
A DHHS site that is a gateway to consumer information. Its goal is to improve consumer access to selected health information from government agencies, their partner organizations, and other reliable sources that serve the public interest.

MEDLINEplus
A consumer-oriented website established by the National Library of Medicine, the world's largest biomedical library and creator of the MEDLINE database. It offers health, drug, and disease information.

MEDLINEplus Evaluating Health Information

MEDLINEplus Healthy Websurfing

ClinicalTrials.gov
A site created by the National Institutes of Health and the Food and Drug Administration to provide patients, family members, and members of the public with current information about clinical research studies and clinical trials.

A Quick Checklist

You can use the following checklist to help make sure that the health information you are reading online can be trusted.

- Can you easily see who sponsors the website?
- Is the sponsor a government agency, a medical school, or a reliable health-related organization, or is it related to one of these?
- Is there contact information?
- Can you tell when the information was written?
- Is your privacy protected?

- Does the website make claims that seem too good to be true? Are quick, miraculous cures promised? (F. W. M. Staff, 2005)

Glossary

A

adipose
fat 55, 56, 68, 79, 206, 290

adrenarche
Adrenarche is known to be an ordinary bodily process that happens to boys and girls as they begin to make the transition to being a teenager. It is a development that happens before puberty, usually between the ages of 6 and 8. During this time certain hormones (biological messengers) begin to increase and may either go unnoticed or can cause changes in the body like new hair growth (Leach, 2013) 277

agranulocytosis
An acute condition marked by severe depression of the bone marrow, which produces white blood cells, neutropenia results, whereby the body is severely depleted in its ability to defend itself. Fever, malaise, and bleeding ulcers of the rectum, mouth, and vagina may be present 234

alkaloid
any of a group of organic basic substances found in plants, many of which are pharmacologically active, e.g., atropine, caffeine, morphine, nicotine, quinine, and strychnine 511

androgens
a male sex hormone, such as testosterone 35

anti-androgen
counteracts the effects of androgens on various body organs and tissues . . . 47, 52, 54, 124, 125, 130, 133, 139, 140, 195, 231, 232, 470, 561, 562, 646

Antiarrhythmics
used to control cardiac arrhythmia, including membrane-stabilizing drugs (e.g. quinidine, lidocaine, flecainide), beta-blockers, amiodarone and sotalol and calcium channel blockers (e.g. verapamil) 512

Antihelminthic
used to destroy or cause the expulsion of parasitic intestinal worms . . 512

antipsychotic
effective in the treatment of psychotic disorders; also, an agent that so acts. Antipsychotics are a chemically diverse but pharmacologically similar class of drugs; besides psychotic disorders, some are also used to treat movement disorders, intractable hiccups, or severe nausea and vomiting 292, 512

anuria
Cessation of the secretion of urine (unknown, 2013b) 233

anxiety
a feeling of unease, such as worry or fear, that can be mild or severe . . 106, 107, 143, 148, 217, 291, 314, 499, 550, 556, 582, 594, 598, 600, 604, 605, 607–609

asthenia
weakness, lack of energy and strength 122, 126

atrophy
The shrinkage or near disappearance of a tissue or organ 41, 53, 59, 60, 225, 613

AUC
a method of measurement of the bioavailability of a drug based on a plot of blood concentrations sampled at frequent intervals. It is directly proportional to the total amount of unaltered drug in the patients blood 182, 512, 513, 635

B

bone mineralization
This is the deposition of calcium hydroxyl apatite salts converting osteoid to rigid bone; dependent on mineral availability (calcium, phosphate and hydrogen ions), enzyme action (alkaline phosphatase), osteocyte activity (osteoblasts and osteoclasts), hormones (parathyroid hormone, thyroid calcitonin) and vitamin D (Mooney, 2009) 640

buccally
A means of administering a drug where it is held in the mouth against the cheek wall 187

BUN
This stands for blood urea nitrogen. Urea nitrogen is what forms when protein breaks down. This test is often done to check kidney function 127, 144, 167, 297, 298, 456, 658

