



PHARMACY

HANDBOOK

A Guide By First Class Honour Students: Helen Su & Eliza Jani



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The authors of this book would like to acknowledge Slidesgo for their contribution to the design of this textbook.

Foreword

The Pharmacy Handbook © is a guide to all three years of the B.Pharm Programme (PHCY220, 310, 320, 432/485, 420) as well as the Intern Year. We hope to be helpful throughout your journey as future pharmacists! Feedback, questions and enquiries are welcome! Contact us at elizajani7@gmail.com or helensuyang@gmail.com.

Warning: Conditions listed in this book are accompanied by visual aids such as graphic imagery that may be deemed disturbing, including photos of infected genitalia.



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University of Otago - First Class Honour Student (2019 - 2023)

- Awarded University of Otago Scholarship in Pharmacy 2021
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- Awarded University of Otago Prestige Scholarship in Pharmacy
- Awarded Aquinas' Academic Excellence 2019, 2020, 2021
- Awarded Council Commendation for Exceptional Performance 2020

Referencing Summary

Please find below - an overall overview of references used throughout this book:

General Resources

1. General Prescribing Guidelines: [BPAC NZ](#), [BPAC Be Quick Guidelines](#)
2. Information on Medicines & Dosing: [NZF](#)
3. Approved/Funded Medicines: [Medsafe](#), [PHARMAC](#)
4. Textbooks: Paul Rutters Community Pharmacy Textbook, Patient Assessment in Community Pharmacy, Pharmacotherapy Principles, Pharmacy Today Healthcare Handbook
5. General Information: [Ministry of Health](#), [Health Navigator](#)
6. Medical Calculations e.g. CrCl, IBW, BMI, BSA, CHADsVASC, HAS-BLED: [MDCalc](#)

Topic-Specific Resources

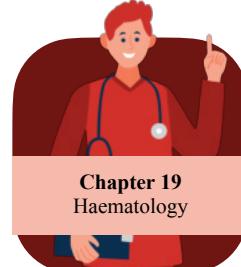
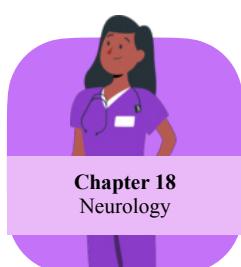
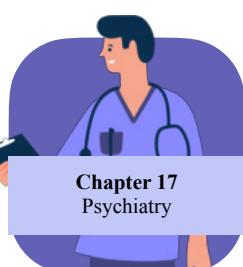
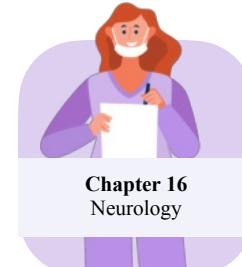
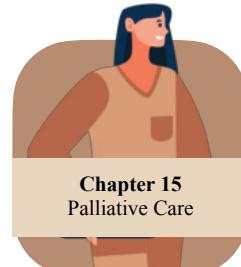
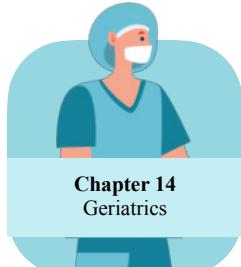
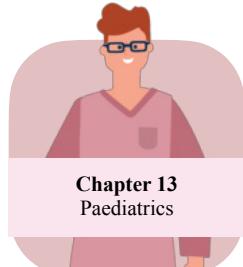
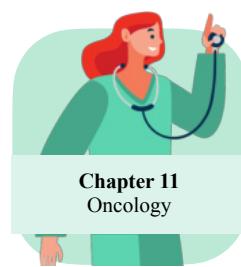
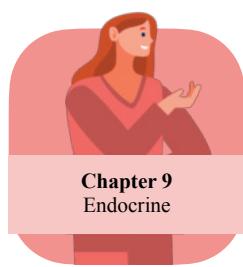
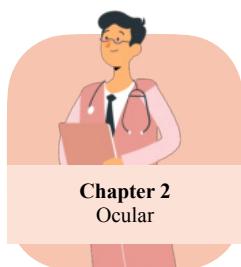
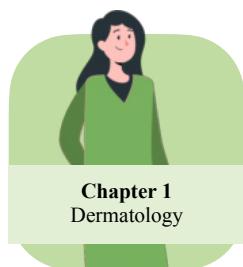
1. Dermatology: [DermNet](#)
2. Sexual Health: [NZHS Guidelines](#)
3. Respiratory: [NZ Respiratory Guidelines](#)
4. Antibiotics: [Starship Paediatric Guidelines](#), [CDHB Pink Book Adult Guidelines](#), [BPAC Guidelines](#)
5. Diabetes: [T2DM NZSSD Guidelines](#)
6. Cardiovascular: [Heart Foundation](#), [CVD Risk Calculator](#)
7. Renal: [Renal Drugs Handbook](#)
8. Pregnancy & Breastfeeding: [Briggs Drugs in Pregnancy & Breastfeeding](#)
9. Psychiatry: [Maudsley Prescribing Guidelines in Psychiatry](#), [American DSM-V](#)
10. Immunisation: [Immunisation Handbook](#), [IMAC](#)
11. Oncology: [EVIQ](#), [Canterbury Guidelines](#)
12. Palliative Care: [Palliative Care Handbook](#), [Morphine](#)
13. Tapering Medications: [TaperMD](#)
14. Geriatric: [Stopp-Start Criteria](#)
15. Law: [Medicines Act 1981](#), [Medicines Regulations 1984](#), [Pharmacy Procedures Manual](#)

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Meet Your Handbook Helpers!

The Pharmacy Handbook uses colour coding and theory to maximise your learning! Each chapter has its own guide - they sometimes emphasise important points or carry fun facts so keep an eye out for them :)





CHAPTER 1

THE DERMATOLOGICAL SYSTEM



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Chapter 1

The Dermatological System

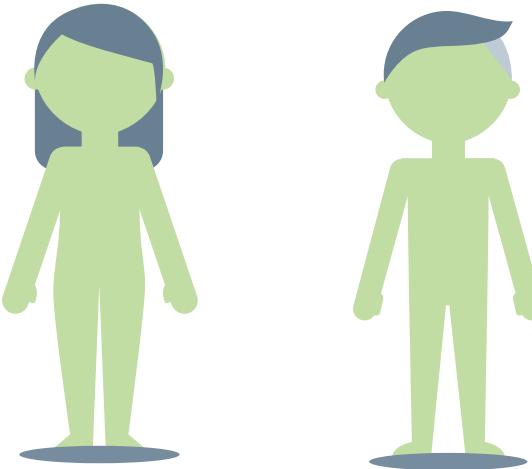
General Overview of Skin Anatomy

Chapter Resources

This chapter aims to cover the various kinds of skin conditions and infections that are commonly seen in community pharmacy practice. [DermNet](#) is a great resource to use when navigating through Dermatology.

Introduction

The skin is the body's largest and primary protective organ, covering its entire external surface and serving as a first-order physical barrier against the environment. Its function includes temperature regulation, protection against ultraviolet (UV) light, trauma, pathogens, microorganisms, and toxins.



The skin also plays a role in immunologic surveillance, sensory perception, control of insensible fluid loss, and homeostasis in general. It is made of three layers, each with a distinct function.

1. The Epidermis

The epidermis, the outermost layer of skin, provides a waterproof barrier and contributes to skin tone.

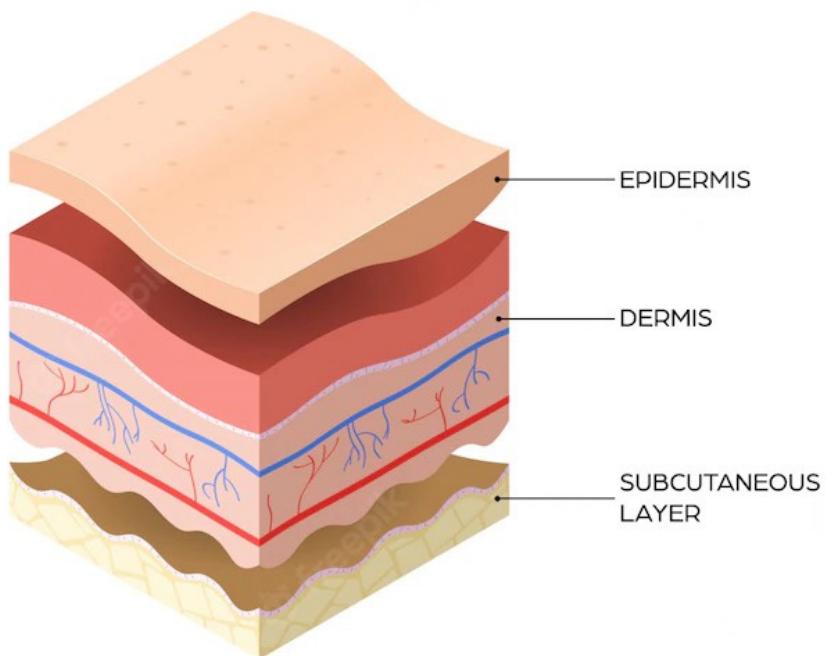
2. The Dermis

The dermis, found beneath the epidermis, contains connective tissue, hair follicles, blood vessels, lymphatic vessels, and sweat glands.

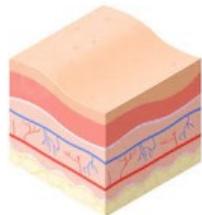
3. The Hypodermis

The hypodermis, the deeper subcutaneous tissue, is made of fat and connective tissue.

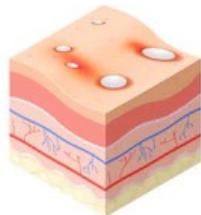
THE LAYERS OF SKIN



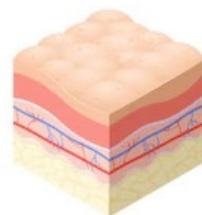
NORMAL SKIN



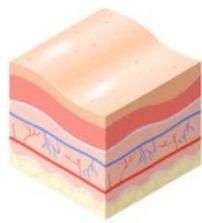
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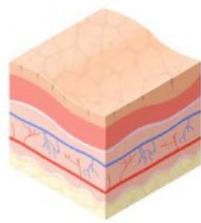
CELLULITE



OILY SKIN



DRY SKIN



VITILIGO



OIL FOR SKIN



WRINKLE



BACTERIAL SKIN INFECTIONS

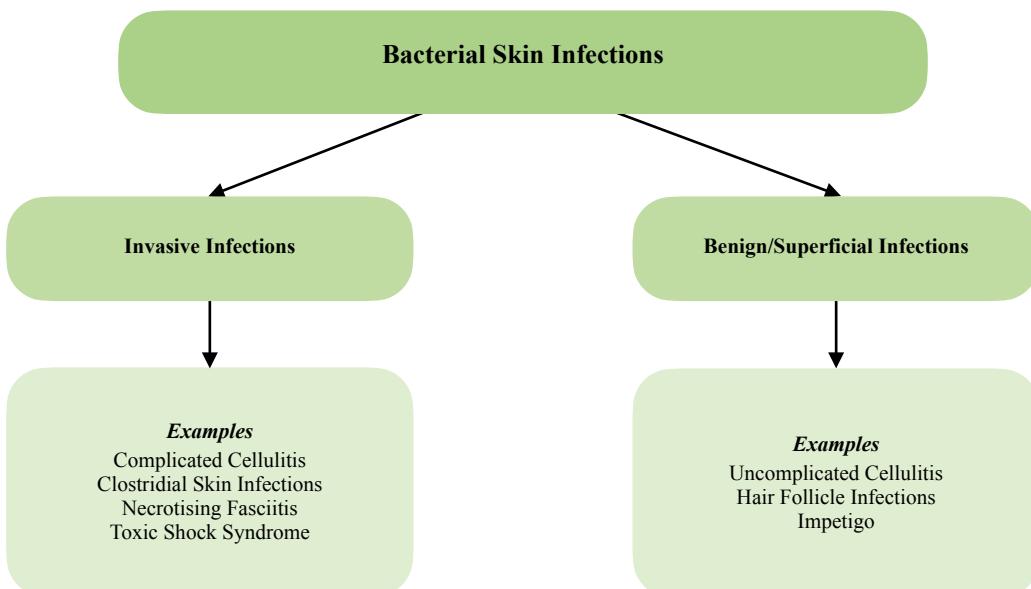
Introduction to Skin Infections

Infections from different pathogens can present clinically with some differences. Bacterial skin infections for example often begin as small, red bumps that slowly increase in size. Skin infections caused by viruses usually result in red welts or blisters that can be itchy and/or painful. Meanwhile, fungal infections usually present with a red, scaly and itchy rash with occasional pustules. We will cover dermatological infections thoroughly throughout this chapter!

If you would like to find out more about different kinds of pathogens, please see the Antimicrobials section in *Chapter 20 - Fever, Pain & Infection*.

Introduction to Bacterial Skin Infections

We will first start off with bacterial skin infections, these can be divided into two sub-categories (see below). While many different kinds of bacterial strains are implicated, you will commonly see Staph & Strep infections!



Cellulitis

[DermNet Cellulitis](#)

Description

Cellulitis is a bacterial infection of the lower dermis and the subcutaneous tissue (fascia, muscles, tendons) that occurs due to the entry of an organism into an open wound (commonly *S. Aureus* and *S. Pyogenes*).



Risk Factors

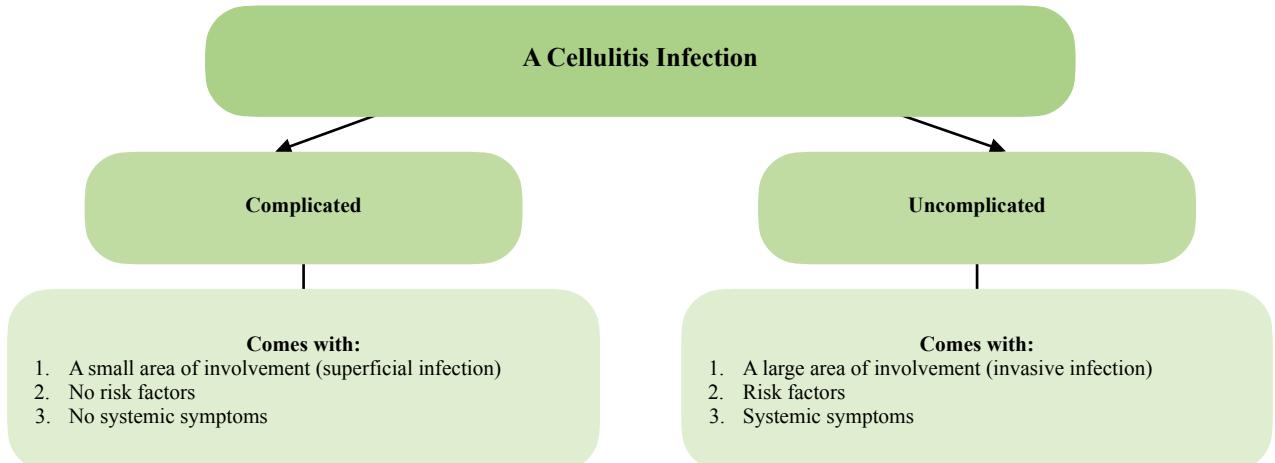
There are many risk factors for cellulitis, those include (but not limited to):

- **An open wound**
- History of skin conditions (cellulitis, eczema, psoriasis, fungal infections)
- History of venous stasis
- Poor circulation in extremities
- Immunocompromised e.g. being homeless, obese, pregnant, or old

Signs & Symptoms

Cellulitis commonly occurs in the leg and generally affects one side of the body.

- It often presents as ill-defined lesions that are red, painful, swollen.
- If systemic involvement, symptoms may include fever, chills, and regional lymphadenopathy.



Red Flags:

Immunosuppression, no improvement after 5 days of treatment, systemic involvement, or haemodynamic instability e.g. tachycardia, hypotension, severe dehydration.



Not Contagious!

It is important to note that cellulitis is not a contagious condition as the bacteria infects deeper layers of the tissue. Thus, it cannot be spread from person-to-person.

Diagnosis

A biopsy culture may be needed to diagnose cellulitis.

Differential Diagnosis

Necrotising Fasciitis

This is a rare but an important differential diagnosis point in cellulitis as necrosis of subcutaneous tissue may mask the visible trauma of cellulitis. Extreme tenderness of the infected area and severity of the patient's illness with the presence of haemodynamic instability can help differentiate necrotising fasciitis from cellulitis.

Monitoring

1. Circle the initial affected area to monitor spread of infection
2. Signs & symptoms e.g. fever, resolution of infection
3. General care e.g. eating frequency, fluid intake
4. Any pre-disposing risk factors

Non-Pharmacological Treatment

Clean, Cut, Cover

1. Wound care and dressing, cut nails
2. Rest & elevate affected area to reduce swelling
3. Cold compress
4. Prevent dehydration and get plenty of rest
5. Keep skin clean and moisturised
6. Control any risk factors (diabetes, fungal infections)
7. Ensure tetanus vaccine and boosters are up to date

Pharmacological Treatment

[BPAC Cellulitis Antibiotic Guidelines](#) [Starship Hospital Antibiotic Guidelines for Cellulitis](#)

Patients will improve within **7-10 days** following treatment. Depending on the severity of infection, treatment approaches will differ.

Uncomplicated Cellulitis

1. Pain Relief
2. Oral Antibiotics
 - *First Line:* flucloxacillin
 - *Alternatives:* erythromycin, cefalexin, co-trimoxazole, vancomycin (MRSA)

Complicated Cellulitis

1. Hospitalisation
2. IV Antibiotics e.g. cefazolin with probenecid
3. Surgical drainage and debridement
4. Pain Relief

Impetigo (School Sores)

[DermNet Impetigo](#)

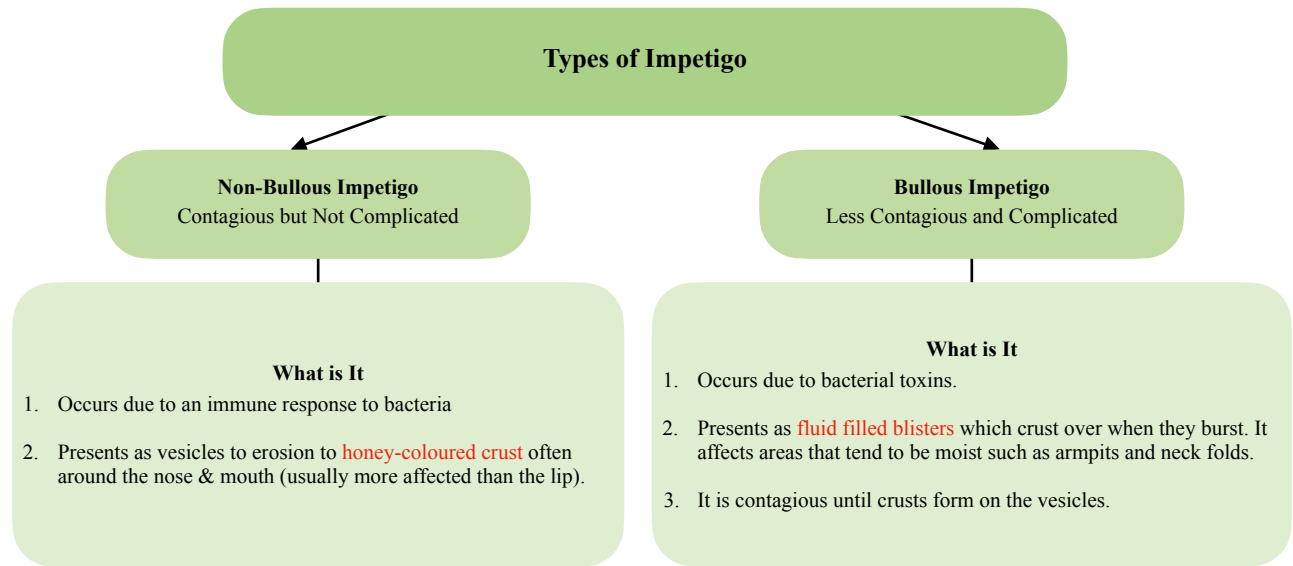
Description

Impetigo is a common and highly contagious bacterial skin infection, also commonly caused by Staph & Streps, that causes red sores on the face. It usually starts as a small red itchy patch of inflamed skin that quickly develops into vesicles that rupture, weep, then crust over and resolve without scarring.



Signs & Symptoms

Two types of impetigo exist:



Red Flags:

Immunosuppression, secondary bacterial infection, fever, regional lymphadenopathy

Risk Factors

- School children mainly, cuts and scrapes
- Close Contact/Crowding

Complications

Systemic spread can lead to kidney complications such as post-streptococcal glomerulonephritis, rheumatic fever, scarlet fever (rare)

Differential Diagnosis

Note that **ecthyma** is a skin infection similar to impetigo, but more deeply invasive - for this reason it is called deep impetigo.

Non-Pharmacological Treatment

“*Clean, Cut, Cover*”.

1. Wash hands often
2. Clean and check the sores every day, gently wash them with warm water and a soft wet cloth for 20-30 minutes or until the hard crust comes off and any blood and pus is cleaned away
3. Cut fingers to prevent scratching and secondary bacterial infections



To Cover or Not To Cover?

Impetigo sores heal faster uncovered - however if the child cannot stop scratching, one would be beneficial to use. Gently pat dry the area, then apply a thin layer of the topical treatment (antiseptic, antibiotic) and then cover with a water-tight dressing. It can be applied on top of the topical treatment as normal.

Pharmacological Treatment

[BPAC Impetigo Antibiotic Guidelines](#)

There are 3 treatment options available. Children can return to school **24h after starting treatment**.

1. Topical Antiseptics

- Hydrogen peroxide cream
- Povidone-iodine ointment

2. Topical Antibiotics

- Fusidic acid
- Mupirocin

3. Systemic Antibiotics

- Flucloxacillin (first line)
- Trimethoprim + sulfamethoxazole
- Erythromycin: if MRSA or flucloxacillin intolerance
- Cefalexin: if flucloxacillin intolerance

Non-Bullous Impetigo (Uncomplicated)

1. *First Line:* Topical Antiseptics
2. *Second Line:* Topical Antibiotics
3. *Third Line:* Systemic Antibiotics

Bullous Impetigo (Complicated)

1. *First Line:* Systemic Antibiotics
2. *Other:* Topical Antibiotics



Using Topical Antibiotics

Due to issues with **resistance** and potential for **contact dermatitis**, topical antibiotics are not recommended unless antiseptics have failed or infection is localised.

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
1st Line Topical Antiseptics	[GENERAL SALE] <i>Hydrogen Peroxide 1%</i> Crystaderm	Hydrogen peroxide is an oxidising agent used in the treatment of non-bullous impetigo	<ul style="list-style-type: none">Apply 2-3 times daily for 5 days (until all sores have healed)Wash and dry skin before applying cream and then cover with a water tight dressing.	<ul style="list-style-type: none">Local irritationCan bleach skin and fabric
	[GENERAL SALE] <i>Povidone-iodine 10%</i> Povidone-iodine	Betadine is an antiviral, anti-bacterial, anti-fungal and anti-protozoal antiseptic due to the microbial activity of iodine.	<ul style="list-style-type: none">Avoid near the eyes and bleaches/stains fabricDo not use hydrogen peroxide and povidone-iodine together as they inactivate each other	<ul style="list-style-type: none">Local irritationStains fabric
2nd Line Topical Antibiotics	[PRESCRIPTION] <i>Fusidic Acid</i> Foban Cream/Ointment	Fusidic acid and its salts are narrow-spectrum antibiotics.	<ul style="list-style-type: none">Apply 2-3 times daily for 5 days	<ul style="list-style-type: none">Dermatitis, hypersensitivity (rash)
	[PRESCRIPTION] <i>Mupirocin</i> Bactroban Ointment	Mupirocin's antimicrobial activity is the result of bacterial protein and RNA synthesis inhibition.	<ul style="list-style-type: none">Apply 2-3 times daily for up to 10 days	<ul style="list-style-type: none">Local reactions including rash, urticaria, pruritus, burning sensation
1st/3rd Line Systemic Antibiotics	[PRESCRIPTION] <i>Flucloxacillin</i> Flucloxacillin (AFT)	Penicillins are antibacterials that attach to PBPs to interrupt cell wall biosynthesis, leading to bacterial cell lysis and death.	<ul style="list-style-type: none">5 day treatment for all (but varying doses and dosing intervals)	<ul style="list-style-type: none">GI upset, thrush, hypersensitivity
	[PRESCRIPTION] <i>Trimethoprim + Sulfamethoxazole</i> Trisul	These are two bacteriostatic antibiotics that work synergistically by blocking a different step in the purine synthesis pathway.	<ul style="list-style-type: none">Take capsules/tablets regularly until finished with a glass of water and food - this will ease GI symptoms.Watch out for allergic reactions, any signs of infections or palpitations/dizziness	<ul style="list-style-type: none">Be careful of signs of infections in cotrimoxazole (BMS)
	[PRESCRIPTION] <i>Erythromycin</i> E-Mycin	Macrolide antibiotic that suppresses protein synthesis	<ul style="list-style-type: none">Avoid grapefruit and calcium fortified foods as these can affect the absorption of the antibiotics.	<ul style="list-style-type: none">Be careful of cardiovascular signs with erythromycin (dizziness, palpitations) — folic acid suppression
	[PRESCRIPTION] <i>Cefalexin</i> Cefalexin ABM	Penicillins are antibacterials that attach to PBPs to interrupt cell wall biosynthesis, leading to bacterial cell lysis and death.		

OSCE points:

- If pregnant: iodine is not recommended, refer

Monitoring

- Spread and/or resolution of the infection e.g. is it going nearby the eye, any secondary bacterial infection
- Improvement of signs & symptoms

Necrotising Fasciitis (Streptococcal Gangrene)

[NF Medsafe](#)

Description

Necrotizing fasciitis (NF), also known as the flesh-eating disease, is a serious bacterial infection that results in the death of parts of the body's soft tissue (necrosis) - it is a rare and life-threatening condition that can happen if a wound gets infected and is commonly caused by the entry of staph & strep through an open wound.



Did You Know?

Medsafe reports found that NF may be associated with NSAID use.

Signs & Symptoms

1. *Early*: Slight trauma at affected area, general malaise, headache, fever, joint and muscle pain
2. *Advanced*: Worsening pain non-proportion to wound, blisters, skin and tissue looks dead
3. *Critical*: Systemic symptoms, coma and death

Pharmacological Treatment

As this condition spreads rapidly, it is crucial to seek treatment early!

Hospitalisation, IV antibiotics, supportive therapy, surgical drainage and debridement, amputation, cosmetic surgery.

Toxic Shock Syndrome (TSS)

[TSS NHS UK](#)

Description

Toxic Shock Syndrome (TSS) is a rare but life-threatening condition caused by bacteria entering the bloodstream and releasing harmful toxins. Bacterial infection of the skin and subcutaneous tissue leads to release of toxic ‘super-antigens’ (produced by staph and strep), which cause an excessive and non-specific activation of the immune system (cytokine storm), leading to multi-organ failure.

Risk Factors

Risk factors for toxic shock syndrome include skin wounds, surgery, and the use of devices, such as menstrual cups, contraceptive sponges or diaphragms.



Did You Know?

TSS is often associated with tampon use in young women, but it can affect anyone of any age – including men and children.



Signs & Symptoms

Early: Redness, swelling, pain at wound site

Late: Fever, hypotension, rash, renal impairment, coagulopathy, respiratory distress syndrome

Pharmacological Treatment

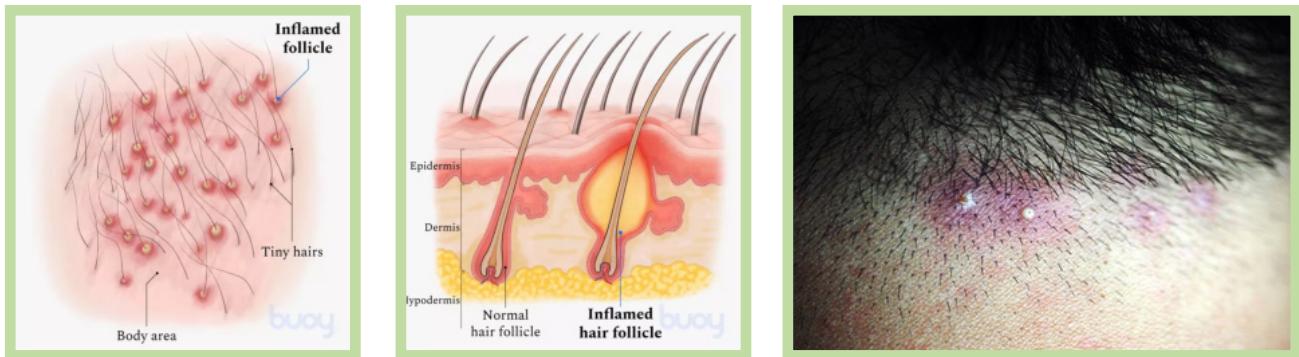
Antibiotics, wound care (drainage and debridement), supportive care, IV immunoglobulin therapy (IVIG)

Bacterial Hair Folliculitis

[DermNet Folliculitis](#)

Description

Folliculitis is an infection and/or inflammation of damaged hair follicles commonly by bacteria (staph/streps). The result is a tender red spot, often with a surface pustule. Infection can often occur as a complication to acne or in areas of high friction.



Signs & Symptoms

1. *Folliculitis*: Clusters of small inflamed pustules that develop around hair follicles, itchy, painful
2. *Boils (furunculosis)*: Severe/deeper infection of follicles in areas of friction, central yellow 'plug', bigger lesions, systemic symptoms.
3. *Carbuncle (conglomeration of boils/furuncles)*: Necrosis, bacteria (pus)

Pharmacological Treatment

Antibiotics (topical, oral, IV), drainage if needed

Leprosy (Hansen's disease)

[Leprosy Cleveland Clinic](#)

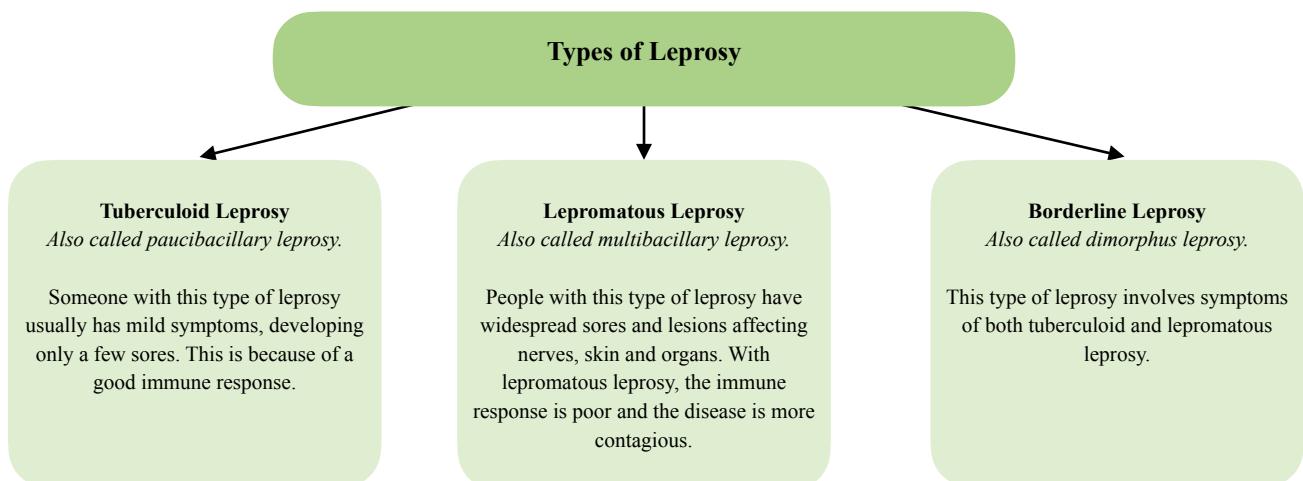
Description

Leprosy, also known as Hansen's disease, is an infection that's been around since ancient times and still exists today. It is caused by a slow-growing bacteria called *Mycobacterium leprae*, which can be transmitted from person to person. It can affect the nerves, skin, eyes, and lining of the nose (nasal mucosa) causing disfiguring sores and nerve damage.



Signs & Symptoms

There are three main types of Leprosy that exist:



Prevention

Tuberculosis vaccine offers some cross protection

Pharmacological Treatment

Leprosy can be cured when detected and treated early and treatment involves multidrug therapy with antibiotics.



Historical Context of Leprosy

For centuries, people isolated and shunned those with leprosy because the disease wasn't understood. Today, effective treatment is available, and there's no need to quarantine people with leprosy

1. *Antibiotics* (multi-drug therapy: dapsone, rifampicin, clofazimine)
2. *Surgical Reconstruction*

Clostridial Skin Infections

Introduction

Clostridium species are anaerobic, gram positive, toxin producing bacteria that cause invasive bacterial infections (such as cellulitis). And thus, much like cellulitis, are caused by entry via an open wound. 2 organisms are responsible: *C.Tetani* and *C.Perfringens*.

Tetanus Disease (Lockjaw)

Health Navigator Tetanus

Description

Tetanus, also known as Lockjaw, is a serious infectious disease caused by the entry of *Clostridium Tetani* and its toxins into a wound - these affect body nerves, causing symptoms such as muscle stiffness and spasms.



The bacteria are usually found in soil, dust, and manure and enter the body through breaks in the skin — usually cuts or puncture wounds caused by contaminated objects.

Signs & Symptoms

- *Early*: Tissue infection, weakness, stiffness, cramps
- *Late*: Spasms, seizures which can be fatal, difficulty chewing and swallowing food (**lockjaw**)

Prevention

1. C. Tetani - Toxoid vaccine (requires boosting) for prevention

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Infanrix-IPV booster (DTaP, polio)	IPV is inactivated or whole killed	4 years
Boostrix booster (DTaP)	Booster	11 or 12 years Unfunded at 45y, 65y, pregnant

Pharmacological Treatment

1. Tetanus Ig (TIG) for immediate protection from toxin
2. Antimicrobial therapy (minor impact)

Clostridium Perfringens Infections

Description

Clostridium Perfringens causes a variety of soft tissue infections including crepitant cellulitis and also other kinds of infections such as food poisoning. C.Perfringens infections are often called gas gangrene because the crepitus present is caused by gas in the underlying tissues.

Signs & Symptoms

- *Early*: Pale skin, fluid filled blisters, discharge, gas production
- *Late*: Severe pain, tachycardia, fever, progression to hypotension and organ failure

Pharmacological Treatment

- IV antibiotics and surgical debridement
- Hyperbaric oxygen therapy

FUNGAL SKIN INFECTIONS

Introduction

Fungal infections seen in the community are either attributable to dermatophytes or candida (also known as tinea infections)



Differential Diagnosis: Fungal Infections & Atopic Conditions

All fungal infections can be differentiated from atopic dermatitis/psoriasis using family history.

This distinction is important as misdiagnosis and prescribing of a steroid will relieve itchiness and redness but organism will proliferate. Furthermore steroid withdrawal can cause the infection to come back stronger and worse.

For this reason, usage of a steroid for a fungal infection (e.g. for itching) should not exceed a maximum of **7 days**.

Tinea infections are very commonly seen in practice and depending on the part of the body they affect, they bear a different name.

- Hands (tinea manuum)
- Feet (tinea pedis or athlete's foot)
- Scalp (tinea capitis)
- Face (tinea faciei)
- Beard (tinea barbae)
- Groin (tinea cruris or jock's itch), and
- Nails (tinea unguium or onychomycosis).

Seborrhoeic Dermatitis (SD, Cradle Cap & Dandruff)

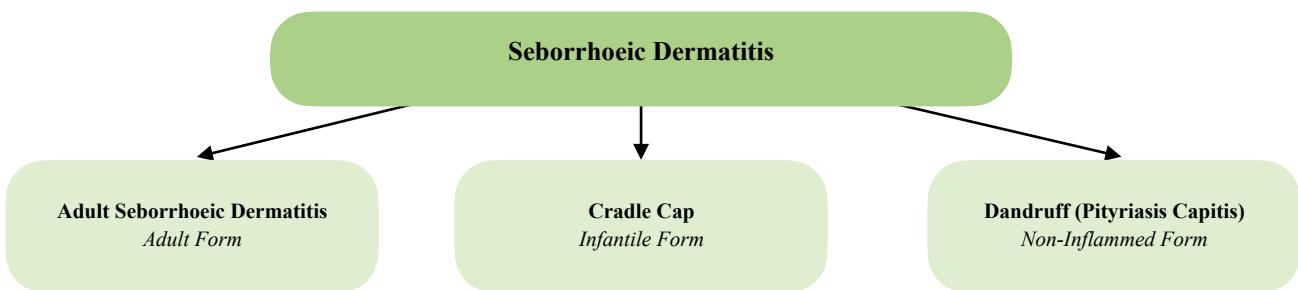
[DermNet Seborrhoeic Dermatitis](#)

Description

Seborrhoeic dermatitis (SD) is an inflammatory, hyper-proliferative, **greasy**, and chronic form of dermatitis that affects mainly sebaceous gland-rich regions of the body such as the face, scalp and trunk.



Three forms of SD exist, each with a different presentation:



Pathophysiology

Adult seborrheic dermatitis and dandruff are both thought to be superficial fungal diseases - particularly by *Malassezia yeasts* given that they make up a high proportion of scalp flora.



Seborrhoeic Dermatitis & Weather

Dry air during the *winter* months will make your SD worse despite the yeast being prevalent in tropical countries. The dermatitis however behaves best during the *summer* due to favourable environmental conditions

Risk Factors

Adult seborrheic dermatitis and dandruff often occur in otherwise healthy patients. However, risk factors associated with dandruff and the severe manifestation of seborrhoeic dermatitis are:

- *Genetics*: Having an oily hair and scalp, family history of SD
- *Age*: young adulthood - middle age
- *Gender*: males are more susceptible than females due to androgen-sebum production
- *Certain illnesses*: particularly neurological (e.g. Parkinson's) and cardiovascular (stroke, HF)

- *Diet*: Eating a diet low in zinc, B vitamins, or certain fats.
- *Lifestyle*: Experiencing excessive stress
- *Immunosuppression*: e.g. HIV, diabetes
- *Pregnancy*: mom's hormones can cause cradle cap

Signs & Symptoms

1. *Infant Cradle Cap (<3 months)*: greasy scaly scalp
2. *Adult Seborrheic Dermatitis*: **minimal itch**, combination oily/dry facial skin, may be scaling or flaking of skin, soreness, pink plaques, folliculitis may be present. Infection is likely in summer but may flare in winter.
3. *Dandruff*: Itchy, dry, flaky scalp with skin flakes being present on eyebrows, beard and shoulders. These may be more severe if the patient is stressed, and they tend to flare in cold, dry seasons.

Differential Diagnosis

Dandruff vs Dry Scalp

Dry scalp and dandruff look very similar and can be difficult to distinguish. Oily, large flakes typically point to dandruff, while dry, smaller flakes signal dry scalp.

SD vs Tinea Capitis

Erythematous scaly lesions seen in tinea capitis closely resemble those seen in SD. However it is important to note that SD does **not** cause hair loss.

SD vs Dermatitis

While SD itself is a form of dermatitis and scalp contact dermatitis is a possible cause of dandruff - unlike atopic/contact dermatitis:

SD is associated with minimal **itch**. Furthermore dermatitis may have a possible **source**.

SD vs Psoriasis

Family history is more prevalent in psoriasis

SD presents with eyelid and ear complications with the patches being more **greasy** than **silvery**.

SD cannot be **felt** if you run a hand through their hair while psoriasis make the scalp uneven and lumpy.

Dandruff vs Adult SD

Dandruff itself is a mild and non-inflamed form of seborrheic dermatitis. However, SD usually presents as defined plaques of greasy, yellow scales that are **not** limited to the scalp; they can be found behind the ears, and on the nose, upper lip, eyelids, eyebrows, and upper chest.

Non-Pharmacological Treatment

Cradle Cap Management (Infants)

1. Regular scalp washing with baby shampoo or aqueous cream, followed by gentle brushing to clear the scales. Baking soda and water work quite well.
2. Do not pick at the scales.
3. May be treated with coconut oil or olive oil applications before shampooing
4. Topical antifungal agents are often prescribed, depending on the extent of the rash

Dandruff Management

1. Mild dandruff may be treated with a gentle daily shampoo. Medicated shampoos may be trialled if this method doesn't work.
2. Many other home remedies exist (although with limited evidence): coconut oil, aloe vera, baking soda, lemon juice, olive oil, apple cider vinegar.

Pharmacological Treatment

There are many treatment options available for the treatment of adult SD and dandruff:



Note

Dandruff is only treated with medicated anti-fungal shampoos. Topical Calcineurin Inhibitors are indicated if topical corticosteroids are needing to be used frequently, as they have fewer adverse effects on facial skin with long term use.

1. *Medicated (Anti-Fungal) Shampoos*: Ketoconazole, Selenium Sulfide, Zinc Pyrithione, Coal Tar
2. *Topical Corticosteroids*: Miconazole + Hydrocortisone
3. *Topical Keratolytics*: Salicylic Acid, Lactic acid, Urea, Propylene Glycol
4. *Topical Calcineurin Inhibitors*: Pimecrolimus Cream, Tacrolimus Ointment
5. *Oral Antifungals*: Itraconazole
6. *Oral Antibiotics*: Tetracycline Antibiotics for secondary bacterial infections

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Medicated (Anti-Fungal) Shampoos	[GENERAL SALE] Zinc Pyrithione Shampoo Head & Shoulders Dry Scalp	Relieve scaling and itching These work by slowing the growth of the fungi that are thought to cause SD. They also slow down dead skin formation to prevent flaking to other locations.	<ul style="list-style-type: none"> Leave on for at least 5 minutes For best results use at least twice a week or as directed by a doctor. Shake before use. Wet hair, massage onto scalp, rinse, repeat if desired. 	• May irritate scalp
	[GENERAL SALE] Coal Tar Shampoo Coal Tar (Midwest)	Relieve scaling and itching Coal tar belongs to a class of drugs known as keratoplastics. Reduces epithelial skin cell turnover rate. It demonstrates antifungal, anti-inflammatory, anti-itch, and antiparasitic properties.	<ul style="list-style-type: none"> Can stain clothes and make scalp more sensitive to sunburn Avoid contact with eyes, nose, mouth, groin or rectum Wet hair/scalp and apply a generous amount of coal tar shampoo, massage into a lather and leave on for a few minutes, protect eyes with a washtowel. 	
	[GENERAL SALE] Selenium Sulfide Shampoo Selsun 2.5%	Relieve scaling and itching Selenium sulfide is an anti-infective shampoo that relieves itching and flaking of the scalp	<ul style="list-style-type: none"> Can discolour hair and stain clothes Wet hair/scalp and apply a generous amount of shampoo, massage into a lather and leave on for a few minutes. 	May irritate scalp May cause unusual scalp oiliness or dryness and hair loss
	[GENERAL SALE, PHARMACY ONLY] Ketoconazole Shampoo 1% or 2% Nizoral Sebizole Dandruff	Relieve scaling and itching Anti-fungal shampoo that targets the fungi that are thought to cause dandruff. Interferes in ergosterol synthesis. <ul style="list-style-type: none"> 1% are General Sale 2% are Pharmacy Only 	<ul style="list-style-type: none"> Discolouration of hair if chemically damaged. Apply to wet scalp twice weekly for up to 4 weeks (may be repeated after a 4 week break); leave preparation on for 3–5 minutes before rinsing 	• May irritate scalp
Topical Corticosteroids + Antifungal	[PHARMACY, PHARMACIST ONLY] Miconazole 2% + Hydrocortisone Micreme H	Anti-Inflammatory/Fungal Reduce inflammation of an acute flare as well as exhibiting anti-fungal activity.	<ul style="list-style-type: none"> Useful for fungal skin infections with inflammatory symptoms. Short term use Contact your doctor if you experience any changes in your vision, including blurred vision. 	Local irritation, hypersensitivity reactions, thinning of the skin,
Keratolytics	[PHARMACY ONLY] Salicylic Acid Salicylic Cream, Egozite Lotion for infants	Hyperkeratotic Softens keratin which allows the shedding of dead cells from the top layer and by decreasing redness and swelling (inflammation).	<ul style="list-style-type: none"> You may experience burning, stinging, peeling. Do not apply to large body areas — especially in infants. Do not apply to non-crusted areas Hair loss may be expected but new hair growth will occur 	Sensitivity, excessive drying, irritation, systemic effects after widespread use
Oral Anti-Fungals	[PRESCRIPTION] Itraconazole Itrazole	Anti-Fungal Triazole fungistatic antifungal with ergosterol-synthesis inhibitory activity.	<ul style="list-style-type: none"> Take with food and until finished. Do not take indigestion remedies, iron or calcium preparations within 2 hours of taking this medicine. Grapefruit or grapefruit juice may interact with this medicine. 	Nausea, diarrhoea, dyspepsia, abdominal pain, dyspepsia vomiting, disguise, cough, headache, dizziness rash, pyrexia
Oral Antibiotics	[PRESCRIPTION] Tetracycline Doxycycline (Doxine)	Secondary Bacterial Infections Inhibit protein synthesis and have anti-inflammatory effects.	Avoid sunlight. Avoid calcium/iron containing products. Swallow whole, take with food and water. Remain upright for at least 30 minutes. Finish the whole course.	N/V, diarrhoea, dysphagia, esophageal irritation

Tinea Versicolor (Pityriasis Versicolor)

[DermNet Pityriasis Versicolor](#)

Description

Pityriasis is a common yeast (usually *Pityrosporum ovale* or *Malassezia*) infection of the skin. This yeast can transform into a pathogenic form and turn off **melanin-producing** cells in the skin, producing asymptomatic flaky patches on the trunk, neck, or arms.



Risk Factors

A number of conditions can trigger conversion of *P. Ovale*

1. *Weather*: hot and humid climates, use of oils, hyperhidrosis (excessive sweating). Pityriasis thus may clear in the winter months and recur each summer.
2. *Immunosuppression*: diabetes, HIV
3. *Age*: young adults

Signs & Symptoms

Patches will manifest differently depending on the skin colour as patches change the colour of melanocytes.

- They appear pink or coppery brown patches on pale skin, and
- Pale brown patches paler than surrounding skin on tanned skin that lasts month to years
- They often present on the chest and back area and may be mildly itchy



Did You Know?

Medical textbooks have historically been biased in using caucasian skin to demonstrate what different skin conditions look like - this was however found to create many health disparities as doctors would fail to recognise the same conditions on melanin-containing skin.

A good example of this is eczema in Māori populations and poorer outcomes we observe. Thus, it is important to pay attention to how the same condition may manifest differently depending on your patient's skin colour.

Pharmacological Treatment

BPAC Tinea Versicolor

Topical antifungal medicines are the treatment of choice for pityriasis versicolor — usual treatment duration for topical antifungals is **2 - 4 weeks**. However, recurrences of infection after successful treatment are common, thus to help prevent relapse, continued intermittent use of topical therapies can be useful e.g. applying selenium sulfide shampoo every month once the rash has cleared will usually prevent recurrence.

Oral antifungals are used when extensive or if topical agents have failed. Short term treatment will clear many cases of pityriasis long term, or at least for several months.

1. Topical Antifungals (for Mild Pityriasis)

- *Shampoos applied on the skin:* Ketoconazole Shampoo, Selenium Sulfide Shampoo
- *Creams/Solutions:* Imidazole creams such as clotrimazole 1%, or miconazole 2%, or econazole
- *Gel:* Terbinafine Gel

2. Oral Antifungals (for Severe Pityriasis)

- *Tablets:* Itraconazole, Ketoconazole, or Fluconazole



Oral Terbinafine is Not Effective

While terbinafine gel is an effective treatment for Tinea Versicolor, however oral terbinafine is not as it is not excreted in sweat so will not reach high concentrations in the stratum corneum to exhibit fungicidal action against Malassezia species

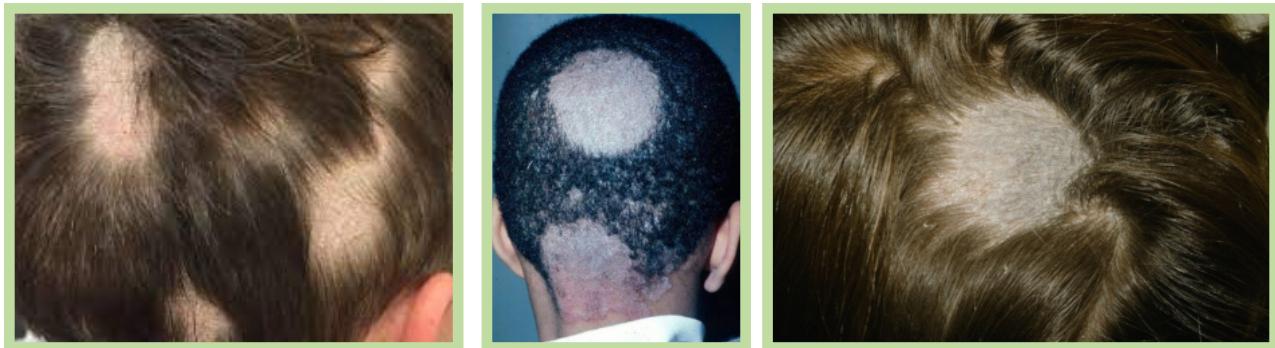
Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Mild Pityriasis Topical Antifungals	[GENERAL SALE, PHARMACY ONLY] <i>Ketoconazole Shampoo 1% or 2%</i> Nizoral Sebizole Dandruff	Shampoo Interferes in ergosterol synthesis. • 1% are General Sale • 2% are Pharmacy Only	<ul style="list-style-type: none"> 2 - 4 weeks treatment Apply the shampoo directly to the skin patches once each day for 3-5 minutes before rinsing off in the shower. Repeat daily for one week, then weekly for one month Avoid contact with eyes and mucous membrane 	Irritation
	[GENERAL SALE] <i>Selenium Sulfide Shampoo</i> Selsun 2.5%	Symptomatic Relief Selenium sulfide is an anti-infective shampoo that relieves itching and flaking of the scalp	<ul style="list-style-type: none"> 2 - 4 weeks treatment Can discolour hair and stain clothes Apply the shampoo directly to the skin patches once each day for 3-5 minutes before rinsing off in the shower. 	
	[PHARMACY ONLY] <i>Econazole Nitrate</i> Pevaryl 1% cream or foaming solution	Cream / Solution Interferes in ergosterol synthesis.	<ul style="list-style-type: none"> 2 - 4 weeks treatment Pevaryl should be applied to the wet body on three consecutive evenings. The foam should not be rinsed off but allowed to dry. 	Local irritation, hypersensitivity reactions (mild burning sensation, erythema, itching)
	[GENERAL SALE, PHARMACY ONLY] <i>Terbinafine Gel</i> Lamisil Dermgel 1%	Gel Interferes with ergosterol synthesis.	<ul style="list-style-type: none"> Apply thinly 1-2 times a day for two weeks in pityriasis versicolor. 	
Severe Pityriasis Oral Antifungals	[PRESCRIPTION] <i>Itraconazole 100mg capsule</i> Itrazole	Triazole fungistatic antifungal with ergosterol-synthesis inhibitory activity.	<ul style="list-style-type: none"> Vigorous exercise an hour after taking the medication may help sweat it onto the skin surface, where it can effectively eradicate the yeast. Bathing should be avoided for a few hours. Take with food and until finished. Do not take indigestion remedies, iron or calcium preparations within 2 hours of taking this medicine. Grapefruit or grapefruit juice may interact with this medicine. 	Nausea, diarrhoea, dyspepsia, abdominal pain, dyspepsia vomiting, disguise, cough, headache, dizziness rash, pyrexia

Tinea Capitis (Scalp Ringworm)

[DermNet Tinea Capitis](#)

Description

Tinea Capitis is a superficial dermatophyte fungal infection of the scalp, involving both the skin and hair, resulting in inflammation and hair loss. It is highly contagious, transmitted via spores or from person to person.



Risk Factors

1. *Animal contact:* Tinea Capitis is often caught from infected kittens and cats (*M.canis*)
2. *Children & Immunocompromised Adults:* more common in children aged 3 to 7 yrs old.
3. *Other:* household crowding and low socioeconomic factors

Signs & Symptoms

Itchy scalp patches, **hair loss** can occur in infected areas (due to the breaking of the hair), inflammation, scaly skin, grey patches that may spread, reddened areas, itch

Complications: permanent alopecia may result with inappropriate and delayed treatment, secondary bacterial infections.

Diagnosis

Wood's lamp examination is diagnostic when hair fluorescence is seen.

Non-Pharmacological Treatment

1. Sharing of potential objects such as hairbrushes, hats, and pillows should be discouraged, and these should be properly cleaned
2. Family pets should be checked by a veterinarian and treated accordingly
3. **Screen contacts** simultaneously as they may be carriers and treat if affected

Pharmacological Treatment

Tinea capitis requires **4 - 6 weeks** of systemic treatment.



Note

Unlike other tinea infections, Tinea Capitis is treated with oral antifungals as first line - this is because topicals **cannot penetrate** the hair root - they thus only have an adjunctive role in helping reduce spore transmission in the first two weeks. Shampoo should be applied for 5 - 10 minutes, three times a week, for 2 to 4 weeks

1. First Line - Oral Antifungals

- Terbinafine (first line)
- Other: itraconazole, fluconazole

2. Adjunctive Tx - Topical Antifungals

- Ketoconazole Shampoo
- Selenium sulfide shampoo
- Betadine (antiseptic)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
First Line Oral Antifungals	[PRESCRIPTION] <i>First Line - Terbinafine</i> Deolate 250mg tablet	For dermatophyte infections Terbinafine inhibits fungal ergosterol synthesis. First line due to its high cure rates, tolerability and low cost.	• Take with or without food at the same each day.	Abdominal discomfort, anorexia, nausea, diarrhoea, dyspepsia, headache
	[PRESCRIPTION] <i>Itraconazole</i> Itrazole 100mg capsule	For candida infections Interferes with cell membrane synthesis	• Take with a full meal, avoid iron, indigestion remedies, or calcium or grapefruit.	Nausea, diarrhoea, dyspepsia, abdominal pain, vomiting, dysgeusia, cough, headache, dizziness rash, pyrexia
	[PRESCRIPTION] <i>Fluconazole</i> Fluconazole (Mylan)	For dermatophyte infections Inhibits fungal ergosterol synthesis.	• Take with food and a glass of water until finished.	GI Upset, N&V, Rash, Allergy
2nd Line Topical Antifungals	[GENERAL SALE, PHARMACY ONLY] <i>Ketoconazole Shampoo 1% or 2%</i> Nizoral Sebizole Dandruff	Anti-Fungal Shampoo Interferes in ergosterol synthesis. • 1% are General Sale • 2% are Pharmacy Only	• Apply the shampoo once each day for 5-15 minutes before rinsing off in the shower. • Repeat daily for one week, then weekly for one month • Avoid contact with eyes and mucous membrane	Scalp irritation
	[GENERAL SALE] <i>Selenium Sulfide Shampoo</i> Selsun 2.5%	Anti-Fungal Shampoo Selenium sulfide is an anti-infective shampoo that relieves itching of the scalp	• Can discolour hair and stain clothes • Wet hair/scalp and apply a generous amount of shampoo, massage into a lather and leave on for a few minutes.	May irritate scalp May cause unusual scalp oiliness or dryness and hair loss
Topical Antiseptic	[GENERAL SALE] <i>Povidone-iodine 10%</i> Betadine	Anti-Fungal Paint Betadine is an antiviral, anti-bacterial, anti-fungal and anti-protozoal antiseptic due to the microbial activity of iodine.	• Wash and dry skin before applying cream and then cover with a water tight dressing. • Avoid near the eyes and bleaches/stains fabric	• Local irritation • Stains fabric

Tinea Corporis (Body Ringworm)

[DermNet Tinea Corporis](#)

Description

Tinea Corporis is a superficial fungal infection (dermatophytes) commonly of the arms and leg. It can affect any part of the body, **excluding** the hands (tinea manuum), feet (tinea pedis or athlete's foot), scalp (tinea capitis), face (tinea faciei), beard (tinea barbae), groin (tinea cruris or jock's itch), and nails (tinea unguium or onychomycosis). It spreads by direct skin-skin contact with an infected person or animal.



Risk Factors

1. *Animal contact:* Tinea Corporis is associated with contact with infected kittens (*M. Canis*)
2. *Climate:* Tinea corporis is found particularly in hot humid climates. It is most commonly seen in children and young adults, however all age groups can be infected including newborns.
3. *Other:* household crowding and low socioeconomic factors
4. *Medical Conditions:* Immunosuppression (HIV, AIDS, diabetes)

Signs & Symptoms

Ringworm usually presents as itchy pink, red scaly, slightly raised patches with a well defined inflamed border and a white healing middle. The lesions are often itchy, inflamed, pustular, dry, scaly.

Non-Pharmacological Treatment

1. Skin should be kept clean and dried thoroughly
2. Loose-fitting light clothing is recommended in hot humid climates
3. Avoid close contact with infected individuals and the sharing of items (to minimise spread)
4. Examination of household members and pets for the source of infection

Pharmacological Treatment

Note: Tinea Corporis, Cruris and Pedis share the same pharmacological treatment. Tinea Summary Table can be found under Tinea Pedis.

1. First Line - Topical Antifungals: Terbinafine, Miconazole, Clotrimazole

- For localised tinea corporis. Once or twice daily is usually sufficient. A typical course is 2 to 4 weeks.
- Application needs to include an adequate margin around the lesion and a prolonged course continuing for at least 1–2 weeks after the visible rash has cleared. However, recurrence is common.

2. Second Line - Systemic Antifungal: Terbinafine, Itraconazole

- Oral antifungal treatment is usually required if tinea corporis is involving a hair-bearing site (as topical treatment cannot penetrate hair root), is extensive, or has failed to clear with topical antifungals.

Tinea Cruris (Jock Itch)

[DermNet Tinea Cruris](#)

Description

Dermatophyte fungal infection of the groin and/or the pubic region arising from contaminated towels and bed sheets or autoinoculation from existing foot infection.



Risk Factors

1. *Climate*: Tinea cruris can affect all races, being particularly common in hot humid tropical climates.
2. *Other*: household crowding and low socioeconomic factors
3. *Medical Conditions*: immunosuppression (HIV, AIDS, diabetes), obesity
4. *Medicines*: topical steroid use

Signs & Symptoms

Inflamed circular red patches, white healing middle, itchy, inflamed, pustular. It presents as an acute or chronic asymmetrical rash. Tinea cruris often causes marked hyperpigmentation in skin of colour — which can persist in residual amounts.

Non-Pharmacological Treatment

1. Careful towelling after washing to avoid transfer of fungi
2. Loose-fitting light clothing is recommended in hot humid climates
3. Avoid close contact with infected individuals and the sharing of items
4. Treatment of triggers such as hyperhidrosis or obesity

Pharmacological Treatment

Note: Tinea Corporis, Cruris and Pedis share the same pharmacological treatment. Tinea Summary Table can be found under Tinea Pedis.

1. First Line - Topical Antifungals — Terbinafine, Miconazole, Clotrimazole

- Once or twice daily is usually sufficient. A typical course is 2 to 4 weeks. Application needs to include an adequate margin around the lesion and a prolonged course continuing for at least 1–2 weeks after the visible rash has cleared. However, recurrence is common.

2. Second Line - Systemic Antifungals — Terbinafine, Itraconazole

- Oral antifungal treatment is usually required if tinea cruris is extensive, or has failed to clear with topical antifungals.

3. Other: *Topical Corticosteroid*

- May be appropriate in Tinea Cruris in severe itching. However only for short term therapy.



Note

Following treatment, residual hyperpigmentation may occur

Tina Pedis (Athlete's Foot)

[DermNet Tinea Pedis](#)

Description

Tinea Pedis is a dermatophyte fungal infection that usually begins between the toes and is commonly in sweaty feet confined within tight-fitting shoes. Spores can survive for months. Infection can spread to other sites of the foot and nail (see Onychomycosis)



Risk Factors

- Fungal infections are more prevalent in summer and in places of hot and humid climates,
- Tight-fitting shoes, sweaty socks, personal hygiene, damp skin (not thoroughly dried), shared communal areas (e.g. changing rooms, public showers), immunosuppression (e.g. diabetes)

Signs & Symptoms

Itching, flaking, fissuring of the skin, smell, white and soggy appearance due to the maceration of the skin.

Complications: 2° bacterial infections in broken skin (looks like oozing, yellow discharge)

Non-Pharmacological Treatment

1. Dry skin thoroughly after showering
2. Do not share towels to prevent transmission
3. Wear cotton socks and change at least once a day
4. Wear open toe shoes
5. Avoid scratching infected skin
6. Wear jandals in communal changing rooms
7. While on treatment, **avoid swimming**

Pharmacological Treatment

Note: Tinea Corporis, Cruris and Pedis share the same pharmacological treatment. Tinea Summary Table can be found here.

1. First Line - Topical Antifungals: *Terbinafine, Miconazole, Clotrimazole*

- Once or twice daily is usually sufficient. A typical course is 2 to 4 weeks. Application needs to include an adequate margin around the lesion and a prolonged course continuing for at least 1-2 weeks after the visible rash has cleared. However, recurrence is common.

2. Second Line - Systemic Antifungals: *Terbinafine, Itraconazole*

- Oral antifungal treatment is usually required if tinea pedis is extensive, or has failed to clear with topical antifungals.

3. Other: *Topical keratolytic cream containing salicylic acid or urea*

- May be appropriate in patients affected by the hyperkeratotic variant of tinea pedis

Summary Treatment for Tinea Corporis / Cruris / Pedis				
Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Topical Antifungals	[GENERAL SALE, PHARMACY ONLY] <i>Terbinafine Gel</i> Lamisil Dermgel 1%	Gel Interferes in ergosterol synthesis.	<ul style="list-style-type: none"> Apply thinly 1-2 times a day for two weeks in tinea corporis Not recommended in breastfeeding 	Local irritation, hypersensitivity reactions (mild burning sensation, erythema, itching)
	[PHARMACY ONLY] <i>Miconazole Cream</i> Miconazole Resolve	Cream Interferes in ergosterol synthesis.	<ul style="list-style-type: none"> Note: Continue miconazole for 10 days after lesions have healed 	
	[PHARMACY ONLY] <i>Clotrimazole Cream</i> Canesten, Clomazol	Cream Interferes in ergosterol synthesis.	<ul style="list-style-type: none"> Apply 2-3 times daily for duration of infection and for 2 weeks after infection has resolved 	Not recommended in pregnancy if application to large areas is required
Oral Antifungals	[PRESCRIPTION] <i>First Line - Terbinafine</i> Deolate 250mg tablet	For dermatophyte infections Terbinafine inhibits fungal ergosterol synthesis. First line due to its high cure rates, tolerability and low cost.	<ul style="list-style-type: none"> Take with or without food at the same each day. Not recommended in breastfeeding 	Abdominal discomfort, anorexia, nausea, diarrhoea, dyspepsia, headache
	[PRESCRIPTION] <i>Itraconazole</i> Itrazole 100mg capsule	For candida infections Interferes with cell membrane synthesis	<ul style="list-style-type: none"> Take with a full meal, avoid iron, indigestion remedies, or calcium or grapefruit. Not recommended in breastfeeding 	Nausea, diarrhoea, dyspepsia, abdominal pain, vomiting, dysgeusia, cough, headache, dizziness rash, pyrexia

Please remember, steroids should not be used for longer than a week - however in the event that the patient is experiencing severe itchiness/discomfort, you may give a steroid + antifungal such as Micreme H or Canesten Plus. After a week, remember to switch onto just an antifungal.

Tinea Unguium (Onychomycosis)

[DermNet Onychomycosis](#)

Description

Onychomycosis is a fungal nail infection, often presenting as a secondary complication to athlete's foot (however it can occur on fingers as well). The initial skin infection is caused by dermatophytes, yeasts, moulds.



Differential Diagnosis

Nail Psoriasis — Presents with pitting, onycholysis, discolouration, thickening and irregular ridging. Look for psoriatic plaques on typical sites (scalp, ears, elbows, knees and flexures).

Signs & Symptoms

White/yellow nail discolouration, thickening of the nail, separation of the nail from the nail bed (onycholysis), rotten looking, nail becomes brittle and crumbles away or falls off.

Red Flags: Refer if >50% of the nail is infected or underlying causative medical conditions (e.g. diabetes)



Infections & Diabetes

If you have a suspicion that your patient's infection could be attributed to high blood sugar, the recommendation is to immediately refer. It is sometimes not recommended to supply a product in the meanwhile because it may not work for the patient while costing them quite a bit. If however, you do choose to supply something, ensure that the patient understands the need to see a GP and that the product supplied is not a replacement for an appointment.

Non-Pharmacological Treatment

Prevention

1. Do not share items e.g. towels used to dry the feet
2. Keep feet cool and dry by wearing cotton socks and breathable footwear e.g. open toed shoes
 - Avoid high heels and narrow toed shoes to prevent nail trauma
3. Wear footwear in communal showers and do not walk barefoot
4. Address any risk factors (e.g. diabetes, athlete's foot)

During Treatment

5. Trim and file down nails
6. Do not wear nail polish during treatment

Pharmacological Treatment

Note: Topicals may be preferred as they don't require a prescription (cheaper than going to the doctor). Oral may be preferred as they offer shorter treatment courses, higher cure rates and fewer relapses.

Please note that duration of treatment is much much longer compared to other kinds of fungal infections - this is because nails take a long time to grow.

1. First Line - Topical Antifungals: Amorolfine nail lacquer

- Mild infections affecting less than 50% of one or two nails may respond to topical antifungal medications, but cure usually requires an oral antifungal medication for several months.
- Note: 8% Ciclopirox is discontinued

2. Second Line - Oral Antifungals: Terbinafine (first line), itraconazole

- Systemic antifungal agents are the most effective treatment for onychomycosis, but cure rates are much less than 100%. Terbinafine is the most effective systemic agent available.

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Topical Antifungals	[PHARMACY ONLY] <i>Amorolfine 5% Nail Lacquer</i> Myconail Loceryl	Fungistatic anti-fungal. Amorolfine is not effective for all fungal nail infections or if the infection is present in the deeper part of the nail.	<ul style="list-style-type: none"> • Apply to infected nails 1-2 times weekly after filing and cleansing, and leave to dry. • Avoid contact with eyes, ears and mucous membranes • Do not use if pregnant or breastfeeding • Takes 9-12 months for toe nails and 6 months for fingernails. Avoid nail varnish during this treatment. 	Local irritation and hypersensitivity reactions (mild burning sensation, erythema, itching)
Oral Antifungals	[PRESCRIPTION] <i>Terbinafine 250mg Tablet</i> Deolate	Fungicidal via ergosterol-synthesis inhibitory activity.	<ul style="list-style-type: none"> • 6 weeks - 3 months treatment duration • Take with food • Take until the medicine is finished 	Abdominal discomfort, anorexia, nausea, diarrhoea, dyspepsia, headache
	[PRESCRIPTION] <i>Itraconazole 100mg capsule</i> Itrazole	Triazole fungistatic antifungal with ergosterol-synthesis inhibitory activity.	<ul style="list-style-type: none"> • Take with food and until finished. • Do not take indigestion remedies, iron or calcium preparations within 2 hours of taking this medicine. • Grapefruit or grapefruit juice may interact with this medicine. 	Nausea, diarrhoea, dyspepsia, abdominal pain, dyspepsia vomiting, disguise, cough, headache, dizziness rash, pyrexia

OSCE Points

- Amorolfine nail lacquer is **contraindicated** in pregnancy/breastfeeding and in children

VIRAL SKIN INFECTIONS

Introduction

Viral skin infections are a common presentation in primary care - we will cover HFMD, Chicken Pox, Shingles, Cold Sores and Warts.

Hand, Foot and Mouth Disease (HFMD)

[Health Navigator Hand Foot and Mouth Disease](#)

[DermNet Hand, Foot and Mouth Disease](#)

Description

Hand, foot and mouth disease is a common, incredibly contagious viral infection that mostly affects children under 10 years of age. This virus is found in faeces, blisters, saliva, a runny noses.



Risk Factors

Hand, foot and mouth disease appears most often in:

- Preschool children
- During warm weather (usually summer/early autumn)

Signs & Symptoms

The disease is usually mild and lasts about 3–7 days.

- *First sign:* mild fever 3-5 days following exposure to virus.
- Painful sores/red blisters inside mouth
- Red or fluid-filled blisters usually on arms/legs (particularly on the palms of hands, or soles of feet but can appear elsewhere) that are **not** particularly itchy or painful
- *Other:* loss of appetite, a sore throat and mouth, a general feeling of weakness or tiredness.

Red Flags: systemic spread, child does not get better within 7-10 days.

Complications

- *Pregnancy:* this disease is rare in healthy adults, catching it during pregnancy can cause baby to develop mild symptoms or miscarry in utero.