C

Calcium channel blockers
medication that slows the movement of calcium into the cells of the heart and blood vessels. This, in turn, relaxes blood vessels, increases the supply of oxygen-rich blood to the heart, and reduces the heart's workload 512

cancerous
malignant 240, 278, 297, 310, 471, 472, 479, 494

capsulitis
Inflammation of a capsule (e.g., of a joint or the ocular lens) or a pseudocapsule (e.g., that formed around a breast implant) 489

Cavg
the average plasma concentration of a drug after administration . . 95

CD4 count
CD4 count is a measure of immune function. By measuring someone's CD4 levels you can see how HIV has affected their immune system, showing the progression of the virus 360, 367

celibate
not having sex 340

cervix
entrance to the uterus - womb . . 59, 75, 76, 327, 329, 330, 332, 333, 338, 342, 344, 385, 391, 433, 439, 620

cisgender
Denoting or relating to a person whose self-identity conforms with the gender that corresponds to their biological sex; not transgender (unknown, 2015a) 53, 508, 509

climacteric
the period during which women gradually lose their reproductive capabilities as a result of aging. Also used as an adjective to describe this period 248, 251

Cmax
The maximum or "peak" concentration of a drug observed after its administration 95, 182, 216, 512, 513

compounding pharmacy
a practice in which a licensed pharmacist, a licensed physician, or, in the case of an outsourcing facility, a person under the supervision of a licensed pharmacist, combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient . . 448

CPA
Cyproterone Acetate 17, 130

cramp
a painful muscles spasm 33, 233, 255, 257, 382, 419, 534, 556

D

detrusor
the smooth muscle of the bladder 257

diaphoresis
perspiration or sweating 149

diplopia
double vision 209, 217

dysuria
painful or difficult urination 521, 635

E

ectopic pregnancy
when the pregnancy develops outside the uterus, usually in a fallopian tube 76, 347, 434, 435, 537

endometrial hyperplasia
This is an abnormal proliferation of the endometrium (ie greater than the normal proliferation that occurs during the menstrual cycle). It is a risk factor for the development of endometrial carcinoma (Tidy, 2014) 59, 81, 90, 92, 96, 97, 103

enterohepatic
Circulation of substances which are absorbed from the intestine and carried to the liverwhere they are secreted into the bile and again enter the intestine. 48, 49, 88, 95, 104, 187, 207

enzyme
An enzyme is a protein produced by the body to speed up a specific chemical reaction in the body. The body produces many different kinds of enzymes for many different body processes, such as digestion and blood clotting. Some inherited diseases are caused by problems with the production of certain enzymes. Doctors may measure the levels of certain enzymes in a person's blood to help diagnose certain types of disease, such as liver problems. 30, 39, 44, 49, 58, 93, 106, 111, 114–116, 120, 121, 127, 130, 144, 158, 168, 174, 175, 202, 207, 232, 269, 285–287, 289, 290, 295, 423, 453, 459, 535, 545, 615, 622, 635

epididymis
the tubes that carry sperm from the testicles 75, 328, 434, 572

erythema multiforme
An acute eruption of macules, papules, or subdermal vesicles presenting a multiform appearance, the characteristic lesion being the target or iris form of lesion over the dorsal aspect of the hands and forearms; its origin may be from drug sensitivity, and the eruption, although usually self limited, may be recurrent or may run a severe course, sometimes with fatal termination (unknown, 2013d) 210

erythema nodosum
An inflammation of subcutaneous tissue marked by the sudden formation of painful nodes on the extensor surfaces of the lower extremities, with lesions that are self limiting but tend to recur (unknown, 2013d) 87, 101, 229