- *Spread:* very rare but spread of the virus can cause or a more serious illness including inflammation of the brain or heart.

Prevention (Spread)

1. Frequent hand washing particularly after using the toilet, when changing nappies, helping them blow their nose or when handling objects/toys children hold/put in their mouths.

Non Pharmacological Treatment

Keep your child home until all the blisters have dried (~1 week)

- *If your child's mouth is sore:* do not give them sour, salty or spicy foods.
- *Hydration:* Make sure they drink plenty of liquids to avoid getting dehydrated e.g. sips of water/juice
- *Blister Care:* do not pierce/rupture, leave to dry naturally, keep clean and apply non-adherent dressings

Pharmacological Treatment

There is no specific treatment for hand, foot and mouth disease - no vaccines, antivirals, antibiotics work and should not be given to children.

1. *Simple Analgesia:*
 - Paracetamol or Ibuprofen
2. *For painful oral/palatal ulcers:*
 - Antiseptic mouthwashes or topical soothing agents (eg. lignocaine)

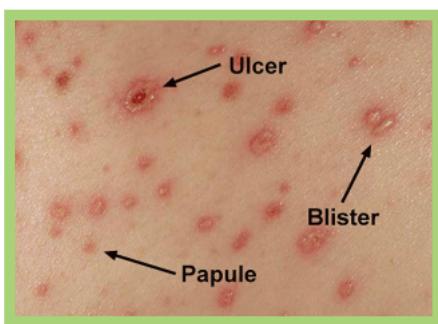
Chicken Pox (Varicella-Zoster)

[DermNet Chickenpox](#) [Health Navigator Chickenpox](#)

Description

Chickenpox is a highly contagious viral infection caused by the varicella-zoster virus that is a common self-limiting childhood infection. It causes:

1. An acute fever and
2. A blistered, itchy rash on the skin



Pathophysiology

VZV has airborne transmission - it infects T cells in **tonsils** and may spread to **blood** and **body**. Until the infection is controlled by the immune system - extensive viral replication & small itchy blisters will form on the skin.

Once a person has had the chickenpox infection, the immune system ‘walls off’ the virus in the sensory nerves, where it will remain latent. However, a poor immune system can cause its reactivation - this is known as Shingles. See the next condition for more information on it.

Risk Factors

- *Age:* children < 10 years old
- *Immunocompromised:* Diabetes, HIV

Signs & Symptoms

In healthy children, chickenpox infection is usually an uncomplicated, self-limiting disease. However, adult chickenpox is much more severe and can be life-threatening. Let's look into a few types:



Duration

It takes **10-21 days** before symptoms appear. A person is most infectious **1-2 days** before the rash appears, until blisters have crusted over.

1. *Congenital Varicella Syndrome*
 - **Mother** develops rash < 4 days before delivery resulting in the infant being affected: deformed limbs, low birth weight, scarring, mental defects

2. *Normal Chickenpox*
 - Small itchy red bumps that turn into fluid-filled blisters, which burst and crust over after 3-5 days.
 - The rash begins on the face and trunk, then spreads to other parts of the body, including the mouth.
 - The blisters clear up within one to three weeks but may leave a few scars.
 - Scarring is prominent when the lesions are scratched and/or get infected with bacteria.
 - Other symptoms: fever, headache, cold-like symptoms, vomiting, diarrhoea, secondary bacterial infection, transient neurological complications (encephalitis)

Complications

- As the blisters are very itchy, secondary bacterial infections are common from the scratching.
- *Other*: viral pneumonia, asthma exacerbations, infections can lead to cellulitis.

Non-Pharmacological Treatment

1. Children should stay away from school until all blisters have crusted over and avoid scratching.
2. Dress children in light, loose fitting clothing or pyjamas - overheating and friction from clothing can worsen itching. A cool bath can also relieve itching
3. Cold compress
4. Keep fingernails trimmed and minimise scratching
5. Rest
6. Because the mouth and throat can be affected, offer soft food and cool drinks. Avoid salty foods and citrus fruits.

Pharmacological Treatment

Children can return to school once all blisters have crusted over

1. Supportive & Symptomatic relief
 - *Fever & Pain*: Paracetamol
 - *Itchiness*: Calamine Lotion, 1st Gen Oral Antihistamines
 - *Itchiness & Inflammation*: Pinetarsol Solution

2. Antiviral Treatment
 - Valaciclovir (first line)
 - Aciclovir (IV if immunocompromised)

3. Antibiotic Treatment
 - For secondary bacterial infections



The Role of Antivirals in Chickenpox

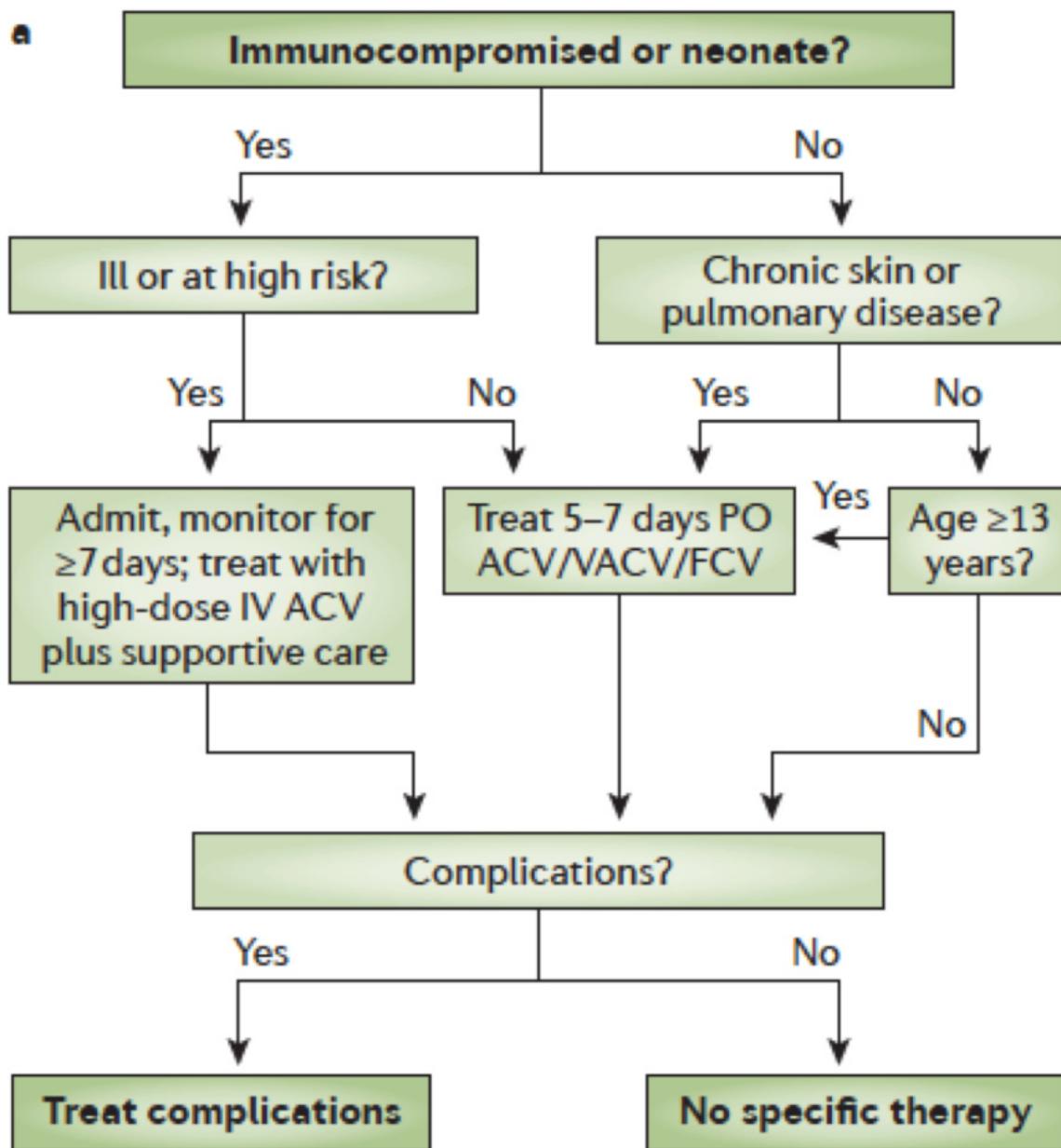
Antiviral therapy is not recommended in otherwise healthy children. However, if there is a high risk, oral antivirals should be initiated **within 24h onset of rash** — they reduce the severity and the duration of disease.

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Supportive Symptomatic Relief	[GENERAL SALE] <i>Paracetamol</i> Panadol	Anti-pyretic mild to moderate pain; pyrexia with discomfort	<ul style="list-style-type: none">Do not take with other paracetamol containing products.No more than 4 doses in 24 hours.	Skin reactions, liver damage.
	[GENERAL SALE] <i>Calamine Lotion</i> Calamine AFT	For itching This lotion contains skin-soothing properties, including zinc oxide.	<ul style="list-style-type: none">Using a clean finger or cotton swab, dab or spread calamine lotion on itchy skin areas.Note that you shouldn't use calamine lotion on or around chickenpox on your eyes.	Local skin irritation and allergic reaction.
	[GENERAL SALE] <i>Topical Tar</i> Pinetarsol Solution, Oil or Gel	For itching and inflammation Helps break the 'itch-scratch cycle'	<ul style="list-style-type: none"><i>Solution or oil:</i> add to warm bath or apply to wet skin and leave on for 2-3 minutes before rinsing<i>Gel:</i> apply to affected wet skin and leave on for 2-3 minutes before rinsing	Skin Irritation
	[PHARMACIST ONLY] <i>Oral Anti-Histamines for Sleep</i> Diphenhydramine	For itching Antihistamines taken by mouth may help prevent you or your child from scratching the rash and blisters, especially during sleep.	<ul style="list-style-type: none">Drowsiness	Dry mouth, drowsiness
Antiviral Treatment (only in high risk)	[PRESCRIPTION] <i>1st Line - Valaciclovir</i> Vaclovir	Valaciclovir is a prodrug of aciclovir and has better bioavailability, fewer doses and a longer duration of action than aciclovir.	<ul style="list-style-type: none">Start within first 24 hours of rash onset	N/V/D, abdominal pain, headache, fatigue, rash, urticaria, pruritus
	[PRESCRIPTION] <i>Alternative 1st Line - Oral Aciclovir</i>	Aciclovir stops the herpes virus growing and spreading. This controls the infection and helps your body's immune system deal with it	<ul style="list-style-type: none">Start within first 24 hours of rash onsetTransient stinging or burning	

Prevention

- Varilrix Vaccine

Vaccine	Vaccine Type	When
Varicella (Varilrix)	Live attenuated vaccine (contraindicated if neomycin anaphylaxis, immunocompromised, pregnant)	15 months



Shingles (Herpes Zoster Virus)

[DermNet Shingles](#)

Description

Shingles is caused by the reactivation of the latent varicella zoster virus due to reduction in immune control of the virus (e.g. sudden homelessness). The virus multiplies within the sensory dorsal root ganglion and then travels back down the sensory nerve to the skin, causing a painful burning vesicular rash along the affected dermatome.



Contagious or Not?

Herpes Zoster (shingles) itself is not a contagious disease and cannot be spread (you **cannot** get shingles from a person with shingles), however shingles can induce chickenpox (varicella-zoster) in those who have never had this infection before. The infection spreads through direct contact with their lesions.

Risk Factors

- Only those who have had a chicken-pox infection
- *Age (major risk factor)*: common in > 60 years old
- *Immunocompromised* (e.g. HIV, immunosuppressant medications)
- *Family History* of Herpes Zoster (shingles)
- *Gender*: Female (changes in hormone)
- *Other*: Major surgery, skin burns, cancer, emotional stress, age

Signs & Symptoms

The course of shingles can be divided into three stages:

	Duration	Symptoms
Stage 1: Prodrome (early symptoms stage)	1 to 3 days PRIOR to rash appearing	<ul style="list-style-type: none"> Before the appearance of the rash - the patient will experience prodromal tingling and burning, localised itching along affected dermatome Commonly affected dermatomes: thoracic (chest/back), ophthalmic Patient here experiences: acute neuralgia, pain, parasthesia
Stage 2: Infectious rash (acute stage)	7 to 10 days duration	<p>This is the stage where a painful unilateral vesicular rash appears along the affected dermatome, often with a sharp cut-off at the anterior and posterior midlines, lasting ~7 days.</p> <ul style="list-style-type: none"> Rash begins as erythematous macules and papules Vesicles form within 12 - 24 hours Pustules form by the third day Lesions crust over in 7-10 days Itching is a prominent and distressing symptom throughout the acute phase, persisting until all crusts have fallen off (2-3 weeks) Other: fever, hypersensitivity, malaise, encephalitis, trigeminal and cranial nerve involvement
Stage 3: Resolution (healing stage)	2 to 4 weeks duration	<ul style="list-style-type: none"> Post-herpetic neuralgia (PHN) occurs here - this is the most common complication of shingles. The condition affects nerve fibres and skin, causing burning pain that lasts long after the rash and blisters of shingles disappear. Once vesicles crust over, patient is no longer infectious

HERPES ZOSTER ASSESSMENT	
Age	<ul style="list-style-type: none"> More common in above 50-60 years If under 50-60 - indicator of autoimmune disease such as HIV
Rash	<ul style="list-style-type: none"> HZ usually presents with a rash but the prodromal pain/tingling/burning may be the first symptom but can occur prior to rash visibility. Even if the rash has not yet appeared, the patient will benefit from monitoring or treatment.
Rash Location	<ul style="list-style-type: none"> HZ typically presents unilaterally, or on just 1 side of the body. The rash also typically affects 1 dermatome, although 2-3 may be involved. HZ near the eye is associated with a high rate of significant complications such as secondary glaucoma, optic neuritis, and even acute retinal necrosis with the risk of bilateral blindness. Urgent referral is needed. HZ oticus typically presents as pain in the ear canal, possibly accompanied by an auricular vesicular rash. Complications include vertigo, tinnitus, osteonecrosis and deafness.
Rash Spread	<ul style="list-style-type: none"> HZ rashes do not usually extend much beyond the affected dermatome. If the patient complains of a widespread rash other conditions should be considered.
Rash Presentation	<ul style="list-style-type: none"> HZ rashes usually begin as erythematous papules, which progresses to pustules in 3-4 days and scabs or crusts over in 7-10 days. Antiviral treatment is most effective within a certain time limit of the rash onset or early identification and referral is crucial. Antiviral treatment should still be considered in patients presenting after 72 hours (within 7 days of rash presentation) if there is continues new vesicle formation or ocular involvement or if the patient is immunocompromised.
Pain Severity	<ul style="list-style-type: none"> Additional symptoms such as fever, headache and malaise may present 48-72 hours before the rash presents.
Medical Conditions	<ul style="list-style-type: none"> Check for immunocompromise
Pregnancy	<ul style="list-style-type: none"> HZ can harm a fetus in the early months but luckily this is rare. Shingles in late pregnancy can cause chickenpox in the fetus or newborn which can eventually develop in HZ in the infant.

Non-Pharmacological Treatment

- Wet compresses may relieve itching, avoid scratching
- Keep the rash clean and dry to reduce the risk of bacterial superinfection
- Avoid topical antibiotics** as they delay healing of the rash
- Avoid clothing made from irritating fabric (e.g wool)
- Cover/protect wound to prevent transmission: absorbent pads, white soft paraffin ointment can be used
- Stay away from immunocompromised people

Pharmacological Treatment

BPAC Shingles Treatment Guidelines

Unlike Chickenpox, the mainstay treatment of Shingles is antiviral treatment.



Initiating Antivirals in Shingles

Oral antivirals should be initiated **within 48 - 72h onset of rash** and continued for **7 - 10 days** — they reduce the severity and the duration of disease.

1. First Line - Antiviral Treatment

- *Oral Antivirals:* Valaciclovir (first line), Aciclovir (first line if immunocompromised)
- *Topical Antivirals:* Aciclovir Eye Ointment

2. Adjunct Tx - Supportive & Symptomatic Relief

Recall that two types of pain exists in Shingles: Acute Neuralgia and Post-Herpetic Neuralgia

Acute Neuralgia

- Pain Relief: Paracetamol or NSAID (first line)
- Itchiness & Drying Lesions: Calamine Lotion

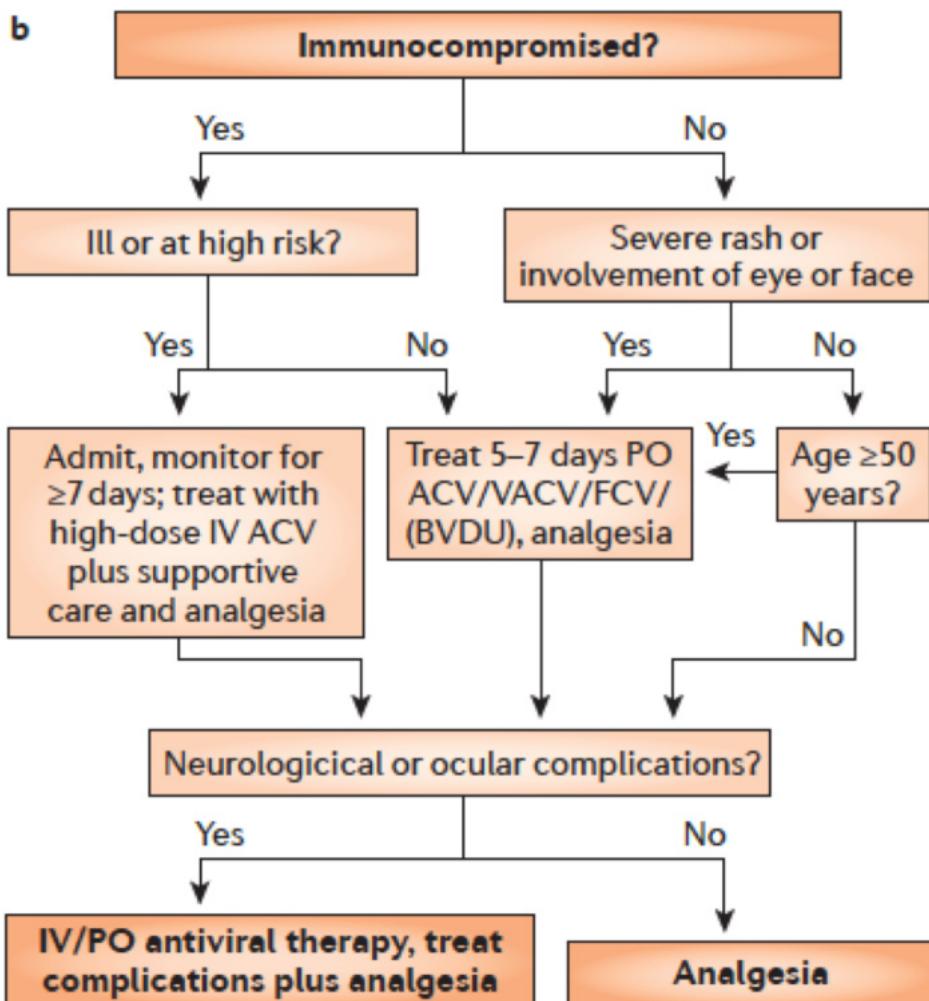
Post-Herpetic Neuralgia (Chronic Pain)

- Low - Mod: Capsaicin Cream
- Mod - Severe: TCAs (Amitriptyline), Gabapentin, Pregabalin
- Severe: Opioids (Codeine), Intrathecal Corticosteroids if all else fail

3. Complications of Shingles

- Oral Antibiotics if secondary infection (*Staphylococcus aureus* or *Streptococcus pyogenes*)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Oral Antivirals	[PRESCRIPTION] <i>1st Line - Valaciclovir</i> Valaciclovir	Valaciclovir is a prodrug of aciclovir and has better bioavailability, fewer doses and a longer duration of action than aciclovir.	<ul style="list-style-type: none"> Start within first 48-72 hours of rash onset and continue for 7 - 10 days. 	N/V/D, abdominal pain, headache, fatigue, rash, urticaria, pruritus
	[PRESCRIPTION] <i>Aciclovir</i> Aciclovir	Aciclovir stops the herpes virus growing and spreading. This controls the infection and helps your body's immune system deal with it	<ul style="list-style-type: none"> Start within first 24 hours of rash onset Transient stinging or burning 	
Topical Antivirals	[PRESCRIPTION] <i>Aciclovir Eye Ointment 3%</i> ViruPOS	Used to treat shingles with ophthalmic nerve division involvement	<ul style="list-style-type: none"> Apply 1 cm of ointment into the lower conjunctival sac 5 times daily (at 4 hourly intervals); continue treatment for at least 3 days after healing 	Local irritation and burning
Supportive & Symptomatic Relief	[GENERAL SALE] <i>Paracetamol</i> Panadol	Pain mild to moderate pain; pyrexia with discomfort	<ul style="list-style-type: none"> Do not take with other paracetamol containing products. No more than 4 doses in 24 hours. 	Skin reactions, liver damage.
	[GENERAL SALE] <i>Calamine Lotion</i> Calamine AFT	Dries lesions and relieves itchiness This lotion contains skin-soothing properties, including zinc oxide.	<ul style="list-style-type: none"> Using a clean finger or cotton swab, dab or spread calamine lotion on itchy skin areas. Note that you shouldn't use calamine lotion on or around chickenpox on your eyes. 	Local skin irritation and allergic reaction.
	[GENERAL SALE] <i>Topical Capsaicin</i> Zostrix	Nerve Pain Produces a burning and stinging feeling in order to distract the person from the nerve pain.	<ul style="list-style-type: none"> Apply regularly to the painful area on the skin - 3 to 4 times daily (not more than every 4 hours). Pain relief begins within the 1st week and increases with regular application over the next few weeks. Review after 4 to 8 weeks. Avoid contact with mucous membranes. Wait until vesicles crust over to apply. 	Local skin irritation and burning.
Antibiotics for Complications	[PRESCRIPTION] <i>Flucloxacillin or Cephalexin</i>	Penicillin antibiotics are used in the management of staph or strep secondary bacterial infections of herpes zoster.	<ul style="list-style-type: none"> Check for allergies Can take with or without food 	Hypersensitivity reactions, GI upsets, skin rashes.



Prevention

- Zostavax vaccine (**live**) recommended for **> 50y** and funded for **those aged 65y (get from GP practice)**
 - If infected, wait **12 months** before receiving vaccination — decreases severity of PHN
 - Wait **7 days** between COVID and shingles vaccine
 - Wait **4 weeks** between live vaccines OR administer on the **same day**
 - Careful in immunocompromised or pregnant individuals.

Vaccine	Vaccine Type	When
Herpes Zoster (Shingrix)	Live attenuated vaccine (contraindicated if neomycin anaphylaxis, immunocompromised, pregnant)	65 years (If infected, wait 12 months before vaccination)

Cold Sores (Herpes Simplex Labialis)

[DermNet Cold Sores](#), [Health Navigator Cold Sores](#)

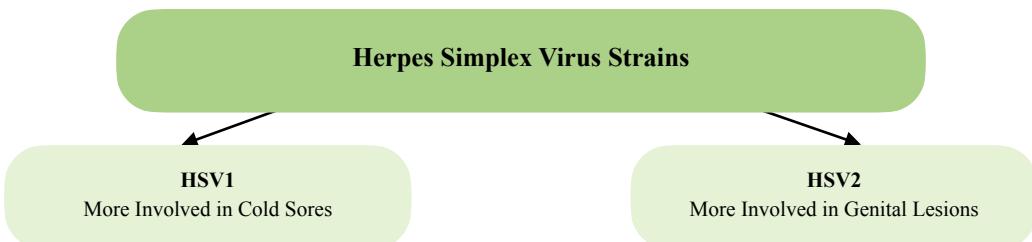
Description

Cold sores are small fluid-filled blisters that appear on the skin caused by Herpes Simplex Virus, usually on the lips, chin, cheeks, or in the nostrils. Infection by this virus is not a reflection of the person's hygiene. Around 80% of people are estimated to carry it but only 20% express symptoms.



Pathogenesis

Two strains of this virus exist. Infection is very common and easily passed from person to person by close personal contact.



Risk Factors

This virus lives in the nerve cells closest to where the cold sore appears - however it remains 'asleep' or 'dormant' until triggers can reactivate it:

- **Sun exposure**
- Viral infection
- Hormonal changes (menstruation, pregnancy, menopause)
- Immune suppression (pregnancy, immunosuppressive drugs, poor diet)



Recurrence

Recurrence is common and often in the same place. Patients tend to experience 2-3 episodes/year. However, patients who are immunocompromised and experience more severe and frequent episodes (6 or more per year) should be **referred**.

Signs & Symptoms

An infection outbreak has four stages. A patient is contagious throughout all stages until all sores are dry.

1. *Prodromal Stage*: a burning or tingling, itching sensation is often present just before the skin lesions develop around the lips (6 - 48h before skin eruption.)
2. *Lesion Appearance*: Over the next 48 hours, a number of fluid-filled blisters begin to appear, which are often painful and itchy.
3. *Lesion Crusting*: Within 24 hours, these blisters burst and form clusters leaving fluid-filled sores.
4. *Resolution*: After 8–10 days, the sores eventually dry, scab over and heal without scarring. This stage can be irritating and painful.

Red Flags: spreading of the cold sore to other parts of the face/body, eyes that become red, watery or sensitive to light, sore that does not heal within 2 weeks.

Differential Diagnosis

1. Angular Cheilitis

Cold sores and angular cheilitis are two conditions that affect the corners of the mouth. While they share some symptoms such as redness, rawness, and inflammation around the corners of the mouth, cold sores are viral (HSV) while angular cheilitis is initially used by the collection of saliva in the corners of the mouth, causing the skin to dry and crack. This can lead to secondary infections (bacteria, yeast, virus).

2. Impetigo

Impetigo has no warning symptoms, us not limited to the mouth area or associated with triggers.



Duration of Symptoms

Generally, symptoms that last longer than **14 days** are unlikely to be due to a cold sore.

Non-Pharmacological Treatment

Area Protection

1. Moisturise and protect the sore with barriers creams e.g. lip balms containing sunblock, petroleum jelly, or zinc oxide (barrier creams)
2. Avoid spicy or rough foods (chips) that may irritate the area, maintain fluid intake
3. Do not scratch or touch area, practice good hand and oral hygienes

Prevention

4. Trigger avoidance e.g. stress, fatigue, sunlight, hormonal changes, pregnancy, menstruation, low immunity, immunosuppressant drugs
5. Trigger management e.g. plenty of sleep, SPF30+ sunscreen

Non Medicated Patches (Compeed)

6. Use Compeed as soon as tingling occurs to protect the sore and prevent scabs from forming, therefore promoting faster healing.
 - The use of creams and patches together may not offer any additional benefit. Adherence of the patch following application of cream may cause difficulty.

Spread Prevention

7. Avoid skin to skin contact with others, especially those with poor immunity (e.g. kissing babies, pregnant women)
8. Do not have oral sex until your cold sore completely heals as you could give your partner genital herpes
9. Avoid sharing items with others

Pharmacological Treatment

Treatment is not necessary as this is a self-resolving condition (**in 7 -10 days**). Treatment serves to reduce the infection period by **~1 day** but does not cure the virus. Treatment should be initiated in the **prodromal phase** (tingling), and cannot be used inside mouth.

1. *First Line - Topical Antivirals*

- Aciclovir Cream, Penciclovir Cream, Idoxuridine

2. *Oral Antivirals (if recurrent infection)*

- Valaciclovir

3. *Symptomatic Relief*

- Paracetamol or Ibuprofen

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
<i>1st Line Topical Antiviral</i>	[GENERAL SALE] <i>Aciclovir 5% Cream</i> Zovirax, Viraban, Viratac	Controls Infection Stop the herpes virus growing and spreading. This controls the infection and helps your body's immune system deal with it	<ul style="list-style-type: none"> • Apply to lesions every 4 hours (5 times daily) for 5–10 days, starting at first sign of attack 	Transient stinging or burning
	[GENERAL SALE] <i>Penciclovir 1% Cream</i> Vectavir		<ul style="list-style-type: none"> • Apply to lesions every 2 hours during waking hours (at least 6 times a day) for 4 days, starting at first sign of attack 	
	[GENERAL SALE] <i>Idoxuridine + Lignocaine + benzalkonium chloride</i> Virasolve	Antiviral (Idoxuridine) For cold sore virus Antibacterial (Benzalkonium) To prevent infections Local Anaesthetic (Lignocaine) To relieve pain and itching	<ul style="list-style-type: none"> • Apply every hour on first day and then every four hours on subsequent days (for 5 days) during waking hours until the cold sore disappears. • Do not use in pregnancy 	Local irritation
<i>2nd Line Oral Antivirals</i>	[PRESCRIPTION] <i>Valaciclovir</i> Vaclovir	Controls Infection Valaciclovir is a prodrug of aciclovir and has better bioavailability, fewer doses and a longer duration of action than aciclovir.	<ul style="list-style-type: none"> • 2 g every 12 hours for one day 	N/V/D, abdominal pain, headache, fatigue, rash, urticaria, pruritus

Non-Medicated Cold Sore Patches	[GENERAL SALE] <i>Non-Medicated Hydrocolloid Cold Sore Patches</i> Compeed	Protection, Hides and Relieves Pain Non medicated patches designed to improve the aesthetic outlook of the cold sore as well as protect it from sunlight.	<ul style="list-style-type: none"> Wash hands. Ensure your skin is clean and dry. Do not use in combination with cream. 	N/A
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Patient Counselling Point for Topical Treatment of Cold Sores:

- Start in the tingling phase
- Dab the cream on gently. Don't re-use the same finger (use a cotton bud) for applying more cream as this can contaminate the medicine in the container or tube.

Common & Plantar Warts (Verruca Vulgaris)

DermNet Warts

Description

Warts are small, fleshy benign growths of the skin or mucous membrane caused by human papillomaviruses (HPV) entry through epithelial defects. They are common on weight-bearing parts of the body (e.g. sole of feet — plantar warts) and on the hands.



Pathophysiology

HPV is a group of common viruses which causes cells to grow abnormally, and over time, these abnormalities can lead to cancer. Immunisation protects against the types of HPV that cause most cervical, anal, genital, mouth, and throat cancers. The virus can be sexually transmissible, and remains latent in nerve endings causing the potential for recurrent disease.

Risk Factors

- Immunocompromise (diabetes, poor diet, certain medicines)

Differential Diagnosis

Corns & Calluses

1. Pinpoint red or black dots (papillary capillaries) are revealed when the wart is pared down. Plantar corns lack the papillary capillaries and thus instead appear as white or yellow keratinised areas of skin
2. Location of a plantar wart is not restricted to pressure sites whereas a plantar callus or corn is.
3. Corn pain is relieved upon footwear removal (not observed with warts), plantar wart pain is constant.

Signs & Symptoms

- No long term health consequences
- Small, fleshy, grainy bumps; flesh, white, pink, tan-coloured, rough to touch, tiny black dots with small clotted blood vessels. Presentation of warts in clusters may indicate a weak immune system.
- If plantar - may cause pain on walking.

Red Flags: Elderly or immunocompromised with atypical warts, anogenital warts (outside of our scope), itch, irregular outline, prone to bleeding, exhibits colour change, **diabetes**.

Non-Pharmacological Treatment

- Suffocate wart with duct tape
- Laser therapy
- Electrosurgery

Pharmacological Treatment

This is a self resolving condition (6 months - 2 years) thus treatment is not only unnecessary but also a slow process (**compliance**). It is usually recommended in immunosuppression or in presence of complications.

1. Keratolytics

- Salicylic Acid + Lactic Acid (Wart Paint, Pastes & Patches)
- Silver Nitrate

2. Other

- Cryotherapy (liquid nitrogen or OTC freezing therapy)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Keratolytics	[GENERAL SALE] <i>Salicylic Acid + Lactic Acid Solution</i> Duofilm	Soften keratin to promote shedding of the layers of the wart.	<ul style="list-style-type: none"> • Soak wart in warm water and rub with pumice stone or a file to remove the top layer of skin. • Apply solution to the wart once a day. • Protect the surrounding skin (e.g. white soft paraffin such as vaseline, plaster) • Repeat until the core of the wart is reached. 	Skin irritation, skin ulceration Warning Do not use in diabetics, over-application can cause skin ulceration.
Cryotherapy	[GENERAL SALE] <i>Dimethyl Ether and Propane</i> Wartner Wart Remover	Freeze the wart to starve it of blood supply and thus oxygen. Treatment is successful when wart turns black.	<ul style="list-style-type: none"> • Shake the bottle well, press down to freeze the metal rounded tip and apply to the wart for a few seconds. 	Skin irritation.

Prevention

- HPV Vaccine: Gardasil 9

Vaccine	Vaccine Type	When
Gardasil 9 (9-valent HPV vaccine)	Non-infectious recombinant vaccine	11 or 12 years Those beginning vaccination at >15 years will need three doses

INFLAMMATORY SKIN CONDITIONS

Introduction

Inflammatory skin conditions are the result of an inappropriate immune response (immune dysfunction) to innocuous substances (allergens) or self proteins (autoimmunity). Their pathophysiology is as follows:

1. *Immediate Response (1st Exposure)*: granulocytes (mast cells, eosinophils, neutrophils, basophils)
2. *Delayed / Acquired response (2nd Exposure)*: helper T cells

Treatment will therefore focus around dampening the immune response. Unlike the previous skin conditions we've observed, these types are not contagious given that they aren't caused by infectious agents. We will look into: acne, dermatitis, psoriasis and urticaria.

Acne (Acne Vulgaris)

[DermNet Acne](#)

Description

Acne is a very common skin condition characterised by the chronic inflammation of sebaceous glands and the increased levels of androgen - it is characterised by pimples, blackheads and whiteheads that appear on the face, neck, chest and back, more commonly in teenagers.

Pathophysiology

The pathophysiology of acne lesions can be broken down to four things:

1. *Hyperseborrhoea (Sebum Production)*
 - Androgens stimulate sebum production by sebaceous glands while estrogen decreases it.
 - Acne is thus commonly seen in the adolescent years during puberty, particularly in teenage boys.
2. *Abnormal Follicular Keratinisation*
 - Spontaneous changes in keratinocytes lead to an increased turnover and an altered keratinisation pattern. **The combination** of sebum and dead skin cells plug hair follicles.
3. *Bacterial Proliferation*
 - This results in bacterial (*Propionibacterium acnes*) entrapment, proliferation, and inflammation, producing more severe acne.
4. *Inflammatory Mediator Release*
 - Inflammation occurs in response to the bacterial interaction with keratinocytes.