Escherichia coli
the name of a germ, or bacterium, that lives in the digestive tracts of humans and animals. There are many types of E. coli, and most of them are harmless. But some can cause bloody diarrhoea. Some strains of E. coli bacteria (such as a strain called O157:H7) may also cause severe anaemia or kidney failure, which can lead to death . 256, 498

exophthalmos
bulging eyeball out of its socket 209, 217

F

flatulence
excess wind 423

G

gastric lavage
stomach washout or stomach pumped out 185

granulomas
inflammation found in many diseases 530

guaiac
used as a reagent in laboratory tests for the presence of occult blood . 482, 483, 485, 486

H

haematocrit
a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells 28, 62, 263, 303, 304

harming yourself
thoughts of intentionally damaging or injuring your body. It is a way of coping with or expressing overwhelming emotional distress . . . 500

hematopoiesis
This is a process of blood cell production and maturation in the bone marrow (AB, 2011) 639

hepatic
Relating to the liver. . . 49, 89, 104, 106, 108, 117, 127, 130, 132, 133, 146, 168, 174, 175, 188, 194, 206, 210, 213, 226, 231, 271, 285, 453, 622

heterogamous species
In reproductive biology, heterogamy or heterogamous is often used as a synonym of heterogametic, meaning the presence of two unlike chromosomes in a sex. For example, XY males and ZW females are called the heterogamous sex 537

homoeostasis
Automatic self-regulation to maintain the normal or standard state of the body under variations in the environment i.e. the body producing sweat to help cool it down on a hot day 67

hormone
a chemical substance produced in the body which has a specific regulatory effect on the activity of certain cells or a certain organ or organs (medical-dictionary, 2014) 10, 15, 19, 26, 28, 32–36, 38, 39, 47–51, 54, 56, 61, 63, 67–72, 74–77, 90, 93, 96, 102, 103, 105, 106, 114, 125, 130, 132, 133, 145, 157, 158, 176, 178, 179, 181, 182, 186–188, 195, 205, 206, 214–216, 224, 226, 231, 232, 248, 249, 251, 253, 254, 261–263, 276, 277, 281, 285, 288, 293, 296, 297, 304, 309, 313, 314, 389, 447–450, 457, 458, 466–470, 473, 482, 488, 496, 499, 502, 506, 511, 516, 520, 533–536, 538, 541, 542, 544, 546, 547, 549–551, 554, 559, 561, 562, 568, 582–584, 587, 589–591, 593, 597–599, 606–608, 611, 612, 614–616, 618, 619, 627, 628, 633, 637, 643, 646

hydrocele
fluid-filled sac 254

hyperkalaemia
An excess of potassium in the blood. If left untreated it can lead to cardiac arrest 233, 234, 238, 322

hypertriglyceridemia
elevated triglyceride concentration in the blood 39, 228, 283
hypogonadism
a low testosterone level or sperm count, or both 104, 105, 225, 293
hyponatraemia
A deficiency of sodium in the blood 233, 238, 324
hypophosphatasia
this is an inherited disorder that affects the development of bones and teeth 269

I
idiopathic
of unknown cause (Dictionary.com, 2014) 81, 207, 278, 318
in-vitro
outside the body 116, 176, 177, 190, 418, 538, 635
in-vivo
within the living organism 116, 177, 635
induration
localised swelling 108, 218
intersex
having the biological characteristics of both the male and female sexes 538, 624, 626
ischaemia
a deficiency in the blood supply to part of the body (unknown, 2013b) 534

J
jaundice
yellow skin and whites of eyes, dark urine, and pale faeces. 33, 87, 90, 96, 100, 103, 107, 168, 209, 210, 217, 228, 286, 348, 351, 352, 354, 484

L
lactation
their breasts discharging milk 76, 77, 93, 98, 106, 146, 478, 533
LD-50
oral lethal dose, 50% of it 174, 186, 214, 239
LDL
Low-density lipoprotein - carries cholesterol to the cells that need it. If theres too much cholesterol for the cells to use, it can build up in the artery walls, leading to disease of the arteries. For this reason, LDL is known as "bad cholesterol" 57, 272–274, 284, 285, 453, 461, 547
Leydig cells
Leydig cells, also known as interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicle. They can secrete testosterone and are often closely related to nerves . . 53, 105, 288, 295
LFT
Liver Function Test 56, 86, 129, 167, 185, 222, 297, 455, 458
LHRH
luteinizing-hormone releasing hormone 125, 146, 158, 169

lipophilic
the ability to dissolve or attach to lipids 52
loss of libido
this is a common problem affecting up to one in five men — and even more women — at some point in their life 144, 500, 543, 544

M
matrix
Estradiol is embedded in the adhesive layer that is applied directly to the skin 452, 454, 627
meibomian glands
also known as tarsal, palpebral, or tarsoconjunctival glands. A type of sebaceous gland on the upper and lower eyelids that open at the edges of the lids 55
melasma
a tan or dark skin discolouration 184, 218, 229
mucin
present in most glands that secrete mucus and is the lubricant that protects body surfaces from friction or erosion 481, 671
mucinous
relating to, resembling or containing mucin 481
myopathy
any disease of the muscles (unknown, 2013b) 513, 534

N
non-restorative sleep
sleep which does not leave you feeling refreshed 582, 583
noncancerous
benign 471–473, 481, 617

O
opioid
a synthetic narcotic that has opiate-like activities but is not derived from opium 484, 513
osteomalacia
Osteomalacia refers to a softening of your bones, which are more likely to bow and fracture than are harder, healthy bones (M. C. Staff, 2014a) 234, 270, 640
OTC
over-the-counter, meaning easily purchased from drug stores and supermarkets 257, 503, 521

P
papilloma
a benign growth on the skin or mucous membrane . 337, 473, 481, 482
paradoxical
not being the normal or usual kind 58
Pathophysiology
The physiological processes associated with disease or injury 481

phlebitis
the inflammation of a vein 86, 217, 226, 228, 245, 255, 530
photosensitivity
an abnormal degree of sensitivity of the skin to sunlight 144, 555
piloerection
hair standing erect and on end 144
polycythaemia
having a high concentration of red blood cells in your blood . . 28, 304, 307
PSA
prostate specific antigen which is a marker for prostate cancer. The higher the PSA level the greater the chance you have prostate cancer . 111, 119, 122, 179, 310–313, 465
Psychotropic agents
a chemical compound that influences the human psyche 513
purulent
containing, discharging, or causing the production of pus . . . 481–483

R
reservoir
Estradiol is contained in a drug reservoir and its release is controlled by a copolymer membrane, it contains more layers than a matrix patch 48, 76, 452, 454

S
sanguineous
containing blood 481
Satellite lesions
Smaller patches of similar-appearing rash to the main rash 521
septicaemia
the presence of microorganisms or their toxins in the blood of a potentially fatal whole-body inflammation 530
serosanguineous
composed of serum and blood 481
serous
producing or containing serum 432, 481
Sertoli cells
A Sertoli cell is a kind of sustentacular cell, and is a 'nurse' cell of the testes which is part of a seminiferous tubule. It is activated by follicle-stimulating hormone, and has FSH-receptor on its membranes 53
SHBG
sex hormone binding globulin . 88, 89, 105, 132, 206, 277–279, 293–295, 456–458
spermatazoa
one of the minute, usually actively motile gametes in semen, which serve to fertilize the ovum; a mature male reproductive cell 537

spermatogenesis
Spermatogenesis is the process by which male spermatogonia develop into mature spermatozoa. Spermatozoa are the mature male gametes in many sexually reproducing organisms. Thus, spermatogenesis is the male version of gametogenesis. In mammals it occurs in the male testes and epididymis in a stepwise fashion, and for humans takes approximately 64 days 53, 103, 104, 295

steroid
any of a large number of hormonal substances with a similar basic chemical structure, produced mainly in the adrenal cortex and gonads 17, 49, 70–72, 77, 79, 88, 93, 103, 105, 112, 113, 115, 124, 125, 130, 139, 140, 158, 186, 215, 224, 225, 231, 246, 276–278, 281, 283, 285, 294, 299, 301, 306, 319, 321–323, 423, 450, 513, 535, 536