Acne Is Not An Infection

Bacteria are involved in acne but they are **not the cause of acne**.

Risk Factors

Notes: Acne has no link to cleanliness level

1. *Genetic*: family history, puberty
2. *Environment*: medicines (steroids, progesterone-high OCs), smoking, stress, diet?

Signs & Symptoms

There are 4 kinds of acne ‘pimples’ that exist: closed comedones (whitehead), open comedones (blackhead), papules & pustules and cysts & nodules. Which ones are present depend on the severity of the acne.



Mild Acne

Has non-inflammatory comedones with a few inflammatory lesions mainly confined to the face.

Moderate Acne

Has many inflammatory lesions that are not confined to the face, that are sometimes painful. Mild possibility of scarring.

Severe Acne

All the above characteristics + nodule and cyst development with widespread lesions involving the upper back and chest. Scarring will usually result.



Psychological Impact

Acne can cause significant psychological impact. Acne of any severity causing psychological upset should be classed as **severe**.

Non-Pharmacological Treatment

- Avoid being in the sun, if you must - use plenty of sun protection (water-based)
- Avoid working in an oily/greasy or sweaty/hot environment
- Don’t scratch or pick at the pimples
- Don’t wear clothing that is tight and rubs on your skin - loose fitting clothes are beneficial, particularly if you have acne on your back/chest
- Don’t use oil-based or soap-based skin-care and makeup products

- Don't over-wash - clean your skin gently twice a day (morning and night) with a mild, non-oily water-based skin cleanser or anti-septic wash designed for acne to degrease it.
- Don't dry roughly - instead pat dry gently.
- You may use products such as tea tree oil, bee venom, polyphenols and other products but note that they have limited evidence of efficacy.
- Include plenty of fruits, vegetables, water in your diet and exercise regularly - high glycemic or dairy diets can exacerbate acne
- Keep hair off your face, especially the forehead

Pharmacological Treatment

[BPAC Acne Treatment Guidelines](#) [DermNet Acne Treatment](#)

Acne usually heals spontaneously. Treatment depends on the severity and aims to clear current lesions, prevent new ones and scarring - following it, improvements should be seen in **2-6 months**.

Mild Acne Treatment

First line treatment is a combination of some of the following:

- Topical Benzoyl Peroxide (+/- clindamycin)
- Topical Azelaic Acid
- Topical Salicyclic Acid (alternative to benzoyl peroxide)
- Topical Antiseptics (Hydrogen Peroxide)
- Topical Retinoids (Tretinoin, Adapalene)
- Topical Antibiotics (Erythromycin and Clindamycin)

Moderate - Severe Acne Treatment (or irresponsive to treatment mild acne)

1. Oral Contraceptives: Ginet (1st Line in Females)
2. Oral Antibiotics: Doxycycline (1st Line in Males), Erythromycin (Alternative)
3. Oral Retinoids: Isotretinoin
4. Systemic Corticosteroids

Category	Ingredients	Mechanism of Action	Counselling	Side Effects
	[GENERAL SALE, PHARMACY ONLY] <i>Benzoyl Peroxide</i> Benzac AC 2.5 % - 10% Gel, Cream or Cleanser	Gel, Cream or Cleanser • Benzoyl peroxide is a topical antimicrobial and keratolytic. • Formulation type depends on patient preference and skin type (gel - oily skin, rinse off cleanser - trunk acne)	<ul style="list-style-type: none"> • Improvement in 6 weeks. Use with oil free moisturiser if dry skin. • Avoid excessive sunlight and do not use if you have dermatitis. • <i>Washes</i> - od or bd for 30 seconds before rinsing thoroughly - good for large body areas • <i>Gels/Creams</i> - od and remove after 2 hours for three days. If tolerated, od at night and leave overnight. 	<ul style="list-style-type: none"> • Skin irritation, dry skin • May bleach fabric (linen, clothing and towels)
	[PHARMACY ONLY] <i>Azelaic Acid</i> Azclear 20% lotion	Lotion • Azelaic Acid is a topical antimicrobial and keratolytic. Less irritant than benzoyl peroxide.	<ul style="list-style-type: none"> • Apply twice daily to clean skin • Improvement in 4 weeks, use up to 6 months 	<ul style="list-style-type: none"> • Local irritation • Hyper pigmentation in darker skins. • Avoid in breast area.

Mild Acne	[GENERAL SALE] <i>Salicylic Acid</i> Clean & Clear	Cream • Softens and descales the skin which reduces comedones. • Exfoliates and unplugs pores	• Less effective than benzoyl peroxide and more skin-dryness causing.	• Skin irritation, dry skin
	[GENERAL SALE] <i>Topical Antiseptics - Hydrogen Peroxide 1%</i> Crystaderm	Cream • Hydrogen peroxide is an oxidising agent and an antiseptic.	• Wash and dry skin before applying	• May bleach fabric
	[PRESCRIPTION] <i>Topical Retinoids</i> Tretinoin or Adapalene 0.1% cream or gel (ReTrive, Differin)	Cream or Gel • Inhibit keratinocyte differentiation and proliferation. Reduce comedones and have anti-inflammatory effects. • Not suitable in patients with inflammatory acne or those with very sensitive skin	• Must apply at night as UV radiation degrades retinoids. • Clean skin with a mild soap cleanser and warm water before applying • Apply thinly one daily - build up application time to avoid adverse effects - up until you are able to leave the cream overnight. • Will worsen acne before it betters it • Apply oil free moisturiser if dry skin • Takes 3-6 months to see an effect	• Skin irritation, dryness and erythema (different to oral retinoids)
	[PRESCRIPTION] <i>Topical Antibiotics</i> Erythromycin 4% Gel Clindamycin 1% solution or lotion	Gel, Solution or Lotion • Address the involvement of the entrapped bacteria to reduce inflammation.	• Apply bd - use alongside benzoyl peroxide or topical retinoid to avoid bacterial resistance	• Skin irritation, constant dermatitis GI disturbances (rarely)
	[PRESCRIPTION] <i>Combination Product</i> Benzoyl Peroxide 5% + Clindamycin 1% Gel (Duac)	Gel, Lotion, Swab Pad, Foam • Prevents bacterial resistance	• Apply once daily at night to clean and dry skin for up to 11 weeks • Takes 4-6 weeks to see an effect	• May bleach fabrics
Moderate Severe Acne	[PRESCRIPTION] <i>1st Line in Females</i> Cyproterone (Ginet)	Tablet Improve estrogen levels which decrease androgen production	• Okay to use in PCOS • Do not use progesterone only	• Risk of VTE
	[PRESCRIPTION] <i>1st Line in Males</i> <i>Oral Antibiotics</i> Doxycycline (1st) or Erythromycin (Alternative)	Tablet • Address the involvement of the entrapped bacteria to reduce inflammation.	• Do not give to children and in pregnancy • Take dose standing up with water and food. Do not lie down for an hour after dose.	• Teeth Chelation
	[PRESCRIPTION] <i>Systemic Retinoids</i> Isotretinoin (Oratane)	Tablet Effective in all four pathogenic processes involved in acne formation.	• Exclude pregnancy up to 3 days before treatment (start treatment on day 2 or 3 of menstrual cycle), and/or conduct pregnancy test. • Contraception method at least 1 month before/after stopping and during treatment for sexually active females of child bearing age • Take with food • Protect yourself from sunlight. • Do not donate blood during treatment and for at least 1 month after discontinuing therapy. • May have decreased night vision, caution if driving or operating machinery. • Avoid wax epilation during treatment and for at least 6 months after stopping.	• Dry eyes, skin, lips, nose (use moisturising creams, ointments, eyedrops) • Monitor liver function and serum lipids 1 month after starting, then every 3 months thereafter • Pregnancy testing during treatment and 5 weeks after stopping • Monitor signs of mood changes

Psoriasis Vulgaris

[DermNet Psoriasis](#)

Description

Psoriasis is a chronic inflammatory autoimmune disorder (overactive T cells attacking healthy skin cells) that cause the rapid buildup of cells. It commonly develops in early adult life, and occurs with periods of relapse and remission, seen as scaling on the skin's surface (lesions) and red patches that are itchy and sometimes painful. The most common forms presented in a pharmacy are plaque & scalp psoriasis.



Risk Factors

1. *Genetic*: family history
2. *Environmental*: medicines (ACEI, NSAIDs, β -blockers, lithium, antimalarials), trauma, smoking, alcohol, potential triggers (menstruation, stress, sunburn)

Differential Diagnosis



Itching

Itch is **not** a predominant feature in psoriasis— consider the possibility of contact dermatitis.

Signs & Symptoms

Psoriasis has a rash characteristic of *salmon pink lesions* with *slivery white scales*, these are usually symmetrical (across scalp, elbows, knees, trunk, gluteal cleft — autoimmune), with well-defined boundaries, and dry, cracked skin, nail involvement (nail psoriasis).

Non-Pharmacological Treatment

1. *Supplements*: fish oil (good evidence), selenium, vitamin B12 (weak evidence)
2. *Sunlight (UV Light)*

Pharmacological Treatment

BPAC Psoriasis Treatment Guidelines

Pharmacy can only treat mild-moderate psoriasis. Severe forms are managed with prescription medicines.

Mild-Moderate Psoriasis (Topical Treatment)

1. First line: Calcipotriol (Vitamin D analogue), Coal tar
2. Emollients/Soap-free substitute: Cetamocragol e.g. Health E moisturiser
3. Keratolytics: Salicylic acid & Lactic acid
4. Topical Corticosteroids: Betamethasone

Severe

1. Phototherapy (UV radiation for moderate-severe psoriasis)
2. Methotrexate, Ciclosporin (very severe)
3. TNF inhibitors (if all else fails)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Vitamin D Analogues	[PRESCRIPTION] <i>Calcipotriol</i> Daivonex 0.005% Ointment	Reduces the proliferation of keratinocytes. Treated areas become less scaly but may remain red.	Apply twice daily. Avoid face Protect affected areas from exposure to excessive UV and/or sunlight.	Local skin reactions, dry skin
Keratolytics	[GENERAL SALE] <i>Coal Tar Solution</i> Coal Tar	Anti-pruritic nature and is keratoplastic – i.e. it normalises keratin growth in the skin to reduce scale build up	For chronic stable plaques, do not use during inflammatory phase May stain bed linen and jewellery. Protect affected areas from exposure to excessive UV and/or sunlight.	Skin irritation and acne-like eruptions *patient compliance as it is messy
	[UNKNOWN] <i>Salicylic acid & Lactic acid</i>	Softens keratin to allow shedding and softens thick scales.	Usually incorporated into emollients to clear scaliness.	Skin irritation.
Topical Corticosteroids	[PRESCRIPTION] <i>Betamethasone</i> Beta-Scalp Application	Corticosteroids have anti-inflammatory, immunosuppressive and antiproliferative properties.	Use for flare ups Apply od - bd for up to one month and then 2-3 days weekly for maintenance Overuse can worsen psoriasis	Thinning of the skin
Emollients	[GENERAL SALE] <i>Emollients</i> BP Health Cetomacrogol cream	Soap free substitute and moisturiser	Used to soften the skin to reduce cracking and dryness	N/A

Urticaria (Hives)

Description

Urticaria is a blanching skin rash caused by physical triggers (pressure i.e., scratching, heat, cold, chemical contact, allergies) or may be idiopathic. It is caused by histamine release by mast cell degranulation triggered by irritants.



Signs & Symptoms

Itchy wheals (hives), localised oedema of the dermis (angioedema). Watch out for **anaphylaxis** signs.

Non-Pharmacological Treatment

1. Avoid triggers (although this may sometimes be impractical)
2. Cold compress for itch

Pharmacological Treatment

1. *2nd Generation Antihistamines* (e.g. cetirizine, loratadine)
2. *Topical Corticosteroids* (e.g. hydrocortisone 1%)

Osce Points

- Educate on potential Atopic March (e.g. food allergy, asthma, eczema)
- Potential sleepiness with anti-histamines e.g. do not drive or operate heavy machinery
- Ask for signs of potential anaphylaxis e.g. throat swelling, SoB
- Seek urgent care if no improvements after 2 weeks

Eczemas (Atopic & Contact Dermatitis)

Resources

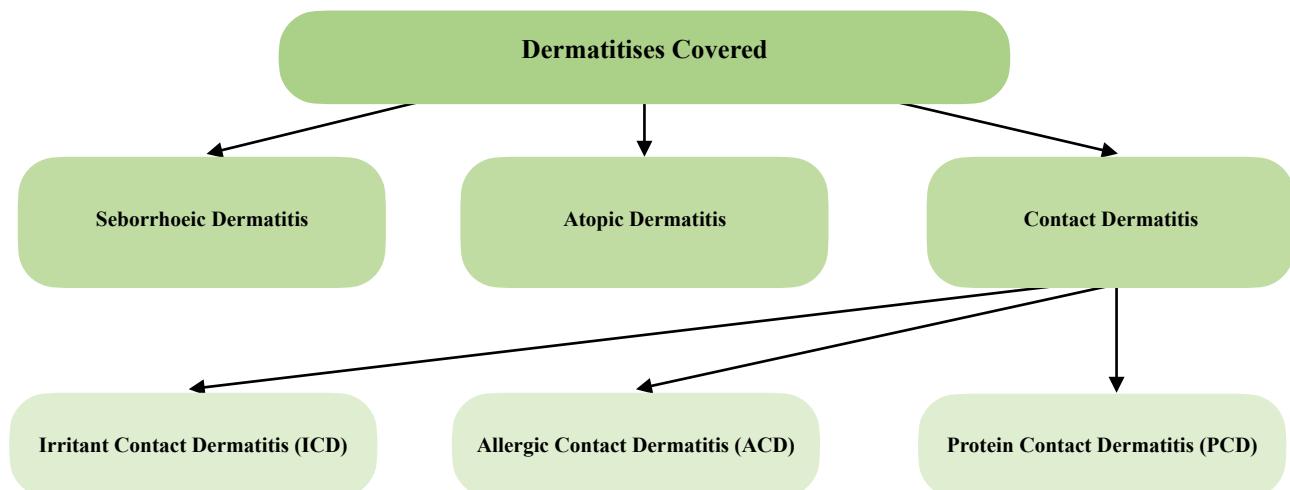
1. [Cleveland Clinic Eczemas](#)
2. [Medical News Today Atopic vs Contact](#)
3. [DermNet - Atopic Dermatitis](#)
4. [Very Well Health Atopic Dermatitis](#)
5. [DermNet Contact Dermatitis](#)
6. [Very Well Health Contact Dermatitis](#)
7. [Health Line Contact Dermatitis](#)

Description

Eczemas or Dermatitises are a group of skin conditions that cause dry and itchy patches of skin due to an overreactive immune system response to small irritants/allergens - triggers differ depending on the type of eczema (see table below) and usually help in distinguish them

Over time, eczemas weaken the skin's barrier function, resulting in poor moisture retention and protection from outside elements. Please note that they are not an autoimmune condition and they are not contagious.

There are seven different types that exist, including seborrheic dermatitis which we covered earlier in Fungal Infections. It is possible for patients to be affected by more than one type of eczema - we will cover only 2 other types: Atopic & Contact Dermatitis, please see next page for a full comparison between the two.



There are 3 sub-types of Contact Dermatitis - which are mainly determined by the allergens involved.

Types	Allergen Involved
Irritant Contact Dermatitis (ICD) e.g. Nappy Rash (Visit Chapter 13 - Paediatrics)	1. <i>Chemical</i> (detergents, solvents, bleaches, shampoo, oils) or 2. <i>Physical</i> (UV, heat, cold, damp)
Allergic Contact Dermatitis (ACD)	Small and inorganic allergens (nickel, latex)
Protein Contact Dermatitis (PCD)	Large proteins which cannot penetrate intact skin

Signs & Symptoms

Eczemas can generally appear on anywhere on your skin and presents as:

- *Dry, itchy skin* that is flaky, scaly or crusty.
- *Skin Rash* - which looks different depending on the person's skin colour. If you have a dark skin tone, an eczema rash can be purple, brown or gray. If you have a light skin tone, an eczema rash can look pink, red or purple.

Complications: can lead to secondary bacterial infections



A Note on Atopic March

Atopic March essentially describes that children with one atopic condition e.g. atopic dermatitis will generally be prone to other atopic conditions due to the fact they are predisposed to having an IgE mediated response predisposition e.g. concurrent food allergy, asthma, eczema, hayfever and so forth.

Diagnosis

- An allergy test.
- Blood tests to check for causes of the rash that might be unrelated to dermatitis.
- A skin biopsy to distinguish one type of dermatitis from another.

Differential Diagnosis

Dermatitis vs Psoriasis

Itching is **not** the predominant symptom as psoriasis is not precipitated by exposure to certain irritants or allergens

Atopic vs Contact Dermatitis

So what is the difference between Atopic and Contact Dermatitis? As we've established, AD and CD are both very common types of eczema that cause itchy, scaly and inflammatory rashes. While their symptoms are similar, the two have a few differences.

Factors	Atopic Dermatitis	Contact Dermatitis
Pathophysiology	Involves IgE	Involves sensitised T Cells
Chronicity	Usually a chronic skin condition that is a combination of hereditary, immune and environmental factors.	Acute skin condition that is not normally hereditary or chronic.
Age	Begins in childhood (and even may present first as cradle cap in infants) but often children can grow out of it (fewer affected in adulthood). Individuals are at risk of developing CD.	Usually affects adults more than children.
Atopic March	Often occurs in people with a family or personal history of asthma/hayfever.	Normally does not relate to other allergic conditions such as hayfever or asthma.

Rash Location	<p>Rash usually appears on both sides of the body and:</p> <p><i>In infants and toddlers</i> Rash appears on the face and extensor surfaces such as the back of elbows and feet</p> <p><i>In children and adolescents</i> Occurs in flexural areas such as the back of knees, front of elbows, front of ankles and the neck skin creases.</p> 	<p>CD rashes appear on the part of the person's body that has come in contact with the irritant or allergen and often have a visible border. These are usually on one side.</p> 
Causes	<p>AD flares occur from time to time and may appear out of nowhere</p> <ul style="list-style-type: none"> • Family history or personal history of eczema • Atopic march: asthma, hay fever, food allergies • Emotional triggers e.g. stress, anxiety, depression • Long hot baths or showers • Soaps or detergents • Dust • Pollen • Sweat • Dry skin • Low humidity 	<p>CD flares occur quickly after you have come into contact with an irritant or allergen. This resolves upon identification, removal and avoidance of the cause.</p> <ul style="list-style-type: none"> • Soaps, detergents, nickel (in jewellery or zippers) • Hair dyes, bleach • Poison Ivy • Shampoos • Perfumes/fragrances • Cosmetics • Exposures to chemicals at work

Non-Pharmacological Treatment

If you avoid the factor causing the reaction, the rash often clears up in 2 to 4 weeks.

1. Avoid triggers (although this may not be practical)
2. Cold compress to relieve itching
3. Prevent scratching e.g. cut nails
4. Bath everyday with warm (not hot) water and use a soap substitute to keep skin moist and clean.
5. Moisturise regularly
6. Avoid soaps
7. Keep person cool as sweating can intensify the itch — wear loose cotton clothing
8. Avoid scratchy fabrics (such as wool, silk and synthetic fabrics e.g. polyester) on skin. Use cotton bedding, underclothes.
9. Wear gloves or barrier creams when exposing hands to abrasive detergents
10. Keep room temperature as regular as possible
11. Use a humidifier if dry air is making your skin dry
12. Use unscented laundry detergent.
13. Stay hydrated and drink at least eight glasses of water each day. Water helps keep your skin moist.

Pharmacological Treatment

BPAC Managing Eczema

There are three main treatment options available to manage dermatitis.

Emollients
Preventative - Use Liberally

Topical Corticosteroids
For Flare Ups - Use Appropriately

Sedating Antihistamines
For Sleep + To Prevent Scratching

1. Emollients

- Emulsifying ointment BP, fatty cream, O/W fatty emulsion, White soft/liquid paraffin (healthE), cetomacrogol with glycerol (Boucher), Sorbolene with glycerin (Pharmacy Health)

2. Corticosteroids

- Mild, moderate, potent (please visit *Adrenal Disorders in Chapter 9 - The Endocrine System* for more information on glucocorticoids and their side effects)

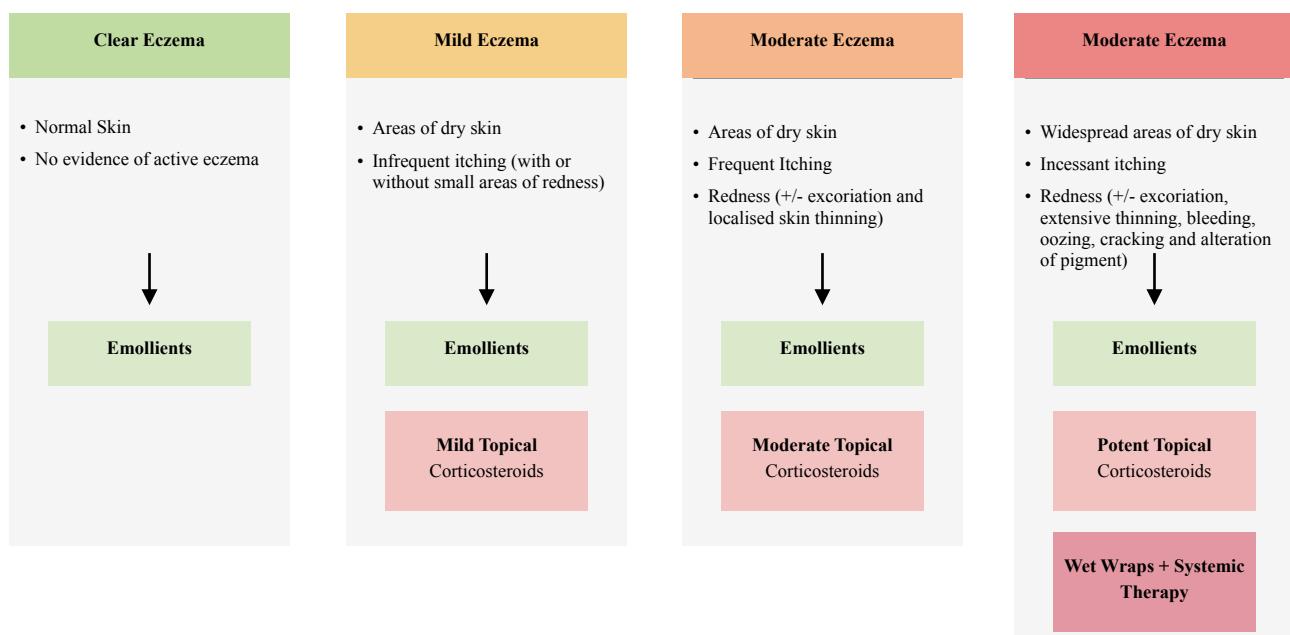
3. Sedating Antihistamines

- Chlorphenamine, Promethazine

4. Other: Antibiotics

- For secondary bacterial infections

NICE ECZEMA MANAGEMENT ALGORITHM



TOPICAL CORTICOSTEROIDS					
Strength & Ingredients		Formulations			
Potency	Active Pharmaceutical Ingredient	Lotions (large areas of skin, or hair)	Cream (large areas of skin)	Ointments (skin with thick scale)	Application (Scalp)
Mild	Hydrocortisone 0.5-1%		15g, 30g, 100g DermAid, DermAssist		
Moderate (2-25x HC)	Clobetasone butyrate 0.05%		30g Eumovate		
	Triamcinolone acetonide 0.02%		100g Aristocort	100g Aristocort	
Potent (100-150x HC)	Betamethasone dipropionate 0.05%		15g, 50g Diprosone	15g, 50g Diprosone	
	Betamethasone valerate 0.1%	50mL Betnovate	50g Beta	50g Beta	100mL Beta Scalp
	Hydrocortisone butyrate 0.1%	100mL Locoid Lotion	100g Locoid Lipocream	100g Locoid	
Very Potent (up to 600x HC)	Clobetasol propionate 0.05%		30g Dermol	30g Dermol	30mL Dermol
	Betamethasone dipropionate 0.05%			30g Diprosone OV	

Absorption: eyelids/genitals (30%) > face (7%) > armpit (4%) > forearm (1%) > palm (0.1%) > sole (0.05%)

How to Apply Corticosteroids



How To Apply

Wait **15-30 mins** between the application of corticosteroids and emollients to ensure absorption. Corticosteroids are applied **first** and can be applied to broken skin, but **not infected skin**.

Fingertip Method

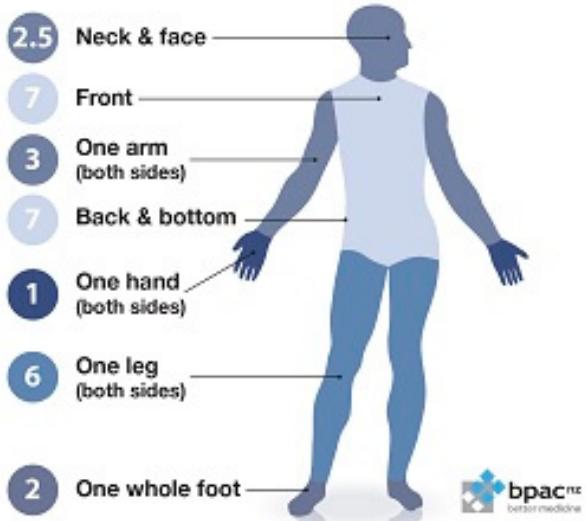
This is a method to help you find out how much of the corticosteroid you need.

- Both hands: 15-30g
- Both arms: 30-60g
- Both legs and trunk: 100g

1 fingertip unit (FTU)



Number of fingertip units to use



OSCE Points

- Cold compresses to reduce scratching
- Educates to apply emollient immediately (within a few minutes) after shower/bath and towel drying to prevent the skin from drying.
- If worsens (e.g. oozing fluid, yellow crusts, blisters, and/or red swelling), go back to GP as this may be a skin infection.
- If persists after course of hydrocortisone, go back to GP.

INSECT RELATED INFECTIONS

Introduction

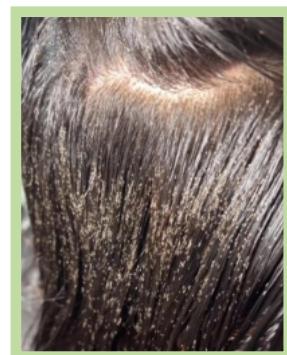
We will cover the following: Head Lice, Bites & Stings and Scabies.

Head Lice (*Pediculosis Capitis*)

[DermNet Head Lice](#)

Description

Head lice are small, wingless insects that infest the human scalp, they move at the root of hair, dropping eggs often at the back of ears and neck hairline.



Pathophysiology

Head lice can only be transmitted by head to head contact. Fleeting contact will be insufficient for lice to crawl from one head to another as they are wingless and do not fly, hop or jump. Humans are the only known host for head lice and pets are not thought to be an intermediary.

Once transmitted lice begin to reproduce; the adult louse lives for approximately 1 month. Throughout this time, the female louse lays several eggs at the base of a hair shaft each night. Eggs hatch after 7 to 10 days, leaving the egg case attached to the hair shaft (known as a nit).

Risk Factors

Most prevalent in children 4 - 11 years old.

Signs & Symptoms

Itching caused by the glue that is secreted by females, in which an allergic response of the scalp to the saliva of the lice and can take weeks to develop.

Complications: secondary bacterial infection, dermatitis.

Diagnosis

- Detection combing to locate the lice and egg droppings

Non-Pharmacological Treatment

There are 3 non-pharmacological approaches we can use when it comes to head lice:

1. Combing e.g. dry/wet
2. Prevention
3. Other Methods e.g. shaving hair, essential oils

Combing

Combing out lice with a plastic detection (fine toothed) comb is an effective way to get rid of this unwanted hitchhiker. Eggs are firmly attached to the hair shaft and need to be manually removed regardless of the treatment used. Two types of combing exist:

Dry combing (~5 minutes)

1. Straighten and untangle the dry hair using an ordinary comb.
2. Once the hair moves freely, switch to a detection comb. Starting from the back of the head, comb the from the scalp down to the end of the hair.
3. After each stroke, examine the comb for live lice.
4. Continue to comb all the hair in sections until the whole head has been combed.

Wet combing (~10-30 minutes - more time consuming)

Applying conditioner or water to the hair before combing loosens the eggs from the hair shaft and makes combing easier.

1. Wash the hair with a normal shampoo.
2. Apply hair conditioner.
3. Repeat steps 1–4 as for dry combing.
4. Rinse out the conditioner.



Wet Combing Alone?

This method can, by itself, be an effective treatment (38-52%), as long as it is done carefully and properly every 2 or 3 days, until no head lice are found for 10 days in a row. This can take 3 to 4 weeks to achieve. However, it is recommended to be used as an adjunct to pharmacological treatment.

Prevention (Reducing Transmission)

Preventing transmission in a house contaminated with a head lice infection:

- Advise your child's school so that teachers can check other children for lice
- Clean combs after using on an affected person's hair; soak in hot water (at least 55°C for 5-10 min)
- Advise children not to share combs or brushes - everyone in the family should have their own combs
- Keep long hair tied up
- Avoid sharing frequently worn hats, hair accessories or sports headgear
- Avoid taking closely grouped photos with anyone who has an active infestation, e.g. selfies with friends
- Cut nails to prevent scratching

Other Methods

- Shaving hair or exposing hair to hot dryer for 30 minutes a day for 1 month
- Natural and herbal treatments e.g. essential oils (Moov range)

Pharmacological Treatment

BPAC Dimethicone Lotion for Head Lice

Treat all members of the family. Inform daycare/school.

1. *First Line - Physical Agents (Suffocant):* Dimethicone Lotion
2. *Second Line:* Permethrin Cream (due to issues with resistance)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Physical Agents	[GENERAL SALE] <i>Suffocants</i> Dimethicone 4% lotion	Kills and suffocates adult and nymph head lice. Lice become immobilised within a minute of exposure. First line treatment as lice cannot develop resistance to it.	• See below for how to use	Transient stinging or burning
Neurological Agents	[GENERAL SALE] <i>Permethrin 5% cream (for crab/pubic lice and scabies)</i> Lyderm	Kills lice	Apply 5% cream over whole body, allow to dry naturally and wash off after 12 hours or after leaving on overnight; repeat application after 7 days	

How to Use Dimeticone

- The lotion is applied to **dry** hair, ensuring that it is spread evenly from the hair root to the tips (ensure to use the product generously and a normal comb can be used to ensure even distribution)
- Pay attention to areas behind the ears and neck.
- Prevent treatment from getting into eyes by holding a towel against them
- Comb wet hair 20 minutes after putting on the lotion, then use a fine toothed lice comb to remove damaged/dead lice or any remaining eggs.
- Leave on for 8 hours/overnight (seal hair in a shower cap or towel) before washing out with shampoo in the morning
- Do not use hair dryers as treatment may be heat sensitive
- Avoid using a conditioner immediately after treatment
- 24 -48 hours after treatment, check hair for live lice or eggs with the conditioner-wet hair comb method and comb them all out until none can be found.
- **Repeat treatment 7 days after first treatment and repeat steps above**
- If treatment fails to clear the lice, a repeated two further applications can be used.

Insect Bites & Stings

Description

- Bite: A bite from mosquito, ticks, fleas, midges, spiders, bed bugs, sand flies, ants
- Sting: Venous stings from wasps, bees, spiders



Signs & Symptoms

- Bite: Red, itchy bump, smooth surface, blister, spreading of localised reactions.
- Sting: Redness and swelling of the area, pain, stinger may still be in wound, spreading of localised reaction, anaphylaxis.
- *Systemic symptoms may occur within minutes of the bite/sting.*

Non-Pharmacological Treatment

1. Cold compress to cool area
2. If pets are the cause - address fleas, ect...
3. **Insect repellent (prevention)**

Pharmacological Treatment

1. *Local Anaesthetic/Antiseptic*: Lignocaine hydrochloride anhydrous + cetrimide (SOOV bite gel)
2. *Aluminium Sulphate*: Stingose
3. *Topical corticosteroid for inflammation*: Hydrocortisone 1%
4. *Oral Antihistamines* e.g. loratadine, cetirizine
5. *Analgesics* e.g. paracetamol

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Pain, itching, inflammation relief	[GENERAL SALE] <i>Aluminium Sulfate</i> Stingose	Relieves pain and itching Aluminium sulphate breaks down the toxins in bites and stings	<ul style="list-style-type: none">• Works best if applied as soon as possible after the sting or bite occurs.• Children must at least be 12 months old	Local irritation, stinging
	[GENERAL SALE, PHARMACY ONLY] <i>Lignocaine hydrochloride anhydrous + centrimide</i> SOOV Bite Gel or Cream	Anaesthetic + Disinfectant This cooling gel helps take away the urge to scratch your skin after an insect bite or plant sting	<ul style="list-style-type: none">• Dab on to affected skin up to 4 times daily.• Children must at least be 2 years old	

Scabies

[DermNet Scabies](#)

Description

Scabies is a contagious, intensely itchy rash caused by a parasitic mite (*Sarcoptes scabiei*) that burrows in the skin surface, affecting trunk and limbs, but **not the scalp**. Scabies rash is a hypersensitivity reaction that arises several weeks **after** the initial infestation. The itching of scabies results from your body's allergic reaction to the mites, their eggs and their waste.



Signs & Symptoms

- Tiny red bumps, intensely itchy especially at *night* (as skin is warmer). Burrows are tiny grey irregular tracts. Typically affects the interdigital web spaces and sides of fingers.

Risk Factors

- Mites from animals

Non-Pharmacological Treatment

- Wash items that may contain the mite in hot water - if washing is not possible, seal in an air tight bag for a week
- Cut nails to prevent scratching
- **Treat all contacts**
- Scabies mites generally do not survive more than 2 to 3 days away from human skin. Children and adults usually can return to child care, school, or work **the day after treatment**.

Pharmacological Treatment



Note

The itch will improve after the first week of treatment but may stay for several weeks after all mites have been killed.

1. Insecticides:

- Permethrin (5% Lynderm cream, **A-Scabies lotion**)
- Crotamiton 10% cream (Itch-Soothe)

2. Oral Anti-Parasitic

- Ivermectin Tablet (if topical therapy is ineffective or inappropriate)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Insecticide	[GENERAL SALE] Permethrin A-Scabies Lotion, Lyderm 5% cream	Kills mites.	Apply 5% preparation over whole body and wash off after 8–12 hours; repeat application after 7 days	Pruritus, erythema, stinging

OSCE Points

- Manufacturer recommends application to the body but to exclude head and neck. However, application should be extended to the **scalp, neck, face, and ears**.
- Repeat application after 7 days.
- Larger patients may require up to 2 x 30 g packs for adequate treatment.
- Can put clothes/towels in air tight bag if can't wash with hot water.
- Explain cream treated the infection and not the itchiness.
- Treatment kills the mites but does not treat the itch and rash - this may last up to several weeks (see GP if this doesn't go away)
- Can give antihistamines for itch
- Can return to school/work a day after treatment

TRAUMA-RELATED SKIN CONDITIONS

Introduction

We will cover the following: corns, calluses, sunburns, wounds, cuts, burns and grazes.