subcutaneous
under the skin 55, 56, 65, 102, 145, 146, 158, 159, 168, 174, 177, 467, 522, 563, 575, 611

sublingually
Beneath the tongue. 81, 89, 517, 535, 633

suicidal thoughts
thoughts of intentionally ending your life 500

synergistically
working together in an interactive manner 281, 288

T

teratogen
Any substance that causes birth defects. 119, 130

teratogenic
having the ability to disturb the growth and development of an embryo or foetus 93, 98, 126

terminal hairs
normal hairs 52

thrombocytopenia
a decreased number of platelets 305, 306, 529

thromboembolism
Blockageof a blood vessel caused by a blood clot carried by the bloodstream from its point of origin . . 33, 81, 92, 98, 207, 210, 226, 244, 591, 592

Tmax
the time after administration of a drug when the maximum plasma concentration is reached; when the rate of absorption equals the rate of elimination 182, 216

transcription
The natural process by which a molecule of RNA is synthsized on the model of a DNA template carrying the necessary genetic information. 47–49, 89, 106

transmen
is someone who was labelled female at birth but has a male gender identity, and therefore transitions to live completely and permanently as a man (LGBT, 2014b) 33, 57, 59–61, 63, 156, 517, 611

transwomen
is someone who was labelled male at birth but has a female gender identity, and therefore transitions to live completely and permanently as a woman (LGBT, 2014b) ... 32, 33, 53, 55, 56, 468, 469, 471, 517, 590

tumorigen
A substance that directly causes tumours to form 239

U

urethra
tube where urine comes out ... 75, 76, 256, 258, 316, 327, 328, 330, 331, 338, 342, 344, 385, 390, 426–430, 435

V

varicocele
collection of widened veins 254

vascular occlusion
blockage of a blood vessel, usually with a clot 530

vellus hairs
very tiny, blonde "baby" hairs 52

venous thromboembolism
a collective term for both 'deep vein thrombosis' (DVT) and 'pulmonary embolism' (PE) 561

viral load
Viral load measures how active HIV is in your body. The higher the viral load the more infectious you would be. Effective HIV medication can keep people's CD4 count high and their viral load so low it is undetectable. However people with HIV's CD4 count and viral load can go up and down depending on their medication, whether they have another STI and their general health 366

vulva
the lips around the opening to the vagina ... 91, 96, 225, 327, 337, 338, 385, 386, 390, 407, 520, 553, 635, 636

Z

zygote
the cell produced by the union of two gametes, before it undergoes cleavage 75, 537

Acronyms

A | B | C | D | E | F | G | H | I | L | M | N | P | S | T | U | V | Y

A

AIDS
Acquired Immune Deficiency Syndrome 358, 367

ALP
Alkaline phosphate 269

ALT
Alanine Transaminase 63, 127, 286, 458–460, 658

AR
androgen receptor 46, 125, 537

AST
Aspartate Transaminase 63, 127, 270, 286, 458–460, 658

B

BNF
British National Formulary 591

BPH
Benign Prostatic Hyperplasia 114, 278, 310

BSE
Breast self-examination 241, 476, 477, 572

BV
Bacterial vaginosis 412–418

C

CAD
Coronary artery disease 284, 285

CSH
Cross-Sex Hormones 619

CSS
steady state serum concentrations 116

D

DCIS
ductal carcinoma in situ 476, 494

DHT
dihydrotestosterone . . 18, 21, 46, 47, 52, 58, 105, 106, 114, 115, 120, 121, 130, 278, 279, 294, 295, 536, 537

DNA
deoxyribonucleic acid 47–49, 54, 106, 139, 140, 224, 226, 645
DVT
deep venous thrombosis 51, 243–245, 247, 255, 569, 590

E
ED
endocrine disruptor 50

F
FDA
Food and Drug Administration 503, 611, 620, 660–662
FSH
follicle stimulating hormone . 67, 68, 77, 78, 89, 103, 104, 169, 175, 206, 226, 281, 288, 455–457, 462