Corns & Calluses

Description

Corns and calluses are caused by response to friction and pressure to the bony prominences of the feet. Repetitive injury results in the skin trying to protect itself from blistering. The basal epidermal cells (keratinocytes) increase in number resulting in thicker prickle cell layer and thicker stratum corneum.



Symptoms

Corn: painful, inflamed

Callus: painless, flattened, yellow-white, thickened skin

Non-Pharmacological Treatment

To get rid of corns and calluses faster, you can use a pumice stone, which will gently remove the top layers of skin. Soak your feet in warm water first, to soften the corn or callus. Dry your feet, then rub the pumice stone gently over the corn or callus. Afterward, moisturize the area with skin lotion.

1. Well-fitting, comfortable, flat footwear
2. Avoid pressure on hand and feet
3. Protective corn plaster or cushion

Pharmacological Treatment (same as warts and verrucas)

Self-resolving

1. *Keratolytics:* Salicylic Acid

Sunburn

Description

Sun exposure causes melanocytes to increase melanin production, causing darkening of the skin. Melanin absorbs UVA and UVB to protect the skin from damage. However, melanin synthesis is slow, therefore skin damage may occur. Sunburn is an inflammatory response where inflammatory mediators cause capillary vasodilation and increased capillary permeability.



Symptoms

Blistering, peeling skin, erythema/severe redness, pain, oedema, tenderness, irritation, chills and fever

Prevention



Medicine-Induced Photosensitivity

Many medications can make you sensitive to sunlight - the below advice is extremely important if this applies to your patient!

1. Slip. Slop. Slap
2. Apply sunscreen 20-30 minutes before exposure, and then every 2 hours
3. Minimise sun exposure, avoid highest sun exposure times (11am-3pm)
4. Wear protective clothing, hats, sunglasses

Pharmacological Treatment

1. *Topical corticosteroid*: hydrocortisone 1%
2. *Topical cream with cooling effect*: aloe vera gel, calamine, moisturisers
3. *Systemic analgesia*

Wound Care

Description

Wounds are a result of a physical injury to the skin or mucous membrane, and have multiple causes; accidental, surgical, underlying diseases, wound development from some skin conditions.

Causes of Wounds

Origin	Cause
Superficial	Scratching, rubbing, picking
Incised	Surgical interventions
Crush	Heavy blow delivered with a cutting tool e.g. sword
Lacerated	Sharp-edged object results in fragments of tissue being torn away
Stab	Pointed tool or weapon
Contused	Injury to tissue under the skin's surface e.g. traffic accidents
Secondary	Primary diseases e.g. diabetic ulcers, pressure ulcers
Other	Bullet wounds, bite wounds, poisoned wounds

Wound Classification

Wound Trauma		
Open Wound	The tissues are traumatised in which there is a break in the skin or mucous membrane	
Closed Wound	The tissues are traumatised without a break in the skin or mucous membrane	
Degree of Contamination		
Clean wounds	Uninfected wounds (primarily closed wounds) with minimal inflammation.	Infection Rate: 1-5%
Clean-contaminated wound	Surgical wounds in which usually sterile areas have been entered i.e. respiratory, alimentary, genital, or urinary tract.	Infection Rate: 8-10%
Contaminated wounds	Open, fresh, accidental wounds with evidence of inflammation	Infection Rate: 15-20%
Dirty / infected wounds	Old, accidental wounds containing dead tissue, and evidence of infection such as pus or drainage	Infected
Wound Thickness		
Superficial	Involves only the <u>epidermis</u> and upper <u>dermis</u>	
Partial Thickness	Involves skin loss up to the <u>lower dermis</u>	
Full Thickness	Involves skin and <u>subcutaneous</u> tissue	
Deep and Complicated	Involves penetration into natural cavities, organ or tissue.	
Wound Complexity		
Simple	Affecting only one organ or tissue e.g. stab wounds	
Combined	Affecting multiple organs and/or tissue e.g. gunshot wounds	
Wound Age		
Fresh	Up to 8 hours from time of injury	
Old	After 8 hours from time of injury	
Wound Healing Time		

Acute	Wounds that heal in the predictable phases as listed under 'Wound Healing' and have excellent potential to recover within 6 weeks (e.g. traumatic wounds, minor wounds, surgical wounds, ect...). Note: all wounds can become chronic off the treatment if incorrect or inappropriate
Chronic	Wounds that do not heal within 3 months and often last for several years. They do not follow the orderly set of stages and in a predictable amount of time. (e.g often stuck in the inflammatory stage for too long). Please see chronic wound management
Degree of Bacterial Load	
Presence of bacteria creates a burden on the wound as they compete for the limited supply of oxygen and nutrients. While achieving sterility is not possible, achieving a manageable bioburden is.	
Wound Contamination	The presence of bacteria within a wound without any host reaction.
Wound Colonisation	The presence of bacteria within the wound which do multiply or initiate a host reaction.
Critical Colonisation	Multiplication of bacteria causing a delay in wound healing, usually associated with an exacerbation of pain not previously reported but still with no overt host reaction.
Wound Infection	The deposition and multiplication of bacteria in tissue with an associated host reaction. Signs of infection: blood tests, increased tiredness, exudate, odour, ect...

Factors Influencing Wounds Healing

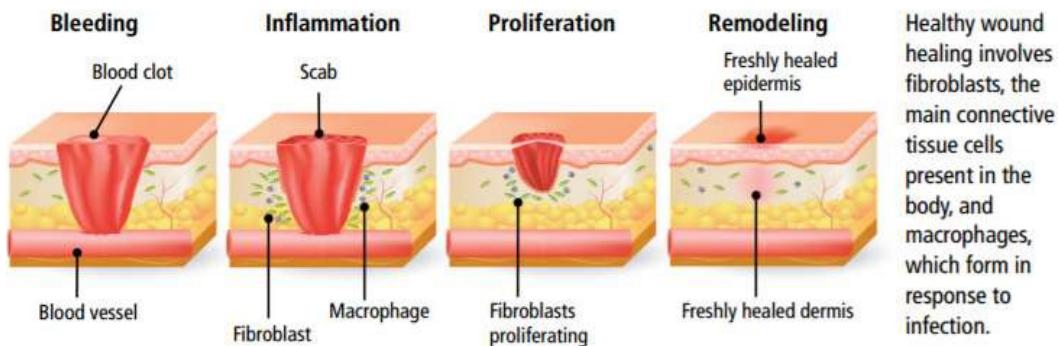
Refer if no sign of improvement after **2-4 weeks**

Local	Systematic
Location e.g. peri-anal (consistent faecal contamination)	Patient Behaviours (smoking, alcoholism)
Foreign body (high degree of contamination)	Poor nutrition or lack of hydration
Poor Blood Circulation	Medicines (NSAIDs, steroids)
Oedema	Chronic diseases (diabetes)
Trauma	Immunosuppression
Size	Type of wound
	Age of patient
	Poor hygiene
	Infection

Wound Healing

In adults, optimal wound healing should involve four continuous and overlapping phases: haemostasis, inflammation, proliferation, and remodelling.

Stage	Description
Haemostasis (Immediate)	Purpose: immediate clotting to prevent more blood leaking out from the body Haemostasis is the process of stopping the blood flow via clotting and it happens immediately, from the first moment of injury. The capillaries contract and thrombose to facilitate this process (haemostasis/clean-up phase)
Inflammatory (0 - 3 days)	Purpose: inflammation controls bleeding, prevents infection and forms scabs (3 - 5 days) After the injury, the injured blood vessels start to leak exudate (made of water, salt, and protein) which causes localised swelling. The exudate allows healing, moves repair cells to the wound site, nourishes the cells and flushes out debris (pathogens). This phase is a natural and crucial part of the wound healing process and is only problematic if prolonged or excessive. Symptoms: Erythema, heat, oedema, discomfort, functional disturbance
Proliferative (3 - 24 days)	Purpose: contract wound edges and reduce overall edges. This is when the wound is rebuilt with new tissue made up of collagen and extracellular matrix. Granulation tissue fills wound which resurfaces the injury by epithelialisation (epidermis layer epithelialisation occurs with cell migrating from wound edges and undamaged hair follicles). A new network of blood vessels must be constructed so that the granulation tissue can be healthy and receive sufficient oxygen and nutrients (angiogenesis (new capillary growth)) In healthy stages of wound healing, granulation tissue is pink or red and uneven in texture. Healthy granulation tissue does not bleed easily. Dark granulation tissue can be a sign of infection, ischemia, or poor perfusion. Epithelialisation happens faster when wounds are kept moist and hydrated. Generally, when occlusive or semi-occlusive dressings are applied within 48 hours after injury, they will maintain correct tissue humidity to optimize epithelialisation.
Remodelling (24 days - 2 years)	Purpose: increase the tensile strength of laid down collagen The collagen that is laid down during the proliferative phase is disorganised making the wound quite thick. During remodelling, the collagen is converted and remodelled into a more organised structure along lines of stress, thereby increasing the tensile strength of the healing tissues. However, even with cross-linking, healed wound areas continue to be weaker than uninjured skin, healed tissue regains about 80% of its original strength. Therefore it will be more likely to be injured again in the future. Symptoms: Skin is lighter in colour due to fewer melanocytes, reduced blood supply and scar size



Complications of Wound Healing

- Haemorrhage:** persistent bleeding that is greater than the normal escape of blood from a wound
- Hematoma:** localised collection of blood underneath the skin that appears as a reddish blue swelling
- Infection:** all wounds, acute or chronic, are considered contaminated as bacteria exists as part of the body's natural flora. However this does not mean infection or sepsis will develop.

Chronic Wound Management

Wound Beds	Colour	Description
Necrotic	Black	Blackened areas are made up of dead tissue. • Debridement is needed to allow healing
Sloughy	Yellow/Grey	Slough is formed by the accumulation of dead cells within the wound exudate. • Desloughing is needed to encourage wound bed cells to grow and heal. • A moist healing environment is needed to prevent wound hardening and facilitate removal.
Granulating	Red	Granulation tissue is red, moist, healthy tissue that fills the wound cavity to allow for epithelialisation. It has an uneven surface due to the development of new capillaries. • Exudate management, a moist environment, protection and support is needed to encourage and maximise healing.
Epithelialising	Pink	Epithelialising tissue is translucent, wrinkles when pressed, has a matte finish, and minimal exudate. • Hydration and protection is needed especially against shear friction and support against any further damage.

Goal of Treatment

- Wounds heal fastest if they are attended to as quickly as possible after an injury. It is important to dress or close the wound using appropriate methods to keep it free from infection.
- We also need to create an optimal wound healing environment by producing a well vascularised, stable wound bed with little or no exudate — Create an environment conducive to healing
- Examine the whole patient. Treat the cause and patient-centred concerns as well as ‘the hole’ in the patient

Non-Pharmacological Treatment

The mainstay for non-necrotic wounds is to promote moist wound healing as this:

- Speeds up angiogenesis and epithelialisation
- Reduce risk of wound infection
- Reduce pain by protecting nerve endings
- Prevents tissue dehydration and cell death
- Enhances autolytic debridement
- Reduces scar tissue

Multiple factors contribute to the decision of appropriate wound treatment: [TIME]

TIME	Description
Tissue (viability)	Is the tissue non-viable or deficient in the wound? If there is a presence of non-viable tissue, necrosis, slough or eschar, then the next step is to determine the best type of debridement that would be the most appropriate for this patient (enzymatic, autolytic, sharps, surgical, mechanical, etc.)
Infection/Inflammation	Are there any visible signs or symptoms of infection? Does the wound appear "angry"? The presence of infection, whether local or systemic, creates a barrier to healing. Presence of edema to the wound bed and/or peri-wound also creates a barrier.
Moisture (balance)	Does the wound appear too dry or too wet? Moisture balance is essential for positive outcomes in wound healing, resulting in the practice of what we now call moist wound healing. So, if the wound is too dry or desiccated, add moisture. If the wound is too moist or macerated—as evidenced by presence of maceration to wound edges and peri-wound—then choose dressings that are designed for moderate to heavy drainage.
Edge of wound (advancement)	Are the wound edges non-advancing or undermined? As we evaluate all aspects of local and systemic barriers, identifying the progress, or lack thereof, of wound edges is another critical point in wound management. When healthy, wound edges appear attached, open, and migrating or contracting. When wounds are improperly dressed, typically in cases with tunneling and undermining,

Wound Care Dressings

Burns & Grawes

Non-Adherent Layer

- Primary Contact Layer: prevents secondary absorbent dressing from adhering to wound and allow exudate to pass through.
- Protective layer coated with an ointment



Atrauman (5cm x 5cm)

- Wear for up to **3 days**
- Can be cut to size
- Not made with natural rubber latex

Waterproof Dressing

- Non absorbent dressing that provides waterproof protection
- Extremely flexible, ideal for contoured areas



Hydrofilm (5cm x 7cm)

- Wear for up to **7 days**
- Shower proof
- Not made with natural rubber latex

Skin Tears

Skin Closures

- Adhesive wound closure strips
- Tran coloured to be less visible



Omnistrops (6cm x 7.6cm)

- Wear for up to **7 days**
- Not made with natural rubber latex

Cuts & Grawes

Adhesive Absorbent Pad

- Adhesive border with a central absorbent pad
- Breathable
- Non-waterproof



Cosmopor E (small, large)

- Wear up to **3 days**
- Not made with natural rubber latex

Waterproof Dressing

- Adhesive film border + central absorbent pad
- Breathable
- Waterproof



Hydrofilm Plus (small, large)

- Wear up to **7 days**
- Shower Proof
- Not made with natural rubber latex

Absorbent Pad

- Designed to be minimally adhered to a wound
- Absorbs fluid produced by wound
- Requires tape/bandage to secure to the body



Non-Adherent Pad (small, large)

- Wear up to **7 days**
- Not made with natural rubber latex

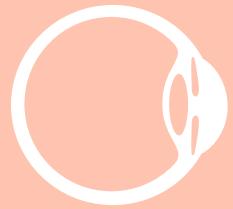
Type of Wound Dressing	Uses	Common Brands
Primary Contact Layer	Prevent secondary dressing from adhering to wound and allow exudate to pass through.	Silicon or knitted fabrics, Atrauman, Atrauman Silicone, Cuticell, Paranet
Film Dressing	Used in later stages of wound healing as a protective layer to prevent new fragile skin from being damaged. Provides fixation to secure non adherent dressing, support epithelialisation	Hydrofilm, Tegaderm, Opsite
Island Dressing	Absorbent centre, support epithelialisation	Primapore Cosmopor E, Opsite Post-op, Hydrofilm Plus
Hydrogel Sheet	Apply to dry or low exuding wounds. Feel cooling when applied and donate moistures. Softens necrotic tissue. Secure with Peha-Haft.	Hydrosorb
Super Absorbent Dressing	Manage heavy exudate.	Zetuvit Plus
Securement	Fixation	Peha-haft, Fixomull
Skin Closure Strips	Skin closure	Omnistrip, Steristrip

Cuts, Burns & Grawes

Pharmacological Treatment

- *Topical Antiseptics:* Crystaderm, Betadine
- *Dressing*

Note: Avoid betadine in pregnancy and breastfeeding



CHAPTER 2

THE OCULAR SYSTEM

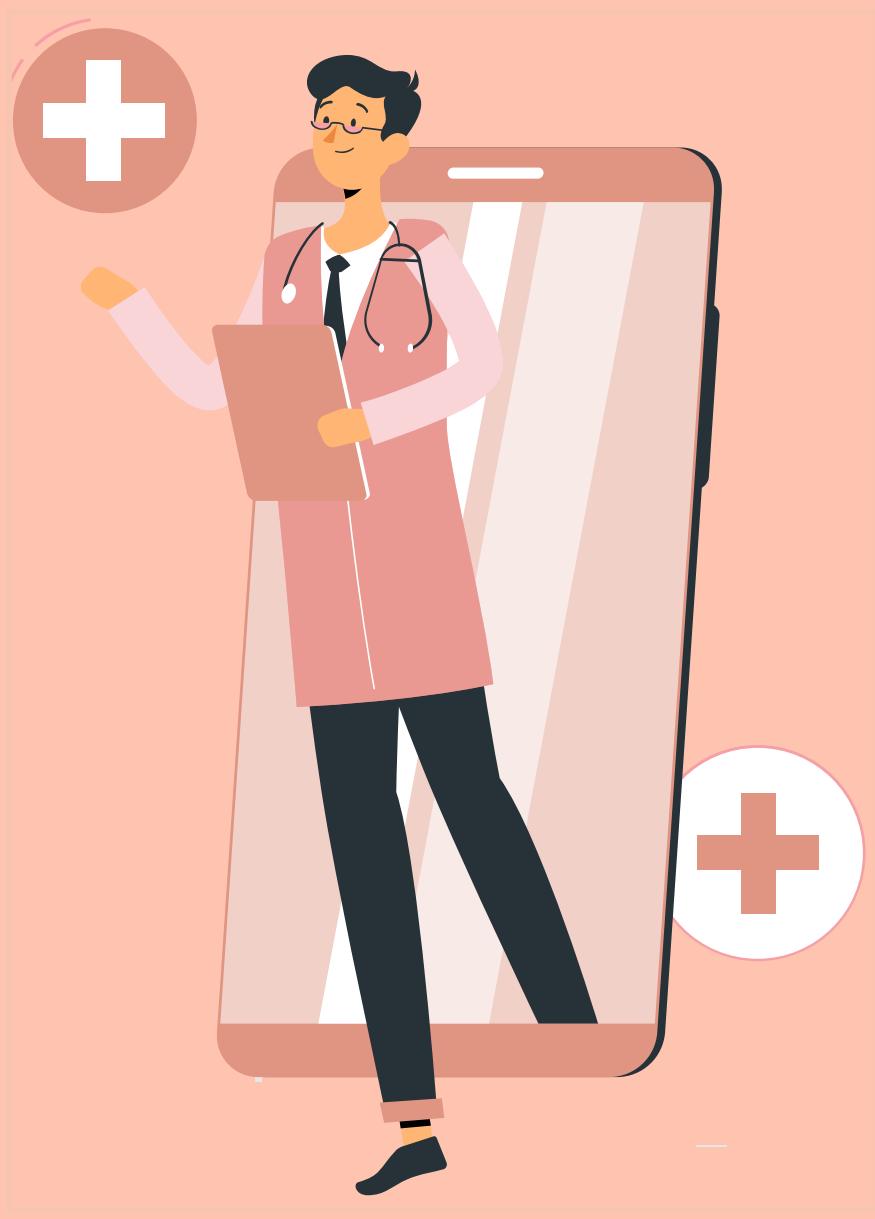


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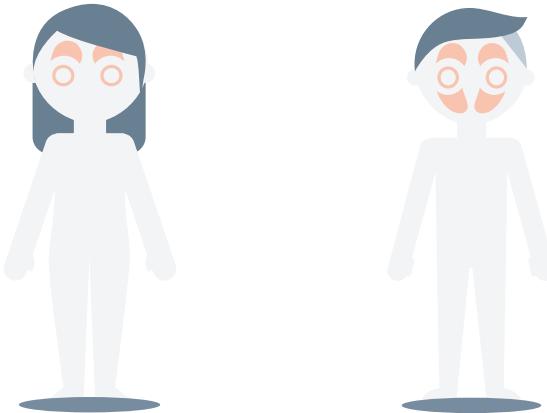
Chapter 2

The Ocular System

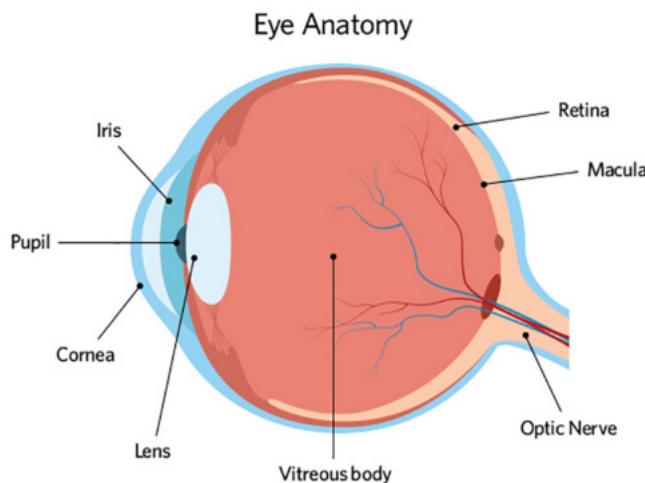
General Overview of Eye Anatomy

Eye Anatomy

Your eye is a slightly asymmetrical globe, about an inch in diameter, that is composed of the following:



4. *Iris*: the coloured part of the eye
5. *Cornea*: a clear dome over the iris
6. *Pupil*: the black circular opening in the iris that allows the penetration of light
7. *Sclera*: the white of your eye
8. *Conjunctiva*: a thin layer of tissue that covers the entire front of your eye, except for the cornea



A Note on Eye Drops

Calculations

1. To calculate *drops to mls* use this ratio: 1 ml = 12 drops and thus 5ml = 60 drops.

Expiry Dates

2. Most eye drops expire after 1 month after being opened - a monthly supply will be needed in that case.

Formulation Choice

3. Eye drops may be preferred over ointments due to the less potential for discomfort and irritation

Application Steps

How to Use Eye Drops Properly

(Using a mirror or having someone else give you the eyedrops may make this procedure easier.)

SafeMedication
Your Trusted Source of Drug Information

- 1 Wash your hands thoroughly with soap and water.
- 2 Check the dropper tip to make sure that it is not chipped or cracked.
- 3 Avoid touching the dropper tip against your eye or anything else — eyedrops and droppers must be kept clean.
- 4 While tilting your head back, pull down the lower lid of your eye with your index finger to form a pocket.
- 5 Hold the dropper (tip down) with the other hand, as close to the eye as possible without touching it.
- 6 Brace the remaining fingers of that hand against your face.
- 7 While looking up, gently squeeze the dropper so that a single drop falls into the pocket made by the lower eyelid. Remove your index finger from the lower eyelid.
- 8 Close your eye for 2 to 3 minutes and tip your head down as though looking at the floor. Try not to blink or squeeze your eyelids.
- 9 Place a finger on the tear duct and apply gentle pressure.
- 10 Wipe any excess liquid from your face with a tissue.
- 11 If you are to use more than one drop in the same eye, wait at least 5 minutes before instilling the next drop.
- 12 Replace and tighten the cap on the dropper bottle. Do not wipe or rinse the dropper tip.
- 13 Wash your hands to remove any medication.

Remember

- Follow directions carefully
- Do not miss doses
- Use the exact number of drops recommended
- Store medications out of reach of children

INFECTIONS, EYELID & OTHER OCULAR CONDITIONS

Introduction

We will cover: conjunctivitis, styes, dry eyes, glaucoma and blepharitis.

Conjunctivitis

[Health Navigator Conjunctivitis](#)

Description

Conjunctivitis is the inflammation of the whites of the eyes (conjunctiva), causing the eye to appear red/pink.



Pathophysiology

Many different kinds of pathogens//allergens are implicated:

- *Bacterial*: Staphs, Streps (pneumoniae), Moraxella, Haemophilus Influenzae
- *Viral*: Adenoviruses
- *Allergic*: Allergens (pollen)

Risk Factors

- Contact lenses
- Allergen exposure
- Exposure to infected persons (bacterial/viral)
- Makeup, swimming in public pools.



Contact Lens Wearer?

Patients who are contact lens wearer should generally be **automatically referred** if they present with ocular conditions - this is mainly because they are at a higher risk of serious complications. An important counselling point is that contacts should not be worn during treatment and **for 48 hours** afterwards.

Signs & Symptoms

SIGNS & SYMPTOMS - CONJUNCTIVITIS						
	Causes	Discharge	Appearance	Lid Swelling	Discomfort	Other symptoms
Mild non-specific conjunctivitis	Tiredness, irritants, rubbing eyes	-	Both eyes are slightly red	-	None or mild irritation	-
Bacterial Conjunctivitis	Bacterial Infection	Purulent, sticky lashes, green/yellow	Generalised and diffuse redness. Both eyes red, but one day or so before the other	Moderate	Gritty feeling (feels like sand is in there)	Sometimes with cough and cold symptoms e.g. Sore throat, cold-like, malaise
Viral Conjunctivitis	Viral Infection (highly contagious)	Clear, watery	(One or) both red	Minimal		
Allergic Conjunctivitis	Allergens (usually pollen)	Clear, watery or clear, sticky	Both red, generalised redness especially in the fornices	Mod-severe	Intense itching	Family history of atopy e.g. rhinitis Sneezing, dripping nose, congestion, dark patches below eyes
Blepharitis	Allergens (usually pollen)	Frothy tears	One or both red	Minimal	Mild irritation	-

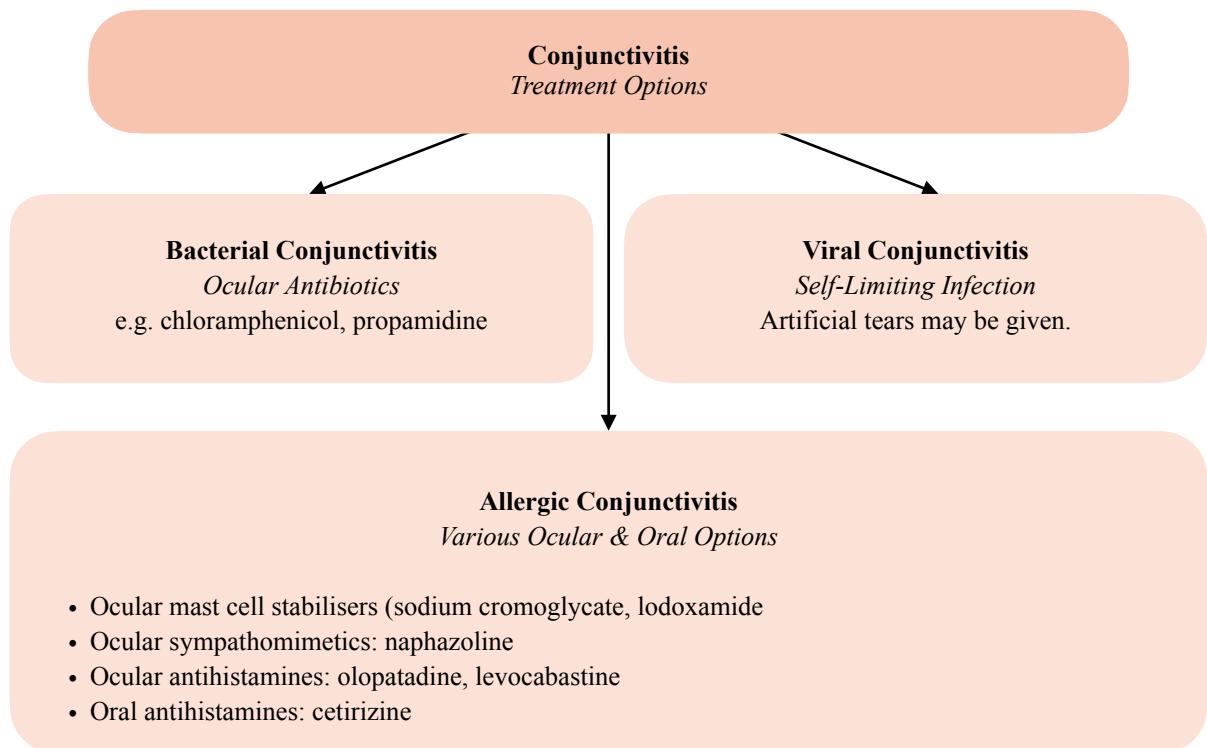
Red Flags: pain, photophobia (sensitivity to light) and reduce visual acuity, babies 3 months old (may have acquired infection from birth), bulging eyes (due to overactive thyroid), blurred vision

Non-Pharmacological Treatment

NON PHARMACOLOGICAL TREATMENT - CONJUNCTIVITIS	
Bacterial Conjunctivitis <i>Self limiting (2-5 days)</i>	<p>Symptom Relief</p> <ul style="list-style-type: none"> • Bathe eyelids with lukewarm water to remove any discharge • Use disposal tissues that you can throw away immediately to wipe eyes e.g. makeup removal pads or a clean facecloth • Start from the end of the eye closest to the nose then towards the outside until eye is clean • You can use artificial tears eye drops for relief from any discomfort. • Antibiotic eye drops are not usually necessary for mild infection. <p>Preventing Spread</p> <ul style="list-style-type: none"> • Wash hands regularly • Avoid touching/rubbing your eyes. • Avoid sharing pillows and towels (changing them frequently) <p>A Note On Breastfeeding Mothers</p> <ul style="list-style-type: none"> • Antibiotic eye drops given for bacterial conjunctivitis are contraindicated in breastfeeding mothers - thus non pharmacological practices are the mainstay • For babies who have contracted bacterial conjunctivitis from their mothers - squeezing breast milk into the affected eye is a common remedy given that it would contain antibodies.
Viral Conjunctivitis <i>Self resolving</i>	<p>Symptom Relief</p> <ul style="list-style-type: none"> • Lubricating eye drops for symptomatic relief • Clean away secretions from eyelids and lashes with cotton wool soaked in water. • Start from the end of the eye closest to the nose then towards the outside until eye is clean <p>Preventing Spread</p> <ul style="list-style-type: none"> • Viral conjunctivitis is very contagious, so take care to wash your hands, use separate towels and avoid touching your face or eyes (until redness/weeping resolves usually in 10-12 days)
Allergic Conjunctivitis <i>Trigger Avoidance</i>	<p>Trigger Avoidance</p> <ul style="list-style-type: none"> • Avoid allergen

Pharmacological Treatment

BPAC Conjunctivitis Antibiotic Guidelines



Bacterial Conjunctivitis

- Note that antibiotics are not required unless patient has severe symptoms - they can speed recovery and reduce relapse
- Also note that ocular antibiotics such as chloramphenicol are okay for use in pregnancy **but not breastfeeding.**

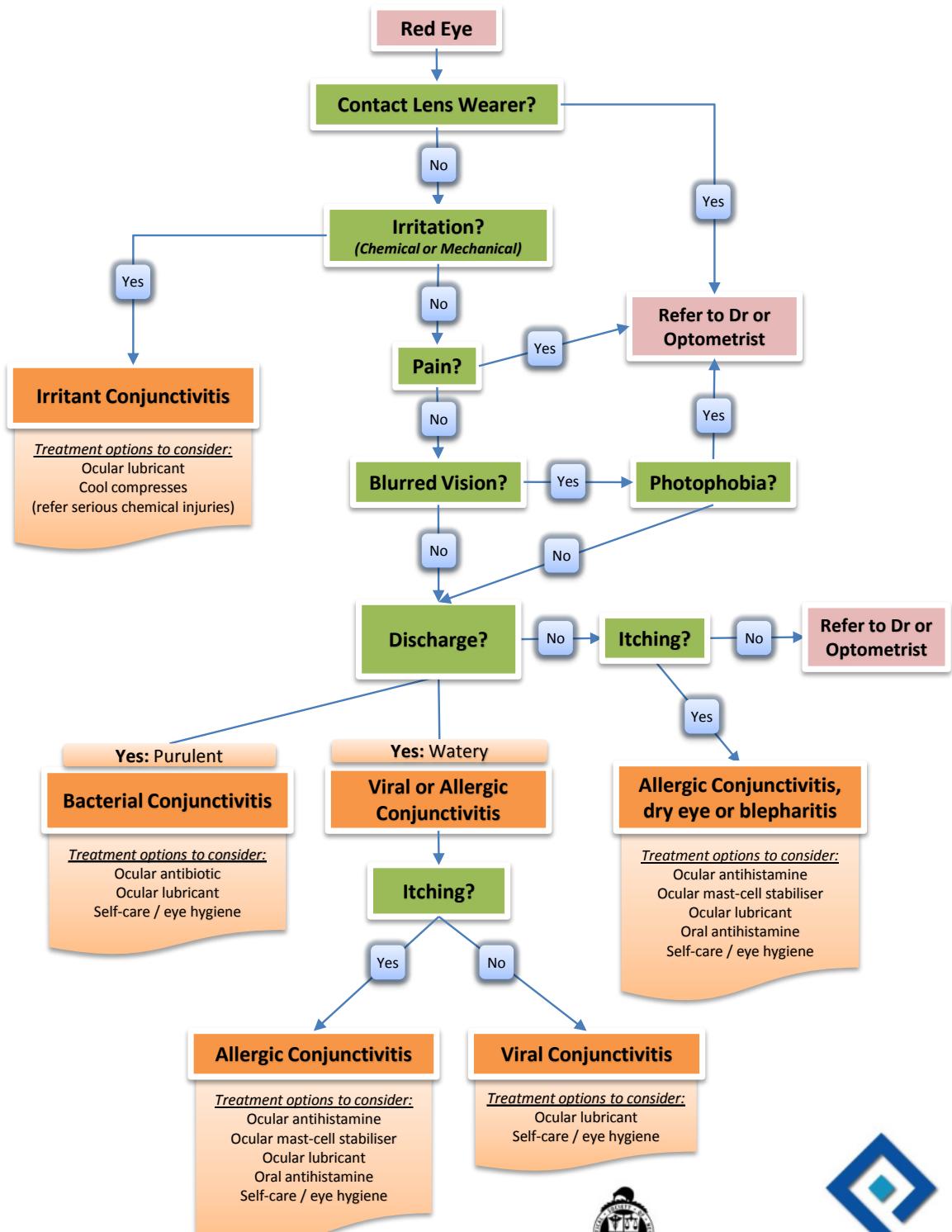
Indication	Category	Ingredients	Counselling	Side Effects
Bacterial Conjunctivitis	Topical Antibiotics	[PHARMACIST ONLY] <i>Chloramphenicol</i> Chlorafast 0.5% Eye Drops	<ul style="list-style-type: none"> Wash hands before treatment Instil 1-2 drop(s) into the affected eye(s) every 2-6 h for 2-3 days. Close eyes for 1-3 minutes to let absorb (but do not blink) Wait 5 minutes until applying another drop Store in refrigerator. Once opened, no need to store in refrigerator. Continue treatment for 48 hours after eye appears normal. To minimise contamination, avoid the tip from contacting the surface of the eye. Max 5 days treatment. Discard 28 days after opening Do not use for children under the age of 2 If the patient wears contact lenses — avoid wearing of contacts during duration of treatment and 24 hours after treatment 	
		[PHARMACIST ONLY] <i>Chloramphenicol</i> Chloramphenicol 1% Eye Ointment	<ul style="list-style-type: none"> Apply a thin ribbon (1-1.5cm) of ointment to the lower eyelid of the affected eye(s) every 3 h for up to 5 days. Continue treatment for 48 h after symptoms resolve. Apply ointment at night and eye drops during the day if using both. Discard 28 days after opening. This product does not need to be stored in the fridge Do not use for children under the age of 2 If the patient wears contact lenses — avoid wearing of contacts during duration of treatment and 24 hours after treatment 	Transient burning and stinging Avoid if family history of blood dyscrasias.
	Topical Antiseptics	[PHARMACY ONLY] <i>Propamidine</i> Brolene	<ul style="list-style-type: none"> 1-2 drops into the eye(s) 4 times daily for up to 1 week 	Eye pain and irritation
		[PRESCRIPTION] <i>Soframycin</i> Framycetin Eye/Ear Drops	<ul style="list-style-type: none"> 2 drops every 1-2 hours reducing to 2-3 drops 3 times daily until after symptoms have cleared. 	Eye pain and irritation
		[PRESCRIPTION] <i>Fusidic Acid</i> Fusidic Acid Eye Gel 1%	<ul style="list-style-type: none"> 1 drop twice daily until 48 hours after symptoms have cleared. 	Eye pain and irritation
	Lubricating Drops	[GENERAL SALE] <i>Dextran + Hypromellose</i> Poly-Tears (Discard 6 months after opening)	Blurred vision, dry eye, ocular discomfort or irritation	1-2 drops in the eye(s) as required
		[GENERAL SALE] <i>Sodium Hyaluronate</i> Hylo-fresh	Blurred vision, dry eye, ocular discomfort or irritation	
Allergic Conjunctivitis	Prophylaxis Ocular Mast Cell Stabilisers	[PHARMACY ONLY] <i>Sodium Cromoglicate 2%</i> Rexacrom, Cromo-Fresh	<ul style="list-style-type: none"> 1-2 drops in each eye 4 times daily. May take 3-6 weeks to reach full effect 	Transient burning and stinging
		[PHARMACY ONLY] <i>Lodoxamide</i> Lomide 0.1%	<ul style="list-style-type: none"> 1 drop in the eye(s) 4 times daily; improvement of symptoms may require treatment for up to 4 weeks 	Burning, stinging, itching, blurred vision, tear production disturbance, ocular discomfort
	Sympathomimetics	[PHARMACY ONLY] <i>Naphazoline</i> Clear Eyes, Naphcon Forte	<ul style="list-style-type: none"> 1-2 drops every 3-4 hours as required, up to four times daily. Do not use for longer than 3-5 days. 	Tansient irritation, blurred vision, mild mydriasis

	Ocular Anti Histamines	<p>[PRESCRIPTION] <i>Olopatadine</i></p> <p>0.1% Eye Drops</p> <p>[PHARMACY ONLY] <i>Levocabastine</i></p> <p>0.05% Eye Drops Livostin</p>	<ul style="list-style-type: none"> 1–2 drops in the eye(s) twice daily 	Local irritation
	Oral Anti Histamines	<p>[GENERAL SALE, PHARMACY ONLY] <i>Loratadine, Fexofenadine Cetirizine</i></p>	<ul style="list-style-type: none"> PRN 	Drowsiness

OSCE Points — Bacterial Conjunctivitis

- Check for any sensitivity to light
- Use for 48 hours after eye appears normal or a max of 7 days
- Instil every 2-6 hours while awake
- ADR: mild stinging or burning, blurry vision
- Contacts wearer?
- Wait 5 minutes before administering a second drop
- Store at room temp (doesn't have to be in fridge)
- Discard after 28 days

Algorithm for the Differential Diagnosis and Treatment of CONJUNCTIVITIS



December 2009



Styes (Hordeola)

[Styes Health Navigator](#)

Description

A stye is a bacterial infection (mostly staphylococcus) involving one or more of the small glands near the base of your eyelashes.



Signs & Symptom

External Style: red, painful lump near the edge of your eyelid that may look like a boil or a pimple, often filled with pus. Red, pain, swollen lids (localised), watery eyes. Self resolving in a few days (shrink or resolve/burst)

Internal Style: As above but more painful and less obvious lesion

Red Flags: pain, photophobia, and reduced visual acuity

Non-Pharmacological Treatment

1. Warm compress 5-10 minutes 3-5 times a day
2. Eyelid cleaning (1 part baby shampoo to 10 parts water)
3. Eyelid Massage
4. Lubricating eyedrops to provide comfort, but this will not treat the problem.
5. Make-up and contact lens wear can make blepharitis worse and irritate your eyes more.

Pharmacological Treatment

1. Antibiotic ointment (not usually needed)

Dry Eye

Health Navigator Dry Eyes

Description

Dry eye is a frequent cause of eye irritation that causes varying degrees of discomfort, leading patients to seek medical care. The condition is chronic with no cure. However, without treatment it can lead to ocular surface damage.

Pathophysiology

Dry eyes occur when the tear film has a dysfunction resulting in inadequate lubrication of the eyes.



Risk Factors

Prolonged screen time, air conditioning, ageing, medicines/medical conditions (diuretics, anticholinergics, isotretinoin, HRT, androgen antagonists, cardiac arrhythmic drugs, β -blockers, SSRIs)

Signs & Symptoms

Burning, irritating, discomfort, watery eyes

Complications: Corneal ulceration if persistent/untreated dry eyes

Red flags: Dry eye in children is rare and therefore should be referred



Dry Eyes Are....Wet?

As odd as it may sound, dry eyes can actually present as constantly and excessively watery eyes that flood down a person's cheeks - so much so that patients often tend to present to the pharmacy not in fact realising they have 'dry eye'. This is known as **reflex tearing** and it is how the body can sometimes try to counter-interact the dryness.

Non-Pharmacological Treatment

Hydration, stop smoking, less screen time

Pharmacological Treatment

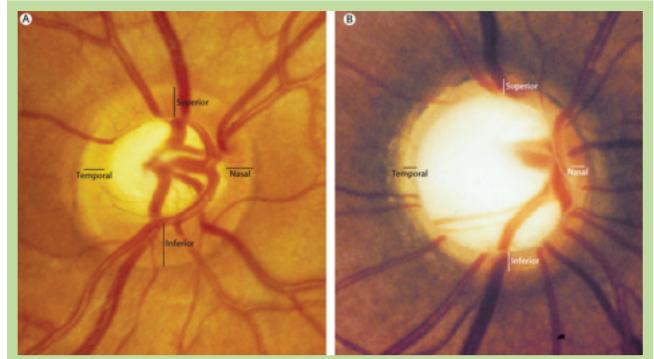
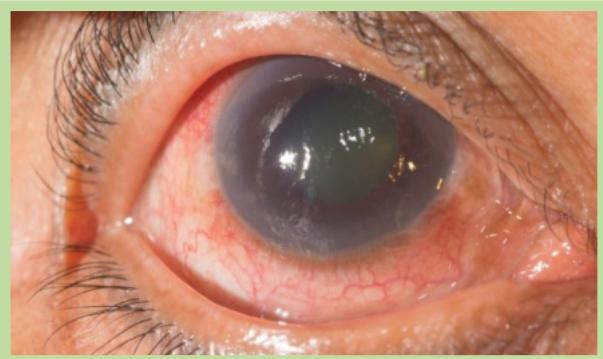
1. Artificial tears
2. Lubricating eye drops and gels

Category	Ingredients	Side Effects	Counselling
Artificial Tears	[GENERAL SALE] <i>Dextran + Hypromellose</i> Poly-Tears (Discard 6 months after opening)	Blurred vision, dry eye, ocular discomfort or irritation	1–2 drops in the eye(s) as required
Lubricating Ocular formulations	[GENERAL SALE] <i>Carbomer (polyacrylic acid)</i> Poly Gel	Transient irritation and blurred vision	1 drop in the eye(s) 3–4 times daily or as required
	[GENERAL SALE] <i>Macrogol-400 + Propylene glycol</i> Systane (Discard 6 months after opening)	Blurred vision, dry eye, ocular discomfort or irritation	
	[GENERAL SALE] <i>Sodium Hyaluronate</i> Hylo-fresh	Blurred vision, dry eye, ocular discomfort or irritation	

Glaucoma

Description

Glaucoma is a group of eye conditions that damage the optic nerve, often caused by an abnormally high pressure in your eye. It is one of the leading causes of blindness for people over the age of 60.



Risk Factors

- Older than 40 years
- Family history
- Short-sighted or long-sighted
- History of migraine or Raynaud's syndrome
- Use cortisone or steroids
- Previous eye injury

Signs & Symptoms

Open-angle glaucoma

- Patchy blind spots in your side (peripheral) or central vision, frequently in both eyes
- Tunnel vision in the advanced stages

Acute angle-closure glaucoma

- Severe headache
- Eye pain
- Nausea and vomiting
- Blurred vision
- Halos around lights
- Eye redness

Prevention

- *Frequent eye checks:* every 1-2 years if at-risk, else every 5 years (every year if >60)

Non-Pharmacological Treatment

- Stop smoking, exercise regularly, balanced diet
- Laser treatment, surgery

Pharmacological Treatment

If you have the condition, you'll generally need treatment for the rest of your life.

Category	Ingredients	Mechanism of Action	Side Effects	Counselling
Prostaglandin Analogues	[PRESCRIPTION] <i>Bimatoprost (Lumigan) Latanoprost (Hysite) Travoprost (Travatan)</i>	Increased drainage of fluid out of eye	<ul style="list-style-type: none"> • Changes in eye colour • Increased growth and thickness of eyelashes • Sunken appearance to eyes • Red eyes and irritation 	
β-Blockers	[PRESCRIPTION] <i>Timolol</i>	Reduce production of fluid in the eye	<ul style="list-style-type: none"> • Shortness of breath • Reduced exercise tolerance • Vivid dreams • Impotence • Irritated eyes 	Not suitable if you have breathing problems such as asthma or COPD .
Alpha-Agonist	[PRESCRIPTION] <i>Brimonidine (Arrow, Alphagan)</i>	Reduce fluid production and increase outflow		
Carbonic anhydrase II inhibitor	[PRESCRIPTION] <i>Brinzolamide (Atopt) Dorzolamide (Trusopt)</i>	Reduce fluid production	<ul style="list-style-type: none"> • Dry mouth and dry eyes • Red eye • Stinging sensation to the eye • Metallic taste • Headache 	
Miotic	[PRESCRIPTION] <i>Pilocarpine (Pilopt)</i>	Acts by opening the inefficient drainage channels in the trabecular meshwork.		

Blepharitis

[Health Navigator Blepharitis](#)

Description

Blepharitis is the inflammation of the eyelids. It usually affects both eyes (bilateral) along the edges of the eyelids and commonly occurs when tiny oil glands near the base of the eyelashes become clogged, causing irritation and redness.

Risk Factors

Several diseases and conditions can cause blepharitis — however they all have one common consequence: excess presence of bacteria on the eyelids and eyelash bases.

Signs & Symptoms

Dry, sore, irritated eyes and eyelids, discharge looks like frothy tears

Red Flags: pain, photophobia, and reduced visual acuity

Non-Pharmacological Treatment

1. Self-care measures, such as washing your eyes and using warm compresses
2. Make-up and contact lens wear can make blepharitis worse and irritate your eyes more.
3. A diet with increased omega-3 fatty acids may also be recommended.

Pharmacological Treatment

Generally:

1. Topical eye antibiotic ointment (chloramphenicol or fucithalmic) followed by
2. Lid cleaning with baby shampoo using a cotton bud (1:10 dilution with water twice daily)
3. Eye lubricants if eyes are dry (artificial tears)

Alternative

4. Antibiotic + Steroid Ointment may be prescribed in severe cases
5. Oral Antibiotics: Doxycycline or Azithromycin
6. Lipiflow and/or intense pulsed light (IPL) therapy.



CHAPTER 3

THE AUDITORY SYSTEM



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Chapter 3

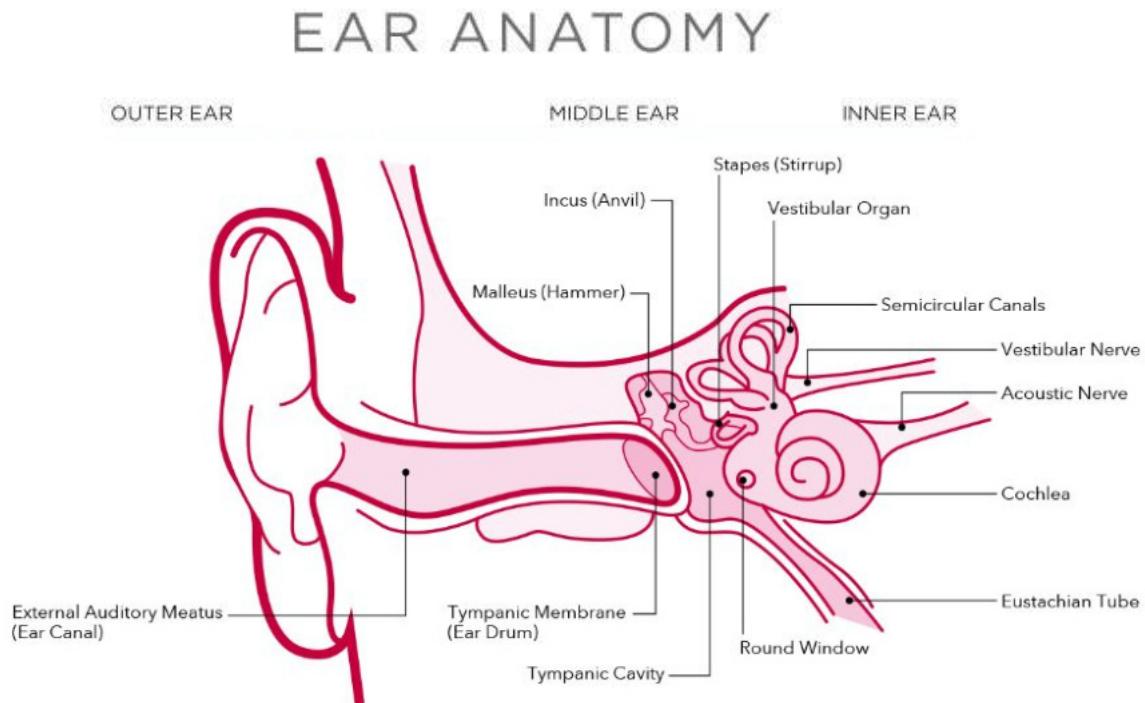
The Auditory System

General Overview of Ear Anatomy

Ear Anatomy

The ear is the organ of hearing and balance. The outer ear consists of skin and cartilage, called the auricle/pinna and the ear canal. The ear drum, or tympanic membrane, is a thin membrane that separates the outer ear from the middle ear. The middle ear is an air-filled chamber containing three small bones called ossicles.

The parts of the ear include:



Cotton Buds

In any ear condition, always **avoid cotton buds** as this cause trauma to the ear

WAX & INFECTION-RELATED AUDITORY CONDITIONS

Introduction

We will cover: earwax, otitis externa and otitis media.

Earwax (Cerumen) Impaction

Description

Ear wax (cerumen) is formed from cerumen-producing glands in the EAM as well as other components, such as dead skin, sweat and oil, and helps to protect the ear from water and infection. Wax buildup occurs when your ear makes earwax faster than your body can remove it.

Risk Factors

Trauma to the ear (recent cleaning of ear), medicines

Diagnosis

Otoscopic examination should reveal excessive wax

Signs & Symptoms

Gradual hearing loss, ear discomfort, itching, tinnitus, dizziness

Red flags: dizziness and tinnitus (inner ear—referral), vertigo, true pain, fever (middle ear infection?)

Pharmacological Treatment

1. *Ear Drops* (softens ear wax): Waxsol, Cerumol, EarClear

Category	Ingredients	Patient Counselling	Side Effects
Ear Drops	[GENERAL SALE] <i>Docusate Sodium</i> Waxsol	Instil drops into ear canal, until it is full, each night for 2 nights	<i>Rarely</i> inflammation stinging, irritation
	[GENERAL SALE] <i>Arachis oil (peanut oil) + chlorobutanol</i> Cerumol	Instil 5 drops into ear canal and leave for 10-30 minutes, repeating if necessary or instil 2-3 drops into the ear canal twice daily for 3-4 days	
	[GENERAL SALE] <i>Carbamide Peroxide</i> EarClear	N/A	

Otitis Externa (Swimmer's Ear)

[Otitis Externa DermNet](#)

Description

Otitis Externa refers to generalised inflammation of the external auditory meatus (EAM) / outer ear canal. It usually occurs as an acute episode but may become chronic (> 3 months) in children.

Risk Factors

The causes of otitis externa can be split into two main groups:

Type of Otitis Externa	Description	Symptoms
Infectious Otitis Externa	<p>Infectious Otitis Externa e.g. Bacterial (90%) or Fungal Infections (10%) or Mixed Bacteria/Fungal</p> <p>Bacterial infections are the most common cause of otitis externa. This is because, as with all skin, the EAM has a normal bacterial flora that remains free from infection until skin defences fail or become damaged. Some common causes that allow the overgrowth of bacteria in the external ear include:</p> <ol style="list-style-type: none">1. <i>Water</i> remaining in the ear after swimming creates a moist environment for bacteria to grow.2. <i>Local trauma</i> to the ear canal allowing bacteria to enter damaged skin, e.g. insertion of objects such as cotton buds, matchsticks and fingers to relieve itching or impacted earwax	<p>Bacterial Otitis Externa (90% of cases)</p> <ul style="list-style-type: none">• <i>Generally</i>: significant swelling, severe discomfort requiring oral analgesics, accompanied by fever• <i>Discharge</i>: scant, white mucus - bloody in chronic infections <p>Fungal Otitis Externa (10% of cases)</p> <ul style="list-style-type: none">• <i>Generally</i>: no symptoms, but can have some discomfort, tinnitus and pruritis usually very itchy• <i>Discharge</i>: fluffy white to off-white discharge, but may be black, grey, bluish-green or yellow
Non-Infectious Otitis Externa	<p>Non Infectious Dermatological Conditions e.g. seborrhoeic, allergic or contact dermatitis, psoriasis, acne</p> <ul style="list-style-type: none">• Primary skin disorders are often precipitants of infectious otitis externa, but they can also be the sole cause of otitis externa.• Can be accompanied by secondary bacterial infections	<p>Atopic Dermatitis</p> <ul style="list-style-type: none">• Very itchy <p>Psoriasis</p> <ul style="list-style-type: none">• Can be itchy <p>Allergic Contact Dermatitis</p> <ul style="list-style-type: none">• Sudden onset <p>Irritant Contact Dermatitis</p> <ul style="list-style-type: none">• Slower onset than ACD

Aetiology: Primary bacterial infection or contact sensitivity

Local causes: Trauma or discharge from the middle ear

General causes: and skin infections.

Signs & Symptoms

It is characterised by redness, swelling, scaling and thickening of the canal skin lining and is accompanied by varying degrees of discomfort, itch, deafness and discharge.

Differential Diagnosis

Symptoms	Diagnosis
Ear Symptom	<ul style="list-style-type: none">• Itch/Irritation/Pain = Otitis Externa• Pain when pressing tragus or moving pinna = Otitis Externa• Pain in mastoid area = Otitis media, mastoiditis (refer)
Discharge	<ul style="list-style-type: none">• If discharge present is not mucopurulent = Otitis externa (EAM has no mucous glands)• Mucopurulent = Otitis Media (refer)
Systemic Symptoms	<ul style="list-style-type: none">• Otitis externa and all forms of dermatitis = do not present with any systemic symptoms• Systemic symptoms e.g. fever, cold symptoms, loss of appetite = Otitis media• Dizziness, tinnitus, deafness = inner ear problems (refer)

Non-Pharmacological Treatment

1. Wear a tight fitting swimming cap to prevent water entering the ear canal
2. Keep ears dry after swimming or showering.
3. Patients prone to recurrences may use acidifying drops after swimming or water sports
4. Avoid poking and scratching the skin of the external auditory canal as damage to the skin and removal of earwax makes the canal more vulnerable to infection



Can I Go Back to Swimming?

Patients with otitis externa should preferably abstain from water sports for at least **7-10 days**.

Pharmacological Treatment

[NZF Acetic Acid for Swimmer's Ear](#), [BPAC Otitis Externa Antibiotic Guidelines](#)

1. *Antifungal + Antibacterial Ear Drops:* Vosol (acetic acid)
2. *Analgesic + Local Anaesthetic:* Auralgan
3. *Pain Relief:* Paracetamol or Ibuprofen
4. *Anti-infective ear drops:* chloramphenicol ear drops
5. *Secondary Bacterial Infection:* Flucloxacillin is the drug of choice

Category	Ingredients	Patient Counselling	Side Effects
Antifungal & Antibacterial	[GENERAL SALE] Acetic Acid 2% Vosol	Preventative use: place 2 drops in each ear morning and evening - especially if trying to prevent infection in unaffected ear. Treatment of infection: carefully remove all wax and debris before placing 5 drops in the infected ear 3-4 times daily.	Transient stinging or burning
Analgesic + Local anaesthetic	[GENERAL SALE] Phenazone + Benzocaine Auralgan Ear Drops	Repeat every 1 to 2 hours until pain is relieved	

Acute Otitis Media (OM)

[BPAC \(Be Quick\) Otitis Media](#)

Description

Otitis media is the inflammation or infection of the middle ear, caused by bacteria or virus. Common in children up to the age of 4 years, following a common cold and results from the virus spreading to the middle ear.

Signs & Symptoms

- Ear pain, impaired hearing, systemic symptoms (fever), purulent discharge if ear drum perforates
- *In children:* lack of attention, irritability, sleep and balance disturbances

Diagnosis

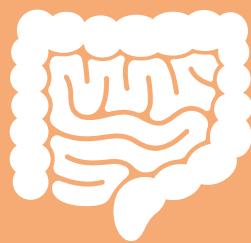
Otoscopy (bulging tympanic membrane, loss of normal landmarks, change in colour)

Pharmacological Treatment

[BPAC Otitis Media Antibiotic Guidelines](#)

Self-resolving within **3 days** usually without the need for antibiotics

1. *Analgesia:* paracetamol, ibuprofen
2. *Antibiotics* if necessary: children < 6 months, \leq 2 years if moderate/severe infection, children who are at risk for developing complications, recurrent infections, no improvement within **48 hours**. Topical ear drops are ineffective.
 - Back-pocket script of **amoxicillin**



CHAPTER 4

THE GASTROINTESTINAL SYSTEM



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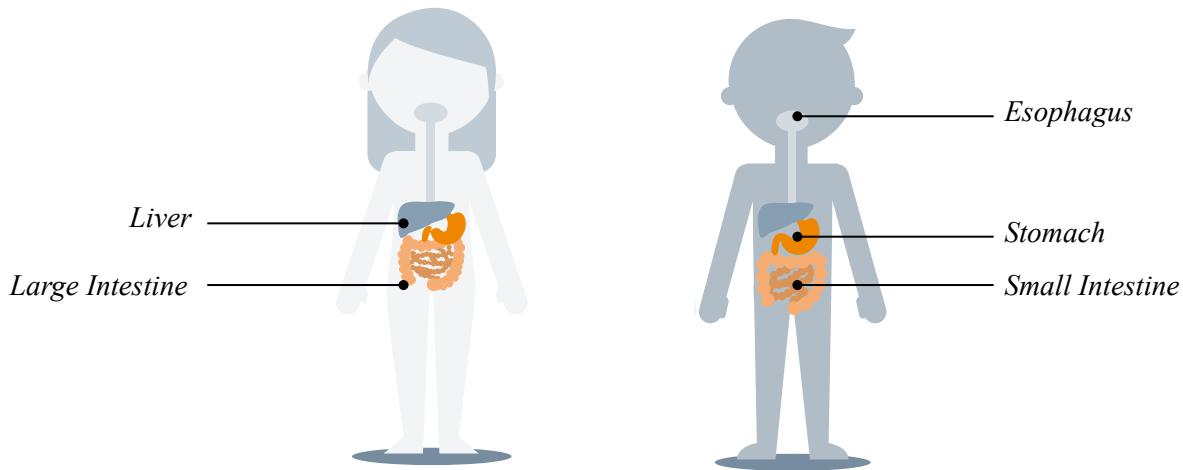
Chapter 4

The Gastrointestinal System

General Overview of the Digestive System

Introduction

The digestive system consists of the gastrointestinal (GI) tract and the liver, pancreas and gallbladder. The GI tract, in particular, is a series of hollow organs that are connected to each other from the oral cavity to the anus - they include the mouth, esophagus, stomach, small intestine, large intestine and anus. A fun fact to start this chapter: did you know that scientists call the gut the second brain?



Purpose

The digestive system is constructed to extract nutrients and energy from food while converting the rest to waste for excretion via bowel movements.



Black Tarry Stools

You will commonly see this symptom throughout this chapter and chapters yet to come. The formation of a black tarry stool is the result of blood interacting with stomach acid - thereby being an indicator that there is bleeding in the GI tract e.g. ulcers. It is always a red flag and always the cause for referral.

COMMON GI SYMPTOMS

Introduction

We will look into the following common symptoms: N/V, constipation, diarrhoea, IBS and haemorrhoids.

Nausea & Vomiting

See *Chapter 11 - Oncology for Chemo-Induced N&V (CINV)*

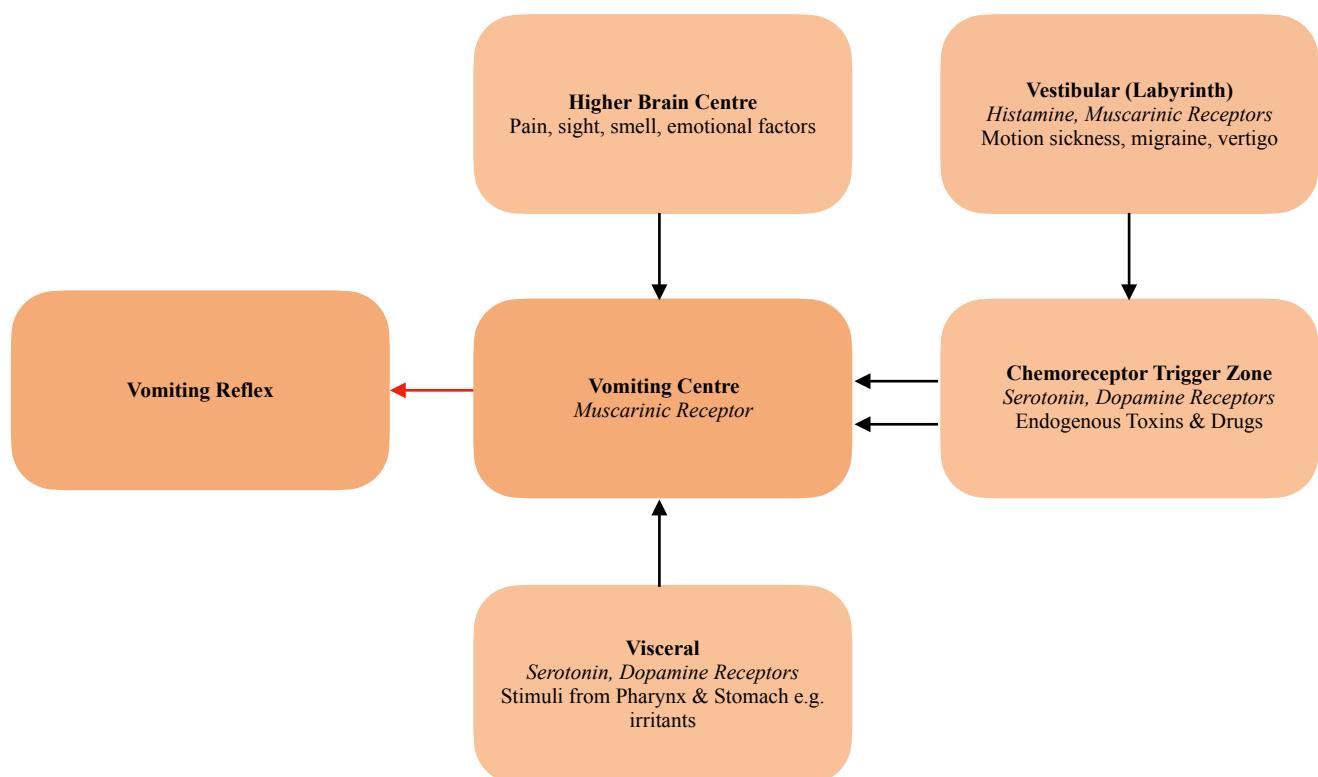
Description

Nausea and vomiting are common gastrointestinal complaints that are considered defence mechanisms when threatening elements enter the body. While vomiting is the act of forceful removal of gastrointestinal contents, nausea is the unpleasant sensation of having the urge to vomit

Pathophysiology

Emetic stimuli that triggers nausea & vomiting can originate from the following four places: visceral, vestibular, the CTZ and the vomiting centre.

These centres are mediated by 4 kinds of receptors: serotonin, dopamine, histamine and acetylcholine. Anti-emetics aim to antagonise these receptors - thus the choice of drug will depend on the causative agent e.g. anti-histamines for motion sickness.



Signs & Symptoms

Nausea, vomiting.

Complications

- Serious metabolic imbalance, dehydration, anorexia
- Deterioration in physical and mental status, treatment withdrawal

Non-Pharmacological Treatment

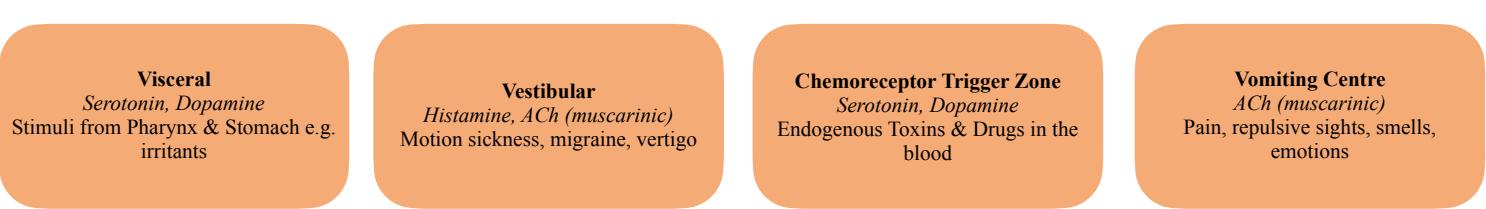
1. Drink clear or ice-cold drinks
2. Eat light, bland foods (crackers, plain bread)
3. Avoid fried, greasy, spicy or sweet foods (stomach irritants)
4. Eat slowly and eat smaller, more frequent meals
5. Do not mix hot and cold foods
6. Drink beverages slowly
7. Ginger
8. Sea-bands

Pharmacological Treatment [Anti-Emetics]

Anti-Emetic Prescribing Guidelines

Given that there are 4 kinds of receptors - there are 4 classes of anti-emetics that exist:

1. *H₁ (Histamine) Antagonists*: Promethazine, Cyclizine
2. *mACh (Muscarinic) Antagonists*: Hyoscine Hydrobromide
3. *5-HT₃ (Serotonin) Antagonists*: Ondansetron, Tropisetron, Granisetron
4. *D₂ (Dopamine) Antagonists*: Metoclopramide, Domperidone, Prochlorperazine
5. *Other*: anti-psychotics, benzodiazepines, steroids and many other drugs are also used in the management of Chemo-Induced N&V (CINV) - see Oncology Chapter.



Ingredients	Mechanism of Action	Patient Counselling	Side Effects
[NON-PRESCRIPTION] <i>1st Gen Antihistamines</i> Promethazine (Allersoothe, Phenergan) - P Meclozine (Sealegs) - P Doxylamine (Dozile) - R Cyclizine (Nausicalm) - R	For stimuli of vestibular origin <i>Block H1 receptors</i> Effective for nausea caused by motion sickness, migraine, vertigo. For stimuli of visceral or CTZ origin <i>Promethazine also blocks D2 receptors</i> Effective for treating and preventing N/V from cancer chemotherapy (cytotoxic), radiotherapy sickness, post-operative N/V, opioids, migraines	<ul style="list-style-type: none"> • Do not drive • Take at night • Do not drink • More effective if taken before the motion sickness begins <p>This medicine may make you sleepy</p>	Drowsiness, sedation
[PHARMACY ONLY] <i>mACh Antagonists</i> Hyoscine (Scopolamine Patch)	For stimuli of vestibular origin <i>Block muscarinic receptors</i> Effective for nausea caused by motion sickness, migraine, vertigo. For stimuli of vomiting centre origin <i>Block muscarinic receptors</i> Effective for nausea caused by pain, repulsive sights, smells, emotions,	Apply 1 transdermal patch to hairless area of skin behind ear at least 5 hours before journey; replace if necessary after 72 hours, or remove at end of journey	Uncommon at anti-emetic doses: Dry mouth, blurred vision, disruption to mental alertness
[PRESCRIPTION] <i>5-HT3 Serotonin Antagonists</i> Ondansetron (Onrex) Granisetron, Tropisetron	For stimuli of visceral origin or CTZ origin <i>Block Serotonin Receptors</i> Antagonists work both peripherally in the GIT and centrally on the CTZ. Effective for treating and preventing N/V from cancer chemotherapy (cytotoxic), radiotherapy sickness, post-operative N/V, opioids, migraines	<i>Disintegrating tablet</i> Place on top of tongue and allow to disperse before swallowing.	Constipation, headache, dizziness, transient rise in hepatic aminotransferases
[PRESCRIPTION] <i>D2 Dopamine Antagonists</i> Metoclopramide, Domperidone Prochlorperazine, Haloperidol, Olanzapine	For stimuli of visceral origin or CTZ origin <i>Block Serotonin Receptors</i> Antagonists work both peripherally in the GIT and centrally on the CTZ. Effective for treating and preventing N/V from cancer chemotherapy (cytotoxic), radiotherapy sickness, post-operative N/V, opioids, migraines	Metoclopramide combined with paracetamol (Paramax) for migraine treatment	Blocking of dopamine in the CNS can lead to movement disorders, fatigue, spasmodic torticollis, stimulation of prolactin release

INDICATIONS & SCHEDULING FOR ANTIEMETIC DRUGS	
Gastroenteritis	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Dopamine Antagonists • Serotonin Antagonists
Opioid-Induced	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Dopamine Antagonists • Serotonin Antagonists
Migraine-Related	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Dopamine Antagonists e.g. metoclopramide prochlorperazine
Motion Sickness & Other Vestibular Causes	<i>Vestibular Stimuli, therefore:</i> <ul style="list-style-type: none"> • Antihistamines • Anticholinergics • Dopamine Antagonists
Chemotherapy-Induced	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Serotonin Antagonists • Corticosteroids e.g. dexamethasone • Dopamine Antagonists e.g. olanzapine, haloperidol • Benzodiazepines e.g. lorazepam
Radiation-Induced	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Serotonin Antagonists • Corticosteroids e.g. dexamethasone • Dopamine Antagonists
Post-Operative	<i>Visceral/CTZ Stimuli, therefore:</i> <ul style="list-style-type: none"> • Serotonin Antagonists • Corticosteroids e.g. dexamethasone • Dopamine Antagonists • Benzodiazepines e.g. lorazepam • Antihistamines

Antiemetics in Pregnancy

Table 1: Antiemetics suitable for use in pregnancy (in order of preference)^{3,4,10}

Medication	Dose	Adverse effects
Metoclopramide	10 mg three times daily	Extrapyramidal symptoms Tardive dyskinesia especially if used for more than 12 weeks
Prochlorperazine	5 mg three times daily	Extrapyramidal symptoms Sedation
Cyclizine	50 mg three times daily	Sedation
Promethazine	25 mg at bedtime, increased to maximum 100 mg daily in divided doses	Extrapyramidal symptoms Sedation
Ondansetron (hyperemesis gravidarum)	4 – 8 mg two to three times daily	Constipation

Domperidone (and ondansetron) are usually not recommended in pregnancy.