G
GGT
Gamma glutamyl transpeptidase 270, 287
GnRH
gonadotropin-releasing hormone .. 28, 67, 157–159, 176, 178–180, 188, 216, 562, 563
GP
General Practitioner, a community-based doctor 12, 34, 156, 253, 259, 312, 315–317, 319, 321, 322, 326, 349, 353, 370, 371, 375, 378, 382, 388, 389, 395, 398, 399, 403, 404, 408, 409, 414, 416–418, 421, 423, 425, 426, 430, 432, 435–437, 439, 441–443, 445, 500, 502, 506, 517, 519, 546, 559, 574, 621
GUM
genitourinary medicine. 326, 341, 363, 364, 371, 388, 389, 395, 404, 408, 409, 414, 416–418, 421, 427, 430, 431, 433, 434

H
HBIG
Hepatitis B immunoglobulin 353
HDL
High-density lipoprotein 57, 222, 272–275, 282, 284, 285, 453, 461
HDL-C
High-density lipoprotein cholesterol 282, 283, 285
HFEA
Human Fertilisation and Embryology Authority 590
HIV
human immunodeficiency virus . 301, 325, 333, 336, 341, 342, 344, 350, 355, 357–369, 371, 392, 393, 399, 407, 411, 426, 430, 436
HNIGS
human normal immunoglobulins 349
HPV
human papilloma virus 337, 338, 340, 341, 393

HRT
Hormone Replacement Therapy . 19, 32, 33, 47, 52, 53, 55, 93, 181–183, 241, 518, 549, 550, 568, 569, 575, 591, 592, 613, 614, 618

HSV
herpes simplex virus 330–333

I

INR
international normalized ratio 108, 141, 213, 229, 297, 308, 309

L

LDL-C
Low-density lipoprotein cholesterol 283–285

LGBT
Lesbian, Gay, Bisexual and Transsexuals 631

LH
luteinizing hormone 67, 68, 77, 78, 103, 104, 145, 146, 158, 169, 175, 188, 216, 226, 281, 288, 456, 457

LMWH
low molecular weight heparin 247

M

MC
Molluscum contagiosum 368–375

mcgs
micrograms 80, 115, 131, 206, 207, 224, 469

MCV
molluscum contagiosum virus 270, 368, 371

N

NGU
non-gonococcal urethritis 426–434

NHS
The UK-wide National Health Service 341, 374, 442, 490, 494, 557–559, 574, 591, 614, 659

NSU
non-specific urethritis 427, 428, 434, 435

P

PCB's
PolyChlorinated Biphenyls, are industrial products or chemicals . . 50

PE
pulmonary embolism 51, 244, 245, 569

PEP
post-exposure prophylaxis 364–366

PID
pelvic inflammatory disease 328, 347, 417, 418, 428, 432–435

PMS
premenstrual syndrome 65, 189, 499, 535, 556

PPC
prescription prepayment certificate 557, 558
PT
prothrombin time 86, 108, 141, 167, 213, 214, 229, 230, 292

S
SPF
sun protection factor 156, 505, 556, 577, 609, 610
SRC
Self-retaining catheter 521
STD's
sexually transmitted diseases 325
STI
sexually transmitted infection . . . 326, 337, 342, 371, 393–395, 399, 408, 413, 414, 418, 419, 421, 426–429, 432, 433, 436–438
STI's
sexually transmitted infections . . 325, 326, 340, 341, 371, 384, 393–399, 402–405, 407, 411, 417, 418, 427–430, 433, 440

T
TBG
thyroxine-binding globulin 89, 206
TFT
Thyroid function test 297, 313, 458
TG
transgender 619
TSE
Testicular self-examination 255, 571
TSH
thyroid-stimulating hormone 313, 466, 483, 485

U
UTI's
Urinary Tract Infection 256, 635

V
VTE
Venous thromboembolism 244, 245, 561, 591

Y
YMMV
Your Mileage May Vary, meaning it might be different for you . . . 458, 552, 574

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