Constipation

Description

Infrequent defecation (<3 times a week), accompanied with difficulty passing of stools and/or hard stools in comparison to usual bowel habit.



Ask! Ask! Ask!

Different people may have different frequencies in bowel movements that are 'normal' to them. While < 3 times a week is an appropriate guideline, it is always important to compare presenting bowel movements to the patient's usual ones in order to establish if there actually is a problem.

Pathophysiology

The large intestine functions to dry faecal matter by removing water and various salts from them prior to their expulsion. It is thus generally agreed that processes that facilitate water resorption will encourage the formation of hard and dry stools - one such example of this is decreased intestinal motility.

Decreased motility causes stools to remain in the colon for too long - exposing them to a longer period of water removal and thus rendering them hard, dry and more difficult to pass.

Risk Factors

Many things can cause constipation - however it is most commonly the result of a deficiency in dietary fibre, a change in lifestyle and/or environment, and medications. Occasionally, it may be also caused if the defecation reflex is ignored.

- *Diet:* Decreased fibre, poor nutrition, inadequate fluid intake
- *Medications:* Opioids
- *Medical Conditions:* IBS, hypothyroidism, diabetes, colorectal cancer, pregnancy
- *Stress Factors:* Pregnancy, sedentary lifestyle, ignorance of defecation reflex

Signs & Symptoms

Less than 3 bowel movements per week, difficult passage of stools, abdominal discomfort, bloating.

Sometimes small specks of blood may be seen due to straining - these usually aren't of worry.

Red Flags

Tarry, red, or black stools may be suggestive of upper GI bleed or ulcers.

Complications

- Haemorrhoids, toxic megacolon (obstruction), delirium, faecal impaction
- Anorexia, nausea, vomiting, abdominal pain, bowel obstruction & perforation.

Non Pharmacological Treatment

First Line in Uncomplicated Constipation

1. Increase dietary fibre (at least 30g a day - fruit, prunes veggies, cereals, grain foods, whole-grain bread)
 - Effects of a high-fibre diet are usually seen in 3 to 5 days.
2. Drink adequate fluid (6-8 glasses of fluid a day)
3. Exercise (regular walking)
4. Respond to the urge to have a bowel movement, do not put it off.
5. Squatting position (45°) rather than at a 90° angle (place a stool under feet to elevate)
6. Fibre supplements: kiwi crush

Pharmacological Treatment (Laxatives)

There are 4 classes of laxatives that exist:

1. Stimulants (6-12 hours)
2. Bulk Forming (12-36 hours)
3. Faecal softeners (24-48 hours)
4. Osmotic laxatives (48-72 hours)

Remembering the differing onsets of action of each respective laxative can guide selection of the appropriate therapy as they can be matched to the severity of the person's constipation e.g quickly acting classes like stimulants are useful in severe constipation.



Remembering Laxatives Using the SBFO Acronym

A way to remember all the laxatives in the order of how quickly they act is by using SBFO:

- “Seek Before Faecal Obstruction”
- “Stimulant, Bulk-Forming, Faecal Softener & Osmotic”

LAXATIVES CONSIDERATIONS	
With Long-Term Opioids	<i>Consider:</i> <ul style="list-style-type: none">• Stimulant (+stool softener) e.g. Docusate Sodium + Senna, Bisacodyl, Picosulfate• Osmotic Laxatives: Macrogols, Lactulose
In Pregnancy & Breastfeeding	Generally all laxatives are fine, but keep stimulants as last line and start with bulk-forming or fibre supplements
In Children	Generally osmotic laxatives are preferred

A Note on Laxative Abuse

Fast-acting classes such as stimulants have the highest potential for laxative abuse - this is because patients can misinterpret an emptied bowel for constipation, leading to the unintended, repeated overuse of the laxative.

This misinterpretation occurs because these medications increase the time needed for the colon to refill again. Enteral loss of water and salts causes aldosterone release which stimulates resorption in the intestine

but increases renal excretion of K⁺ (double loss of K⁺). The resulting **hypokalaemia** promotes a reduced peristalsis, thereby the increased time needed.

On the other hand, intended laxative abuse can occur - which describes the use of these medications for the purpose of loosing weight by eliminating unwanted calories. Intended, or not, the **long term use of laxatives weakens bowel muscles) and loss of electrolytes**. Counselling and screening for suitability is important.

Ingredients	Mechanism of Action	Patient Counselling	Pros/Cons	Side Effects
[PHARMACY, PHARMACIST ONLY, GENERAL SALE] <i>Stimulant Laxatives</i> Docusate + Senna (Laxsol) Picosulfate Sodium (Ducolax) Bisacodyl (Bisacodyl) Glycerol (Glycerol Suppository)	Time taken: Effect in 6-12h Dose: OD before bedtime Combination softeners and stimulants increase GI motility by directly stimulating the nerves in the bowel, causing muscle contractions and in this way gets the bowel moving. Docusate is a stool softer, acting to increase surfactants to soften stools.	<ul style="list-style-type: none"> Take before bedtime so that it aligns with morning bowel movement Do not take for more than 5-7 days (dependence) 	Pros <ul style="list-style-type: none"> Fast acting Can help get rid of initial stool plug Cons <ul style="list-style-type: none"> Should not be used if intestinal obstruction is suspected Cause greater side effects (cramping, diarrhoea) Has the most potential for laxative abuse. 	
[GENERAL SALE] <i>Bulk Forming Laxatives</i> Psyllium Husk (Metamucil, Konsyl-D, Bonvit)	Time taken: Effects in 12-36h Dose: OD or BD Contain polysaccharide polymer fibres which do not get broken down but instead soak up intestinal water. This mimics increased fibre consumption hence increasing faecal mass. This in turn, stimulates bowel muscles and prompts peristalsis	<ul style="list-style-type: none"> Patients should increase fluid intake at the same time to avoid intestinal obstruction (thus not suitable in HF patients due to fluid restriction) Be careful, medicine swells when in contact with water. Stir powder in liquid for 3-5 seconds and drink promptly. If on other medicines, take 1-2 hours before them as they can interfere with absorption. 	Pros <ul style="list-style-type: none"> Gentlest class Safest long term option Useful for people with small, hard stools due to a change in diet Cons <ul style="list-style-type: none"> Take time to work Not appropriate if experiencing symptoms like bloating Some options not palatable 	Flatulence, Abdominal discomfort, Diarrhoea Electrolyte imbalances, dehydration Stimulants - urine discolouration and colic
[GENERAL SALE] <i>Faecal Softener Laxatives</i> Docusate Sodium (Coloxyl) Poloxamer (Coloxyl Drops Paediatrics)	Time taken: Effect in 24-48h Dose: BD Medicine acts like a detergent, enabling water and fats to be incorporated in stool which makes it softer and easier to pass. These are recommended for mild constipation (e.g.: haemorrhoid prevention.) Rarely used alone (often used with a combined stimulant)	<ul style="list-style-type: none"> Patients should increase fluid intake 	Pros <ul style="list-style-type: none"> Good for mild constipation if a bulk-forming laxative is not suitable More gentle than stimulants Cons <ul style="list-style-type: none"> Take time to work Not supported for chronic use 	
[GENERAL SALE] <i>Osmotic Laxatives</i> Lactulose (Laveolac) Macrogols (Molaxole) Sodium Citrate/Sodium Lauryl Sulfoacetate/ Sorbitol (Micolette, Microlax)	Time taken: Effect in 48-72h. Dose: BD Draw water into the colon from the surrounding tissues via altering the osmotic balance. This softens stools and increases bowel movement frequency. You can mix macrogols with food and fruit juice for children.	Patients should increase fluid intake Notes: Available as an oral liquid for patients that can't swallow tablets. Brush teeth after administration of lactulose due to high sugar content.	Pros <ul style="list-style-type: none"> Well tolerated Cons <ul style="list-style-type: none"> Side effects 	

Diarrhoea

Description

Increase in frequency (≥ 3 a day) in the passage of soft or water stools relative to the usual bowel habit. It can also be accompanied by an urgency to go to the toilet or stomach pain and cramping. There are three types of diarrhoea that exist:

Types of Diarrhoea	
Osmotic Diarrhoea	This kind of diarrhoea occurs when certain factors prevent the normal and regular absorption of water and electrolytes - causing them to remain in the bowel.
Secretory Diarrhoea	This kind of diarrhoea occurs when electrolytes are secreted into the bowel, causing water buildup. This can be caused by many things including bacterial toxins, medications, infections and so forth.
Exudative Diarrhoea	Exudative diarrhoea is associated with damage to the intestinal mucosa, leading to the release or oozing of mucus, blood, and plasma proteins from cells as result of inflammation or injury. This increases the fluid content of feces and is present in ulcerative colitis, Crohn's disease, or radiation.

Risk Factors

1. *Diet:* Food intolerances (e.g. lactose)
2. *Medical Conditions:* Acute Gastroenteritis (virals, bacterial infections), IBS, IBD, Coeliac Disease
3. *Medications:* **Antibiotics**, Antidepressants (SSRIs), antacids & PPIs, chemo



A note on Antibiotic Associated Diarrhoea (AAD)

Antibiotics disrupts the normal GIT microflora, allowing the proliferation of pathogens - this can commonly result in diarrhoea typically a few days after taking antibiotics. This is however self-resolving upon cessation of the drug with usually no damage to the GIT. Patients prone to AAD can be given *prophylactic probiotics*.

Signs & Symptoms

≥ 3 bowel movements a day, dehydration, N/V, abdominal cramping, flatulence, tenderness

Red Flags: Bloody stools, >4 days duration or recurrent, more than 10 runny bowel motions a day

Non-Pharmacological Treatment

1. Replenish fluids (at least 1 cup after each loose bowel movement)
2. Avoid irritating foods and drinks (e.g. caffeine, alcohol, tobacco, sugar alcohol-containing foods e.g. sugar free gum, sorbitol, mannitol, xylitol)
3. Add semi-solid and low-fibre foods gradually as your bowel movements return to normal
4. BRAT Diet (high in K⁺): bananas, rice, apple sauce, toast.
5. Other: try soda, crackers, rice or chicken, bulking foods like bran, potatoes, apricots
6. Avoid milk/milk products (yoghurt/buttermilk are okay), high fat foods

Pharmacological Treatment (Anti - Diarrhoeals)

Please note that anti-diarrhoeals are not appropriate in all situations - an example of this is when food poisoning (gastroenteritis) is the cause. In these cases, it is best to not halt the bowel movements to allow the flushing out of the bacteria and use oral rehydration salts. If anti-diarrhoeals are appropriate, options include:

1. *Anti-Motility Agents*: Loperamide, Diphenoxylate
2. *Absorbents and Bulk Agents*: Psyllium
3. *Opioids*: Morphine, Codeine
4. *Anti-Secretory Agents*: Bismuth subsalicylate (not in NZ)
5. *Probiotics*: effective in treating and preventing diarrhoea (especially in those taking antibiotics)

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Fluid Replacement Therapy	[GENERAL SALE] Oral Hydration Salts (Enerlyte, Electral) (Pedialyte - for paediatrics)	Rehydration of lost electrolytes	Use after every loose motion to replace electrolytes lost in diarrhoea	N/A
Anti Motility	[GENERAL, PHARMACY, PRESCRIPTION] Anti-Motility Agents (Loperamide Diamide Relief) (Diphenoxylate Diastop)	Increase intestinal transit time by slowing motility, and enhance absorption of water and electrolytes. Loperamide also decreases urgency & faecal incontinence by increasing sphincter tone Do not give under 12	Use after every loose motion	Nausea, abdominal cramps, headache
	[GENERAL SALE] Absorbents & Bulk Agents (Psyllium Metamucil)	Bulk agents fibres solidify the stool by decreasing its fluid content which decreases diarrhoea.	Stir in powder and drink immediately	Flatulence, Abdominal Discomfort
Opioids	[CONTROLLED DRUGS] Morphine, Codeine	Anti-diarrhoeal effect occurs at a lower dose compared to analgesia: decreases stomach emptying by slowing motility, decreases contractions, and increases fluid and electrolyte absorption	May be addictive	Sedation, N&V, Constipation

Caution in providing loperamide to children <12 years (advise to see GP) as diarrhoea in young children is often caused by gastroenteritis.

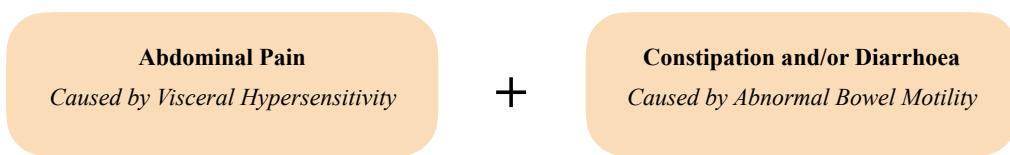
Irritable Bowel Syndrome (IBS)

Description

Irritable bowel syndrome (IBS) is one of the most common GI tract conditions seen in primary care. It can be defined as a functional bowel disorder (i.e. absence of abnormality) affecting the **large** intestine, without any deterioration in the patient's general health. It is a collection of symptoms associated with abdominal pain and bloating that is accompanied by a change in bowel habits - often resulting in alternations of diarrhoea (hurrying of food) and constipation.

Pathophysiology

IBS is not very well understood — there is instead much of a focus on the symptoms it causes:



1. *Abdominal Pain*: occurs due to visceral hypersensitivity, a situation where the sensory nerve endings in the intestinal wall have an abnormally strong response to stimuli e.g. stretching following a meal.
2. *Abnormal Bowel Motility*: foods containing short chained carbohydrates such as lactose and fructose often trigger symptoms by drawing in water. This can lead both to diarrhoea, gas, bloating and visceral hypersensitivity.

Risk Factors

1. Acute Gastroenteritis e.g. Novovirus, Rotavirus
2. Short-chain carbohydrates e.g. apples, beans, cauliflower
3. **Stress**

Signs & Symptoms

IBS manifests with a **group** of symptoms

1. *Abdominal pain, bloating & discomfort*
 - Felt in the lower left abdomen quadrant and is usually relieved by defecation or passage of wind
2. *Changes in bowel movement patterns*
 - Either diarrhoea- or constipation-predominant
 - Symptoms occurring at least 3 times a month
 - Feeling of incomplete defecation
 - Presence of mucus



Fun Fact

Women affected by IBS tend to be more constipation - predominant

IBS tends to be episodic. The patient might have a history of being well for a number of weeks or months in between bouts of symptoms. Often, patients can trace their symptoms back many years, even to

childhood.

Red Flags: <16y or >45y with recent change to bowel habit (associated with malabsorption syndromes), change in nature and severity of pain, pain that is not normally in the left lower quadrant, blood in stool

Diagnosis

The diagnosis is suggested by the presence of long-standing colonic symptoms, without any deterioration in the patient's general health.

Non-Pharmacological Treatment

1. Smaller and more frequent meals - avoid missing meals and increase dietary fiber to 20-35g daily
2. Low FODMAP diet*
3. Avoid irritating foods - processed, recooked food, limit fresh fruits to three portions per day
4. Avoid irritating drinks - reduce intake of alcohol and fizzy drinks.
5. Adequate hydration - drink at least eight cups of fluid per day, especially noncaffeinated drinks.
6. Physical activity
7. Manage stress



*FODMAP Foods

FODMAP foods are foods that contain certain types of carbohydrates. They include short-sugars that can cause symptoms in the digestive systems of susceptible individuals e.g. apples, beans, cauliflower (foods that make you gassy)

Pharmacological Treatment

1. *Laxatives for constipation:* Stimulant, bulk-forming
2. *Antidiarrhoeals for diarrhoea:* Loperamide
3. *Anti-spasmodics:* Peppermint oil (Mintec), Hyoscine butylbromide (Buscopan IBS Relief)
4. *Probiotics:* Lactobacillus, Bifidobacterium

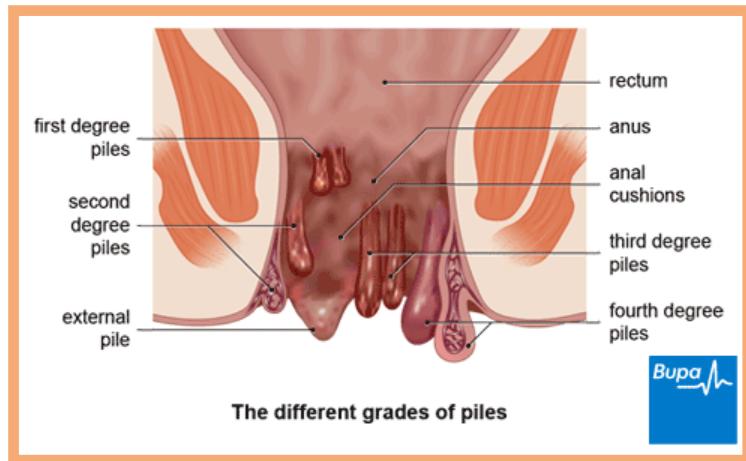
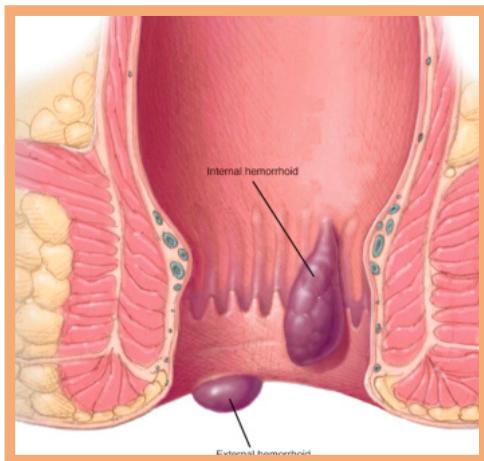
Haemorrhoids (Piles)

[Health Navigator Haemorrhoids](#)

Description

Haemorrhoids are swollen and inflamed veins in the anus and lower rectum (anorectal region). Patients might feel embarrassed talking about symptoms, and it is therefore important that any requests for advice are treated sympathetically and away from others to avoid embarrassing the patient.

Two anatomical types exist: *internal* (inside rectum), *external* (under the skin around the anus).



Risk Factors

1. *Physiological*: Increased pressure in lower rectum
2. *Mechanical*: Straining, prolonged periods of sitting, heavy lifting, pregnancy, childbirth, obesity
3. *Anatomical*: Degeneration of elasticity of connective tissue due to ageing causes veins to fill with blood / impaired venous return
4. **Stress**

Signs & Symptoms

The way a haemorrhoid may feel to a patient can indicate whether it is internal or external - generally internal haemorrhoids are mostly painful while external haemorrhoids are painful/itchy.

1. *Internal*: Painless bleeding, irritation, inner **pain** during bowel movements, itchiness, protruding lump
2. *External*: **Itching** and irritation around the rectum/anus, dull ache pain that worsens at defecation, discomfort, swelling around anus, bleeding (this is not a red flag and usually expected with haemorrhoids)

Red Flags: Symptoms persisting ≥ 3 weeks, sharp or stabbing pain at defecation which may last a few hours (anal fissure or tear), symptoms such as N/V, weight loss, loss of appetite, extreme loss of blood

Non-Pharmacological Treatment

Resolve underlying cause e.g. constipation

3. Increase fibre intake and fluid intake
4. Avoid straining, do not resist the urge to go
5. Avoid sitting for long periods of time, exercise regularly
6. Adopt a squatting position so that you are not sitting at a 90 degree angle or use a stool to lift legs
7. Clean area with wet paper towel to prevent irritation of affected area
8. Epsom salts bath, witch hazel, aloe vera are all effective home remedies
9. Ensure to massage piles regularly as this can relieve stagnation and pressure.

Pharmacological Treatment

Treatment of haemorrhoids is generally symptomatic as these are usually self-resolving within **7-14 days**.

There are three products available:

1. Proctosedyl
2. Ultraproct
3. Anusol

Classification	Ingredients	Patient Counselling	Side Effects
Local anaesthetic + Corticosteroids	[PHARMACY ONLY] Proctosedyl <i>Ointment Suppository</i> (Cinchocaine + Hydrocortisone)	Use after bowel movement. Do not use for more than 1-4 weeks Apply with finger (external), or with cannula (internal) Caution in pregnancy	Over-usage can lead to local skin thinning, stretch marks and local irritation.
	[PRESCRIPTION] Ultraproct <i>Ointment Suppository</i> (Cinchocaine + Fluocortolone Hexanoate + Fluocortolone Pivalate)	Use after bowel movement. Do not use for more than 1-4 weeks Apply with finger (external), or with cannula (internal)	Local irritation & systemic adverse effects with prolonged use
Astringents	[GENERAL SALE] Anusol <i>Ointment Suppository</i> (Zinc oxide + Peru Balsam + Benzyl Benzoate)	Use after bowel movement. Apply with finger (external), or with cannula (internal) Zinc precipitates surface proteins, thus producing a protective coat over the haemorrhoid.	Local irritation

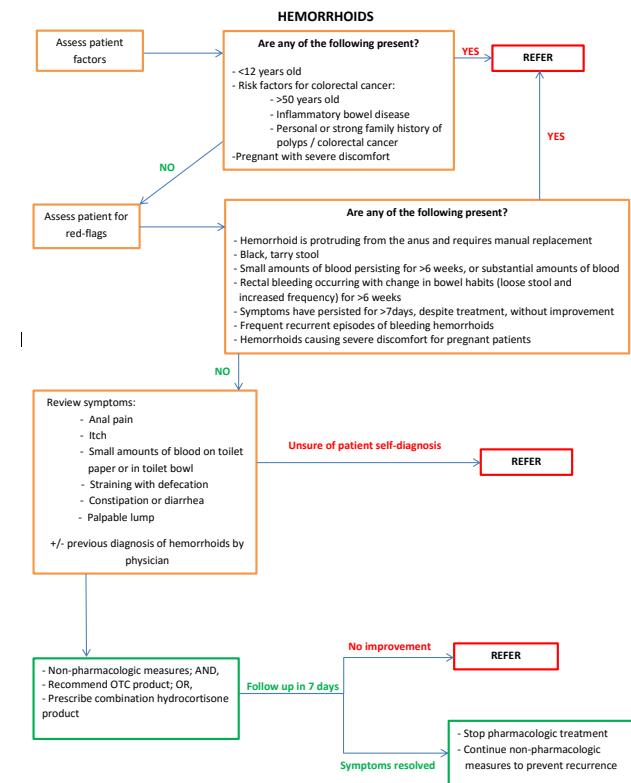
OSCE Points

- Ointment products contains applicator — figure out whether piles are external or internal.
- Smear a little ointment (about the size of a pea) around the anus and in the anal ring with a finger, using the fingertip to overcome the resistance of the sphincter
- Applied to clean area, ideally after defecation, describes correct amount to use (about the size of a pea) smeared around the anus (for external haemorrhoids)
- Wash hands before and after using
- Red flags (sharp, stabbing pain, bleeding a lot)

- Cold compress, warm bath
- Avoid straining, diet, respond to urge to go

PHARMACIST ASSESSMENT -- HEMORRHOIDS

Patient information	
Name:	HSN:
Address:	DOB: (<12 → refer) <input type="checkbox"/> male <input type="checkbox"/> female
Telephone:	<input type="checkbox"/> Pregnant (refer if severe discomfort)
Medical History:	
<input type="checkbox"/> Family or personal history of colorectal cancer or polyps → refer <input type="checkbox"/> History of inflammatory bowel disease → refer <input type="checkbox"/> Previous diagnosis of hemorrhoids → helps confirm patient self-diagnosis	
Drug History:	
Review of Symptoms	
Any red flags present? <input type="checkbox"/> Bleeding dark in color, large amounts, small amounts lasting >6 weeks, or frequent recurrent episodes of bleeding hemorrhoids <input type="checkbox"/> Mass protruding out of rectum needing manual replacement <input type="checkbox"/> Severe pain <input type="checkbox"/> Symptoms been present for more than 7 days despite treatment <input type="checkbox"/> Frequent, recurrent episodes of bleeding hemorrhoids <input type="checkbox"/> Yes to any → refer	
Are symptoms consistent with the diagnosis of hemorrhoids? <input type="checkbox"/> Burning, irritation, swelling, itching + / - pain in anal area <input type="checkbox"/> Bright red blood on toilet paper, in toilet bowl <input type="checkbox"/> Associated with constipation or diarrhea <input type="checkbox"/> Palpable lump <input type="checkbox"/> Straining with defecation <input type="checkbox"/> Yes → Continue <input type="checkbox"/> No, consider other causes, refer	
Has the patient tried any non-pharmacologic or pharmacologic treatment for hemorrhoids? <input type="checkbox"/> No <input type="checkbox"/> Yes → What? Effect?	
Treatment recommended	
<input type="checkbox"/> General treatment measures: - Increase fibre and fluid intake - Sitz bath - Avoid long periods on the toilet <input type="checkbox"/> OTC hemorrhoid product <input type="checkbox"/> Prescription for hemorrhoidal product <i>(Note: OTC products should be used preferentially as first option, depending on patient preference)</i>	



BACTERIAL GI INFECTIONS

Introduction

The gastrointestinal tract is unique in the sense that it has an established, local and protective microflora. However, there are an enormous number of microbes that cause disease in the digestive tract, we will first focus on bacteria.

Helicobacter Pylori (H. Pylori)

[BPAC \(Be Quick\) H.Pylori Infection](#), [BPAC H.Pylori Treatment Guidelines](#)

Description

Helicobacter Pylori (H. Pylori) is a gram negative (-) bacteria that can infect your gut and induce (1) reflux, (2) ulcers, and (3) GI cancer.



Fun Fact

Barry James Marshall, the scientist that discovered that H.Pylori could cause ulcers, drank a solution with the bacteria on purpose to prove this to the science community, who at the time believed that the sole cause of ulcers were stress. He later developed ulcers and revolutionised its treatment worldwide.

Pathophysiology

H. Pylori is transmitted via contaminated food or water and it can spread through faecal matter, vomit or saliva. It survives in the gut mucus layer due to its urease activity - this is an enzyme that converts urea → ammonia + **CO₂**. By this mechanism, the bacteria:

1. Creates a neutralising environment that hides it from the immune system, and
2. Weakens the mucous layer, resulting in the sensitive stomach lining being irritated by both the bacteria in the acid.

Risk Factors

- *Genetics*: Māori or Pasifika Ethnicity
- Use of NSAIDs (particularly aspirin)
- Smoking, excess alcohol
- History of pre-disposing GI issues

Signs & Symptoms

Often asymptomatic. Symptoms are **worse** on an **empty** stomach.

1. *Reflux*: abdominal pain, N/V/D, bloating, flatulence, heartburn
2. *Peptic Ulcers*: dull, gnawing ache, weight loss, bloating, burping, N/V, black tarry stools
3. *Cancer*

Red Flags

In patients presenting with dyspepsia-like symptoms:

- Evidence of GI bleeding: anaemia, bloody / black stools, bloody / coffee-ground vomit
- Age ≥ 55 years at first presentation or ≥ 45 years for Māori, Pacific, or Asian patients
- Family history of gastric cancer with age of onset < 50 years
- Other: difficulty swallowing, palpable abdominal mass, unexplained weight loss, sharp, sudden, persistent stomach pain

Diagnosis

1. Breath Test (gold standard but unfunded)
2. Stool/Faecal Antigen Test
3. Antibody Blood Test

Non-Pharmacological Treatment

1. Staying hydrated and keeping fluids up
2. Diet: reduce meal sizes, avoid large meals before bedtime, avoid trigger foods
3. Limit alcohol intake
4. Weight loss (if obesity a risk factor)
5. Cessation of any causative medications

Pharmacological Treatment

[BPAC H.Pylori Treatment Guidelines](#)

Treatment mainstay is to:

1. *Reduce Stomach Acid* e.g. PPI, antacids
2. *Resolve the Infection:* Antibiotics

Treatment Guidelines in Patients with a H.Pylori Infection		
Infection	Treatment	Description
Suspected H.Pylori Infection	PPI Trial	For 4-8 weeks. If symptoms persist, test for H.pylori infection
Confirmed H.Pylori Infection	First Line Treatment	<p>1. <i>Triple Eradication Regimen for 7-14 days</i></p> <ul style="list-style-type: none"> • Omeprazole (20mg bd) and — see duration of treatment if ulcers are present (NZF) • Clarithromycin (500mg bd) and • Amoxicillin (1000mg bd) or Metronidazole (400mg bd) <p>Please note, if patient has had a previous exposure to:</p> <ul style="list-style-type: none"> • Any macrolide antibiotic → omeprazole + amoxicillin + metronidazole • Metronidazole → omeprazole + amoxicillin + clarithromycin • Both macrolide and metronidazole → refer to gastroenterologist
		<p>2. <i>Quadruple Eradication Regiment for 14 days</i></p> <p>If still testing positive after 3 months of above treatment</p> <ul style="list-style-type: none"> • Omeprazole (20mg bd) and • Bismuth (120 mg qid) and • Tetracycline (500 mg qid) and • Metronidazole (400 mg tid)
	Third Line Treatment	<p>3. <i>Gastroenterologist Referral</i></p> <ul style="list-style-type: none"> • If first line and second line fail to clear the infection/signs/symptoms

Monitoring

- Confirmation of infection eradication is not usually required if symptoms resolve - need to wait **3 months** after treatment to conduct follow-up testing.
- If symptoms persist, retest (e.g. faecal antigen test) after 3 months, then consider second line treatment.
- Patients should be advised not to take PPIs within two weeks of testing, or antibiotics or bismuth compounds within four weeks of testing, to prevent false negative results.

Prevention

Subunit Vaccine (3 oral doses for children) - Fusion of H. pylori urease with E. coli heat labile toxin

Bacterial Gastroenteritis

Description

Also known as food poisoning, tummy bug or traveller's diarrhoea - bacterial gastroenteritis describes the irritation of the digestive tract that occurs in response to either an intoxication or infection by a bacteria.

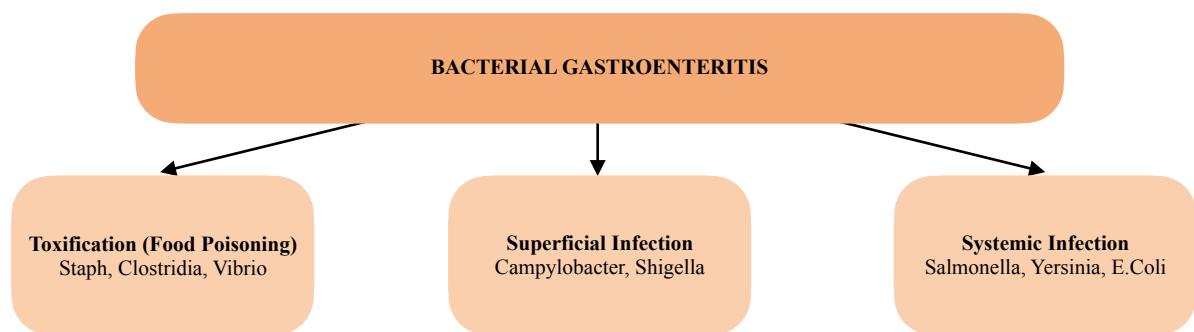


Intoxication vs Infection

Food Poisoning is an **intoxication** rather than an **infection**. *Food Infection* occurs when live bacterial cells are ingested and these cells go on to grow in the digestive tract to cause symptoms. *Food Intoxication* occurs from eating a food that contains a toxin produced by bacteria.

Causative Agents

Bacteria/bacterial toxins (in food or water) are the most common causative agents for food poisoning, superficial, and systemic infections.



	Food Intoxication	Superficial Infection	Systemic Infection
Duration	Lasts 24 hours	Lasts Days	Lasts Days
Management	Self Limiting	May not be self-limiting	Not self-limiting
Symptoms	Mainly diarrhoea but no fever (or any systemic symptoms)	Mainly diarrhoea + low fever	Mainly diarrhoea + high fever
Bacteria	<ul style="list-style-type: none">• Staphylococcus Aureus (Gram +ve, Intestine)• Clostridium Perfringens & Botulinum (Gram +ve, Intestine)• Vibrio Parahaemolyticus & Vulnificus (Gram -ve, Intestine)	<ul style="list-style-type: none">• Campylobacter Jejuni (Gram -ve, Gastrointestinal)• Shigella Dysentery Shigellosis (Gram -ve, Intestine)• Listeriosis Monocytogenes (Gram +ve, Gastrointestinal)	<ul style="list-style-type: none">• Salmonella (Gram -ve, Intestine)• Yersinia (Gram -ve, Gastrointestinal)• Escherichia Coli (Gram -ve, Gastrointestinal)

Risk Factors

Older adults or very young children are more vulnerable to the symptoms of gastroenteritis, and are also at a higher risk of complications.

Signs & Symptoms

Diarrhoea, vomiting, abdominal pain are classic signs of a GI infection.

1. *Food poisoning*: lasting 24 hours, diarrhoea, vomiting, cramps, **no fever**
2. *Superficial infection*: **low-grade fever**, systemic symptoms, abdominal pain, N/V/D, can last for days.
3. *Systemic infection*: N/V/D, **fever**, abdominal pain, can last for days.

Non-Pharmacological Treatment

1. *Food Poisoning*
 - Fluid replacement, rest, probiotics
2. *Infection*
 - Breastfeed your baby e.g. breast milk, formula, cow's milk (if the child's one year and older), clear soup, rice water are all suitable
 - Fluid replacement 5mL/min (25ml/5 min) — Can use straw or chill solution

Pharmacological Treatment

1. *Food Poisoning*
 - **No** need for antimicrobials
 - **No** anti-motility agents (we need to flush away bacteria/toxins)
 - Oral Rehydration Salts: Plasmalyte, Pedialyte, Gastrolyte, Enerlyte
2. *Infection*
 - Antibiotics (depending on the bacteria)
 - Oral Rehydration Salts: Plasmalyte, Pedialyte, Gastrolyte, Enerlyte

VIRAL GI INFECTIONS

Introduction

We will look into one viral GI infection: viral gastroenteritis

Viral Gastroenteritis

Description

Also called stomach flu or tummy bug, viral gastroenteritis is an intestinal infection caused by viruses (**norovirus, rotavirus, enteroviruses e.g. poliovirus**). Transmitted via contaminated food or water, or through contact with an infected person.

Signs & Symptoms

Diarrhoea, abdominal cramps, N/V, and sometimes fever

	Description	Signs & Symptoms
Norovirus	A group of viruses that cause stomach or intestinal infection, leading to vomiting and diarrhoea. Transmitted via contaminated food and water.	Sudden diarrhoea and vomiting, stomach pain, fever, malaise
Rotavirus	Rotavirus is a highly infectious virus of the gut, causing severe vomiting and diarrhoea. It is transmissible via the oral-faecal route. It is self-resolving within 1 - 2 weeks.	Severe gastroenteritis (vomiting, diarrhoea — temporary lactase deficiency), low-grade fever, malaise, dehydration, extra-intestinal disease (neurological disease, trigger for inflammatory/autoimmune complications)
Enterovirus (Poliovirus)	Polio is a highly infectious viral disease that can cause paralysis (muscle weakness). It affects the bowel, then nervous system, causing meningitis and paralysis. It is not as prevalent now due to immunisation but could be brought into NZ by travellers and immigrants. It is transmitted via the oral-faecal route. The pathogenesis of poliovirus consists of GI replication of the virus (virus excreted for 2-8 weeks), spread to lymphoid tissue, invasion of blood and potential BBB penetration.	Diarrhoea, vomiting, abdominal pain, fever, runny nose, sneezing, cough, skin rash, mouth blisters, body and muscle aches, paralysis . <i>Poliovirus</i> : Headache, diarrhoea, tiredness, stiffness of neck and back (meningitis), pain in limbs/back/neck with or without paralysis

Non-Pharmacological Treatment

- Maintain hydration and electrolytes: Fluid replacement 5mL/min (25ml/5 min) — Can use straw or chill solution
- If vomiting is an issue, try saltine crackers and small sips of water.
- Reintroduce age-appropriate diet when possible — lactase levels may be temporarily reduced due to diarrhoea
- Avoid contact with case, strict hygiene
- Breastfeed if your baby is breastfeeding e.g. breast milk, formula, cow's milk (if the child's one year and older), clear soup, rice water are all suitable

Pharmacological Treatment

Infection resolves within few weeks without treatment.

- Oral rehydration salts: Plasmalyte, Pedialyte, Gastrolyte, Enerlyte

Prevention

Rotavirus

Vaccine	Vaccine Type	When
Rotarix	Live Oral Vaccine	6 weeks, 3 months

Poliovirus

Cocooning +

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Infanrix-IPV booster (DTaP, polio)	IPV is inactivated or whole killed	4 years

FUNGAL GI INFECTIONS

Introduction

We will look into one fungal GI infection: oral thrush. From here onwards, you still notice that many medications begin to become culprits behind various oral health conditions. A few examples of things we will look into are listed below. Please visit the sub-section ‘Medicines-Related GI Conditions’ for conditions specifically caused by medications.

Medicines & Oral Health

As we will look into later, medicines may be the culprit behind many oral health conditions.

- Dry Mouth (Xerostomia)
- Abnormal Gum Bleeding
- Gingival Hyperplasia
- Oral Thrush (Oral Candidiasis)
- Oral Ulcers
- Oral Mucositis (Stomatitis)
- Medication-Related Osteonecrosis of the Jaw (MRONJ)
- Medicines & Developing Teeth

Medications with anticholinergic activity are common culprits as they cause a dry mouth (saliva is a protective factor)

Anticholinergic activity of medications

Class	Drugs	Relative anticholinergic potency
Antihistamines	H ₁ receptor antagonists, first-generation: brompheniramine, carbinoxamine, chlorpheniramine, clemastine, cyproheptadine, dimenhydrinate, diphenhydramine, doxepin, doxylamine, hydroxyzine, meclizine, triprolidine, others	High
	H ₁ receptor antagonists, second-generation: fexofenadine, cetirizine*, loratadine, desloratadine, levocetirizine, others	Low
Antiparkinson	Benztropine, trihexyphenidyl	High
	Amantadine, bromocriptine, entacapone	Low
Analgesic	Opioids: codeine, hydrocodone, fentanyl, meperidine, methadone, morphine, oxycodone, tramadol, others	Low
Antimuscarinic, overactive bladder	Darifenacin, fesoterodine, flavoxate, oxybutynin, solifenacain, tolterodine, trospium	High
Antimuscarinic, spasmolytic	Atropine, belladonna-containing medications, clidinium-chlordiazepoxide, dicyclomine, hyoscymamine, glycopyrrrolate, homatropine, methscopolamine, propantheline, scopolamine (hyoscyine)	High
Antimuscarinic, inhaled bronchodilator	Ipratropium, tiotropium	High (local effect)
Antimuscarinic, ophthalmic drops (mydriatic/cycloplegic)	Atropine, cyclopentolate, homatropine, scopolamine	High (local effect)
Cardiovascular	Disopyramide	Low
Gastrointestinal	Antiemetics (eg, hydroxyzine, meclizine, promethazine, scopolamine); also refer to first-generation antihistamines above	High
	Domperidone, loperamide, prochlorperazine	Low
	H ₂ receptor antagonists (cimetidine, famotidine*)	Low
Muscle relaxant	Orphenadrine, tizanidine	High
	Cyclobenzaprine*, baclofen, methocarbamol	Low
Psychotropic	Antipsychotics, first-generation: chlorpromazine, fluphenazine, loxapine, methotrimeprazine (levomepromazine), thioridazine, trifluoperazine	High
	Antipsychotics, first-generation: haloperidol, perphenazine*, others	Low
	Antipsychotics, second-generation: clozapine	High
	Antipsychotics, second-generation: olanzapine*, quetiapine*, iloperidone, risperidone, others	Low
	Benzodiazepines: chlordiazepoxide, clonazepam, temazepam, triazolam	Low
	Selective serotonin reuptake inhibitor (SSRI) antidepressants: citalopram, fluoxetine, fluvoxamine, paroxetine*	Low
	Tricyclic antidepressants: amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, others	High
	Carbamazepine, lithium, nefazodone, oxcarbazepine, phenelzine, trazodone	Low
Other neurologic		

Oral Thrush (Oral Candidiasis)

[Health Navigator — Oral Thrush](#)

Description

Opportunistic fungal infection in the mouth caused by *Candida albicans*. Many people carry this organism as part of their natural mouth flora. The yeast reproduces and invades the moist surfaces of the mouth creating inflammation and tissue damage.



Risk Factors

- *Age*: Neonates/babies, elderly, ill-fitting dentures
- *Medicines*: broad spectrum antibiotics, drugs causing dry mouth e.g. antihistamines, immunosuppressants, inhaled corticosteroids
- *Medical conditions*: Diabetes, dry mouth, immunosuppression
- *Environmental*: Smoking, nutritional deficiency (Vit B)



Oral Thrush & Steroid Inhalers

Inhaled corticosteroids e.g. Fluticasone, Symbicort are a common cause of oral thrush - often due to patients forgetting to rinse their mouth after using them or just in general having poor oral hygiene. It is always important to screen for potential causative medications and emphasise during counselling the need for good oral hygiene. A helpful tip is to keep the steroid inhaler next to your toothbrush!

Signs & Symptoms

- Creamy-white, soft elevated patches on the tongue or inner cheeks that **can** be scraped off, discomfort, burning, irritation.
- Can also appear on pharynx (due to steroid inhalers).

Non-Pharmacological Treatment

- Rinse mouth after steroid inhaler use.
- Maintain good oral hygiene (brush teeth, avoid overuse of antiseptic mouthwashes that alter mouth flora — **chlorhexidine** has some anti-candida activity).
- Giving probiotics if someone is prone to thrush caused by antibiotics

Pharmacological Treatment

1. *Topical Antifungals*: Miconazole Gel, Nystatin Drops
2. *Oral Antifungals*: Fluconazole, Itraconazole

Note: If thrush has occurred to a baby, **may need to treat nipple after a feed with miconazole** - see *Chapter 12 - Men & Women's Sexual Health* for more information.

Category	Ingredients	Dosing	Patient Counselling	Side Effects
Topical Antifungals	[PHARMACIST ONLY] <i>First line in >6yrs</i> Miconazole Oral Gel 2% (20 mg/g) (Daktarin, Decozol)	<p>Frequency: Apply FOUR times daily after food. Use for at least 1 week after symptoms resolve</p> <p>Infants (6-24 months): 1/4 of measuring spoon (or 20mg/kg/day)</p> <p>Adults: 1/2 of measuring spoon (do not give if on warfarin)</p>	<ul style="list-style-type: none"> Place gel onto the tongue using the measuring spoon supplied. Keep gel in the mouth for as long as possible before swallowing. Avoid placing gel at the back of the throat. Treatment should be continued for 1 week after symptom resolution. In younger kids, give dose in several smaller ones in different areas of the mouth (avoid back of throat.) Avoid in babies as they can choke on the thicker gel. If dentures are involved, apply the gel directly to them in the evening and leave overnight. Improvements are seen within 1-2 days, if no improvement after 2 weeks, seek medical advice 	N&V Rash
	[PHARMACIST ONLY] <i>First line in <6yrs</i> Nystatin Oral Drops (Nilstat)	<p>Frequency: Take 1ml FOUR times daily after food for 7 days. Use for at least 2 days after symptoms resolve</p> <p>Infants >1 month old & adults: 1ml FOUR times daily</p>	<ul style="list-style-type: none"> Give under tongue and hold in mouth for as long as possible If no improvement after 7 days, seek medical advice 	
Oral Antifungals	[PRESCRIPTION] Fluconazole (Milan)	<ul style="list-style-type: none"> Take with food and a glass of water until finished. 		GI Upset N&V Rash Allergy
	[PRESCRIPTION] Itraconazole	<ul style="list-style-type: none"> Take with food and a glass of water until finished. Contraception should be used in women of child-bearing potential during treatment and for 1 week after the last dose (ask pregnancy status) 		

PARASITIC GI INFECTIONS

Introduction

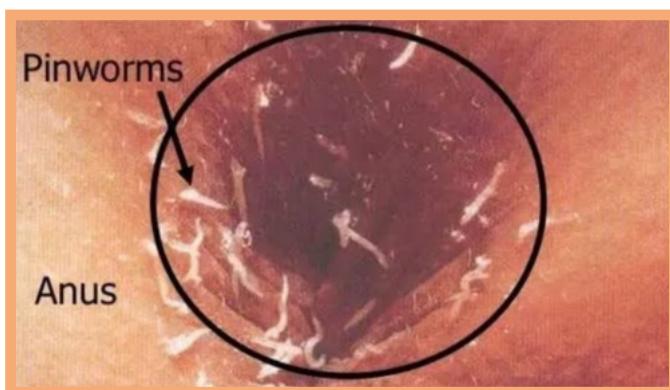
We will look into three parasitic infections: threadworms, cryptosporidium and giardia lamblia infections.

Threadworms (Pinworms)

[DermNet Pinworms](#)

Description

Threadworms are tiny parasitic worms (*Enterobius vermicularis*) that infect the large intestine of humans. Eggs are transmitted via the faecal-oral route (auto-infection), retroinfection, and/or inhalation. Eggs usually get lodged under fingernails after scratching the anal region which are then ingested by finger sucking. A perpetuating cycle occurs if it is not treated.



Risk Factors

- School-aged children, household members
- **Recent travel**

Diagnosis

- ‘Sticky tape’ test: use clear adhesive tape in the anal region to catch any eggs. Best done first thing in the morning, prior a shower.
- Adult worms can be seen with the naked eye (thin, white, wriggling threads), often in the faeces.

Symptoms

Nighttime itching around the rectal area (caused by the mucous produced by females when laying eggs), sleep disturbances, irritability, abdominal pain.

Complications: UTIs, secondary bacterial infection

Non-Pharmacological Treatment

Good Hygiene

1. Have a shower at night and then again in the morning to remove infected eggs and any eggs laid over night. Wash around the anus well.
2. Frequently change bed clothes/bedding/towels/underwear/sleepwear. Eggs stick to this materials - wash in hot water and keep separate to other washing material, else keep in airtight sealed bag.
3. Avoid shaking bed linen/duvet/towels in the morning
4. Frequently vacuum furniture, bedroom, and **around the toilet** to remove any eggs
5. Avoid scratching perianal area, cut nails and scrub them- depositing of eggs under fingernails can cause re-infection
6. Avoid eating food in the bedroom due to the higher risk of contact with eggs

For Children:

1. Undress children in the shower so that eggs do not get deposited on the bed or carpet.
2. Wash hands after attending to them.
3. Dress them in snug, fitting clothes to prevent scratching

Pharmacological Therapy

All contacts must be treated

1. *Antihelmintics*: Mebendazole, Pyrantel — both also come as chocolate squares (chewable tablets)
2. *Itch Relief*: Hydrocortisone (topical)

Category	Ingredients	Patient Counselling	Side Effects
Anthelmintics	[PHARMACY ONLY] <i>First line</i> Mebendazole (Vermox) Pyrantel (Combantrin)	<ul style="list-style-type: none">• 100 mg (1 chocolate square) as a single dose; if reinfection occurs second dose may be needed after 2 weeks• Treat family contacts	GI upset mostly
Anti-inflammatory (itch-relief)	[PHARMACIST ONLY] Hydrocortisone cream 1%	<ul style="list-style-type: none">• Wash the anal area with warm water and soap & avoid scratching.	None unless inappropriate use

Osce Points

- Recent travel
- **Check for broken or weeping perianal skin**

Cryptosporidium Infections

Description

Cryptosporidium is a microscopic parasite that causes the diarrhoea disease, cryptosporidiosis. Oocysts transmitted via faecal-oral route

Signs & Symptoms

Prolonged diarrhoea, stomach pain, nausea, weight loss

Pharmacological Treatment

1. Nitazoxanide (broad spectrum thiazolidine antiparasitic)

Giardia Lamblia Infections

Description

Giardia is a tiny parasite that causes the diarrhoea disease, giardiasis. It is found on surfaces, in soil, for, or water that has been contaminated with faeces from infected animals. Cysts transmitted via faecal-oral route

Signs & Symptoms

Prolonged diarrhoea (temporary lactase deficiency), abdominal pain, bloating, weight loss

Pharmacological Treatment

1. Metronidazole (but resistance..)



Did You Know?

Metronidazole is an antimicrobial that requires cessation of alcohol while on treatment - it causes something called a 'disulfiram-like' reaction.

INFLAMMATORY GI CONDITIONS

Introduction

Before we look into inflammatory conditions, it is first important to understand how they come about.

The gut immune system, also known as the Gut-Associated Lymphoid Tissue (GALT) is a complex structure that allows the absorption of nutrients whilst protecting the GI tract from microbes.

Immune factors help the barrier maintains its integrity to ensure any ingested microbes remain in the gut lumen. In the event that the epithelium senses bacteria, M Cells will transport those antigens into Peyer's Patches, which are localised areas of lymphoid cells that project onto the lumen of the gut. This activates the travel of sensitised T cells towards the tissue to help eliminate any pathogens.

If the barrier is healthy and intact

Antigens will remain in the gut and not infiltrate/penetrate other structures. T-cells will thus proceed to die by apoptosis as they aren't needed.

If the barrier is leaky

Antigens will not be contained within the gut - this results in the further recruitment of T-cells resulting in inflammation. While this is useful in the destruction of microbes, it can also extend to the barrier itself as inflammatory mediators generally aren't specific. This can eventually open doors to a vicious cycle of chronic inflammation where further microbes enter tissue and further inflammatory mediators are recruited.

Inflammatory Bowel Disease (IBD)

Description

IBD is a group of chronic inflammatory conditions of large or small intestine. It is the result of a dysbiosis that occurs as a result of environmental changes and a genetic predisposition. Translocation of luminal antigens due to a faulty barrier function results in an inflammatory response.



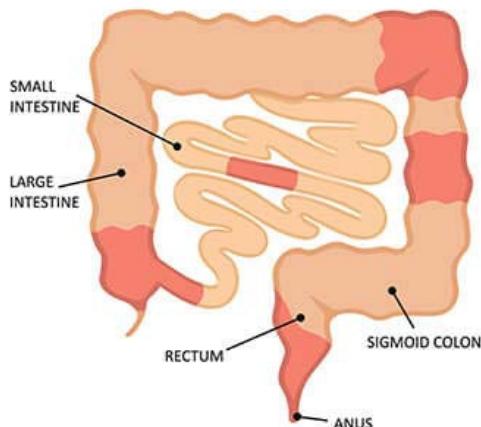
IBS ≠ IBD

Whilst often confused, Inflammatory Bowel Syndrome **is not** Inflammatory Bowel Disease. IBS is a chronic syndrome made up of a group of symptoms. IBD, on the other hand, refers to inflammation or chronic swelling of the intestines. An easy way to remember this is focus on the fact that the latter is a *disease*.

There are 2 types exist: Crohn's Disease (CD) and Ulcerative Colitis (UC).

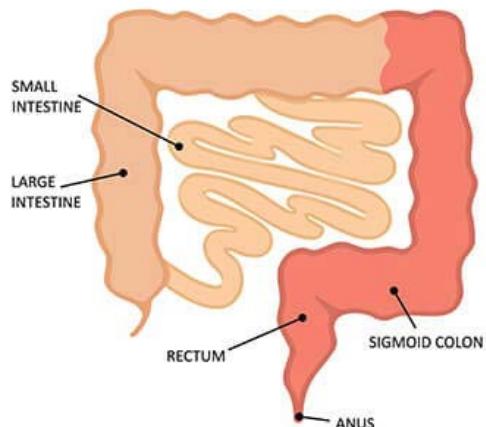
CROHN'S DISEASE

PATCHY INFLAMMATION THROUGHOUT SMALL AND LARGE BOWEL



ULCERATIVE COLITIS

CONTINUOUS AND UNIFORM INFLAMMATION IN THE LARGE BOWEL



	Crohn's Disease	Ulcerative Colitis
Continuity	Discontinuous patchy gut inflammation with skip lesions	Continuous and uniform inflammation with no skip lesions .
Affected Areas	Can affect ANY part of the GIT (mainly ileum and colon)	Affects the large intestine only (colon) .
Level of Damage	Transmural inflammation, affecting all layers of the bowel wall.	Superficial inflammation, affecting only the mucosa and submucosa of the colon.
Bloody Diarrhoea	Rare	Common
Strictures	Common	Rare
Fistulae	Common	Rare
Role of Smoking	Increases likelihood of developing	Decreases likelihood of developing
Bowel Cancer Risk	Low Risk	High Risk

Mild - Mod Severity	<ul style="list-style-type: none"> Frequent diarrhoea Mild abdominal pain 	<ul style="list-style-type: none"> Up to 4 loose stools (may be bloody) Mild abdominal pain
Mod-Severe Severity	<ul style="list-style-type: none"> Frequent diarrhoea Abdominal pain Fever, weight loss, anaemia 	<ul style="list-style-type: none"> 4-6 loose stools per day (may be bloody) Moderate abdominal pain Anaemia
Very Severe	<ul style="list-style-type: none"> High fever, severe weight loss Persistent vomiting Evidence of intestinal obstruction or abscess 	<ul style="list-style-type: none"> More than 6 blood loose stools per day Fever anaemia, rapid heart rate

Risk Factors

- Genetic:* immune regulation genes
- Environment:* diet change, stress, frequent antibiotic use, smoking, microflora/infection

Diagnosis

No diagnostic test. Recommend gastroenterology assessment (history, presentation, endoscopy, blood tests for inflammation & infection)

Signs & Symptoms

IBS comes with three sets of symptoms:

- General Symptoms e.g. constipation, diarrhoea, bloating, gas AND
- Intestinal Symptoms: diarrhoea (blood, mucus), rectal bleeding, anaemia, abdominal pain, fatigue, weight loss (reduced appetite), fever
- Extra-intestinal symptoms: ocular, ulcers, mouth, liver, biliary tract (gallstones), kidneys, skin manifestations, osteoporosis, thromboembolic event, arthropathy, circulation.

Complications: Colorectal cancer

Non-Pharmacological Treatment

- Smoking cessation (protective factor in UC, but need to focus on **long term health risks**)
- Healthy diet (reduce trans/sat fats, artificial sweeteners, processed meat)
- Exercise & Weight loss (weight gain can occur with steroid use)

Pharmacological Treatment: Note the use of **different** formulations (oral, suppositories, enemas)

[Inflammatory Bowel Disease BPAC Guidelines](#) [Starship Guidelines for Inflammatory Bowel Disease](#)

- Aminosalicylates:* Mesalazine, Olsalazine, Sulfasalazine
- Corticosteroids:* Hydrocortisone, Beclomethasone, Budesonide, Prednisone
- Antibiotics:* Metronidazole, Ciprofloxacin
- Immunosuppressants:* Methotrexate, Azathioprine, Mercaptopurine, TNF Antagonists, Cyclosporin
- Biologics:* Infliximab, Adalimumab

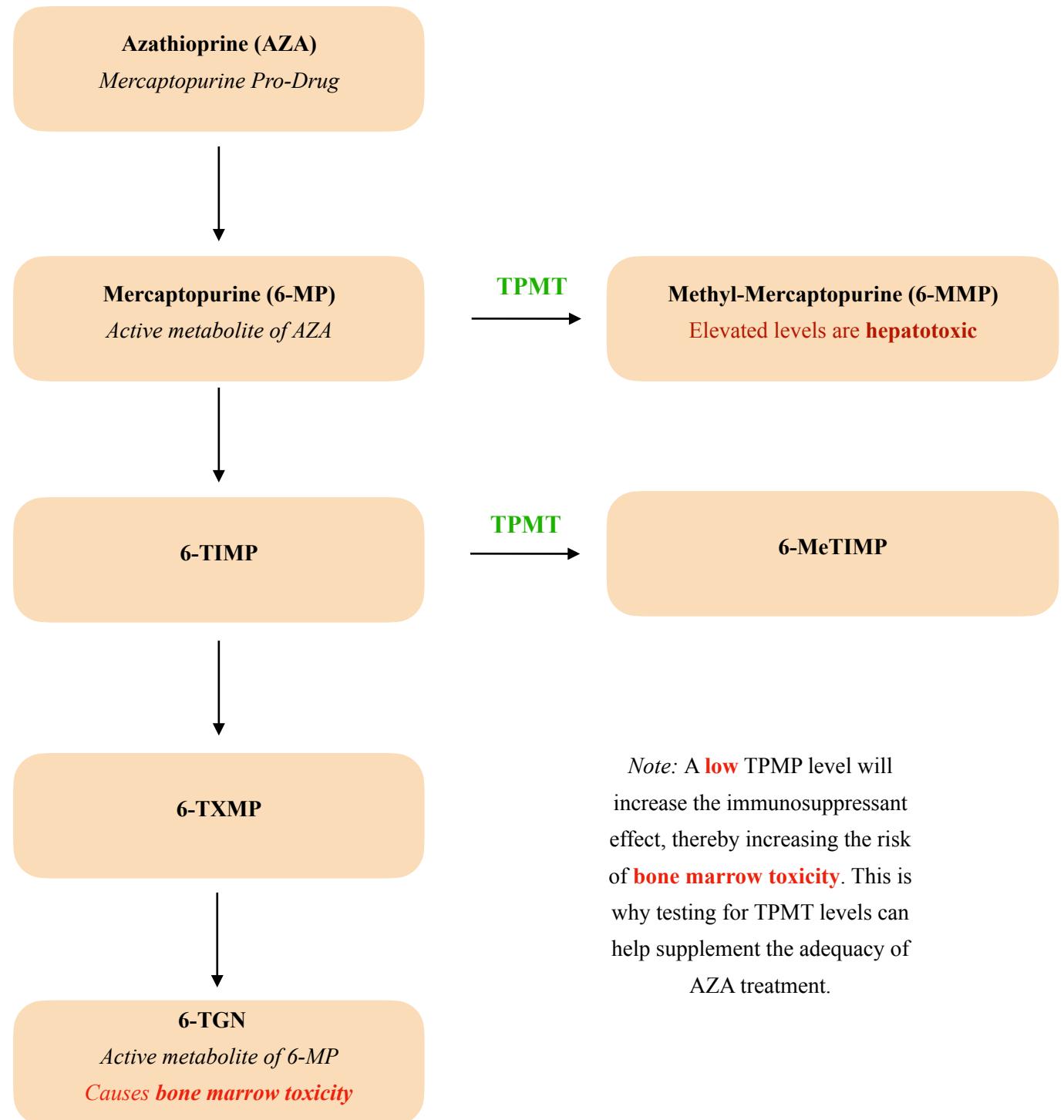
Class	Ingredients	Mechanism of Action	Patient Counselling & Usage Guidelines	Side Effects
Anti-Inflammatory	<p>[PRESCRIPTION] <i>Aminosalicylates (5-ASA/ Mesalazine/mesalamine)</i></p> <p>Asacol (pH Sensitive Release at > 7) (Suppository / Tablet)</p> <p>Pentasa (Time Sensitive Delayed Release) (Enema / Suppository / Granule sachet)</p>	<p>Structurally similar to NSAIDs. Mesalazine (5-ASA) decreases inflammation by blocking cyclooxygenase and inhibiting prostaglandin production in the colon.</p> <p>Originally used sulfasalazine (5-ASA + sulfapyridine). However the sulpha component was associated with ADE. Aminosalicylates only contain 5-ASA.</p> <p>pH sensitive release: good for reaching the colon and the terminal ileum — high concentrations in specific areas → UC</p> <p>Time sensitive release: provides an even coat all throughout the GI tract (release at all pH) — low concentrations in all areas → Crohn's</p>	<ul style="list-style-type: none"> First line for mild to moderate IBD. Predominantly for UC (ASA not as effective in Crohn's) Use along with oral/topical formulations for targeted delivery Corticosteroids or ASAs are often initiated for symptoms when waiting for a IBD assessment Report unexplained bleeding, bruising, fever, malaise, purpura, sore throat, ADR 	ASAs increase the risk of blood dyscrasias and other blood disorders. N/V/D, abdominal pain, headaches
	<p>[PRESCRIPTION] <i>Glucocorticoids (Prednisone is mainstay)</i></p> <p><i>Oral:</i> Prednisone, Budesonide <i>IV:</i> Methylprednisolone, HC <i>Enema:</i> HC <i>Rectal Foams:</i> HC</p>	Immunosuppressants. Inhibit phospholipase A2, up regulate anti inflammatory proteins and decrease expression of pro-inflammatory proteins. Need to taper if used orally >2 weeks. Careful of HPA suppression.	<ul style="list-style-type: none"> For acute treatment if ASA is ineffective, or if severe symptoms Used for flare ups to induce remission, not for IBD maintenance treatment (avoid long-term use) Monitor risk of osteoporosis and osteonecrosis with oral corticosteroid use 	Skin thinning, easy bruising. Effects on carbohydrate (promotes gluconeogenesis and worsens hyperglycaemia), protein (skeletal muscle wasting, HTN) and fat (redistribution of body fat)
Antibiotics	<p>[PRESCRIPTION] <i>Antibiotics</i></p> <p>(Metronidazole, Ciprofloxacin)</p>	N/A	<ul style="list-style-type: none"> Usually short-term when inducing remission if evidence of infection e.g. abscesses in conjunction with incision and drainage or perianal fistulising disease. 	N/A
Immuno Supressants	<p>[PRESCRIPTION] <i>Immunomodulatory</i></p> <p>Azathioprine → Mercaptopurine, Methotrexate</p>	<p>Azathioprine (prodrug): metabolised to mercaptopurine which disrupts DNA/RNA cell division by acting a false nucleotide in the cell cycle of T and B cells. TPMT Testing is recommended to ensure this therapy is appropriate.</p> <p>MTX: folic acid antagonist, inhibiting normal cell division. Also a immunosuppressant.</p>	Azathioprine/mercaptopurine: <ul style="list-style-type: none"> For acute treatment if ASA is ineffective. May be combined with corticosteroids until remission is achieved Compatibility in pregnancy? <p>MTX:</p> <ul style="list-style-type: none"> MTX Monday, Folic Acid Friday Contraindicated in pregnancy 	Blood dyscrasias
Biologic Response Modifiers	<p>[PRESCRIPTION] <i>Biologics</i></p> <p>(Adalimumab, Infliximab)</p>	Biologics work by interrupting immune system signals involved in the inflammatory process that result in damage to tissue.	<ul style="list-style-type: none"> Do not give live vaccines when using a biologic Consider flu vaccine Patient to report any signs of sickness 	Hypersensitivity reactions (including malaise, dizziness, vomiting, diarrhoea, fever, rigours, myalgia, arthralgia, rash, hypotension and interstitial nephritis—calling for immediate withdrawal), dose-related bone marrow suppression

Monitoring

- Control of disease: Markers of inflammation: CBC, CRP, ESR, TPMP, prevention of flares, S/S
- Liver and kidney function, Electrolytes (if dehydrated)

TPMT Testing

- Provides an indication as to whether AZA therapy is appropriate for the patient. Low levels TPMP may be a contraindication due to bone marrow toxicity.



Mouth Ulcers (Minor Aphthous Ulcers)

Description

Mouth ulcers is a collective term to describe superficially painful oral lesions. They are a form of stomatitis (inflammation on inside of mouth) due to damaged epithelium and its underlying lamina propria. Most causes are **idiopathic**.



Risk Factors

- Trauma, **stress**, irritation, food sensitivity, nutritional deficiencies, family history
- Infections, inflammatory disorders, radiation
- Medicines: NSAIDs, β -blockers, cytotoxic agents, OCs, immunosuppressants (methotrexate, azathioprine, chemotherapy)

Signs & Symptoms

Roundish, grey-white lesion, painful, <1 cm in diameter, located on side of cheeks, tongue, inside of lips.

Non-Pharmacological Treatment

1. Pain relief
2. Salt water (saline mouthwash)
3. Sucking on ice
4. Avoiding irritating foods (acidic, spicy, salty, abrasive)
5. Reduce stress
6. Keep well hydrated to avoid dry mouth

Pharmacological Treatment

Self-resolving within 7-14 days

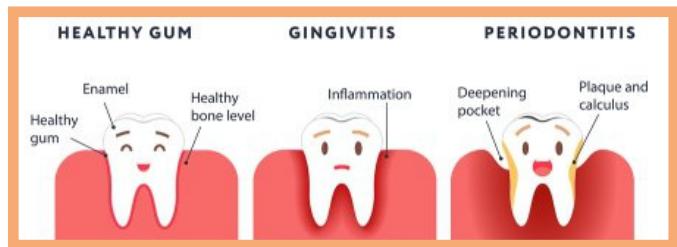
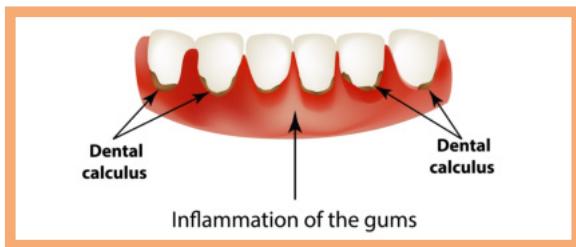
- *Antiseptic Mouthwashes*: Chlorhexidine — *avoid alcohol-based mouthwashes & lauryl sulfate*
- *Anti Inflammatory*: Bonjela
- *Anti-Infective + Anaesthetic*: Medijel
- *Corticosteroid*: Oracort, Kenalog
- *General Pain Relief*: Panadol

Category	Ingredients	Patient Counselling	Side Effects
Antiseptic Mouthwash	[GENERAL SALE] <i>Chlorhexidine Mouthwash</i> Corsodyl	These fight the bacteria, viruses and fungi that can cause infection, they also reduce pain and encourage quicker healing. Use twice a day and rinse mouth well after brushing your teeth; toothpaste can inactivate some mouthwash ingredients.	N/A
Anti-inflammatory pain reliever	[GENERAL SALE] <i>Choline Salicylate gel</i> Bonjela	<ul style="list-style-type: none"> Wipe the surface and apply to affected area not more often than every 3 hours Avoid prolonged or excessive use, do not use in under 4 months old. 	N/A
Anti-infective + Local Anaesthetic	[GENERAL SALE] <i>Aminoacridine + Lignocaine</i> Medijel Gel	<ul style="list-style-type: none"> Apply gel to area; repeat application after 20 minutes if necessary 	Local Irritation
Corticosteroid Anti-inflammatory	[PHARMACIST ONLY] <i>Triamcinolone Dental Paste</i> (Oracort, Kenalog)	<ul style="list-style-type: none"> Most effective if applied in the ‘prodromal’ phase. Apply a small amount to coat lesion with a thin film, preferably at night; may also be applied after meals if required Refer if no improvement after 7 days treatment. Caution in diabetes 	May cause occasional exacerbation of local infection

Gingivitis

Description

Inflammation of the gums caused by excess build-up of plaque on teeth consisting of bacteria and food particles. If left untreated, it will progress into periodontitis (spontaneous bleeding, taste disturbances, bad breath, difficulty while eating).



Risk Factors

Diabetes, cigarette smoking, poor nutritional status, poor oral hygiene. Worsens during pregnancy. Medicines causing gum bleeding (NSAIDs, warfarin, heparin) and gum hypertrophy (phenytoin, ciclosporin).

Signs & Symptoms

Swollen, red gums which bleed easily with slight trauma (brushing teeth), visible plaque, bad breath

Red flags: unprovoked bleeding gums

Complications: Can lead to Gingival Hyperplasia and Periodontitis

Non-Pharmacological Treatment

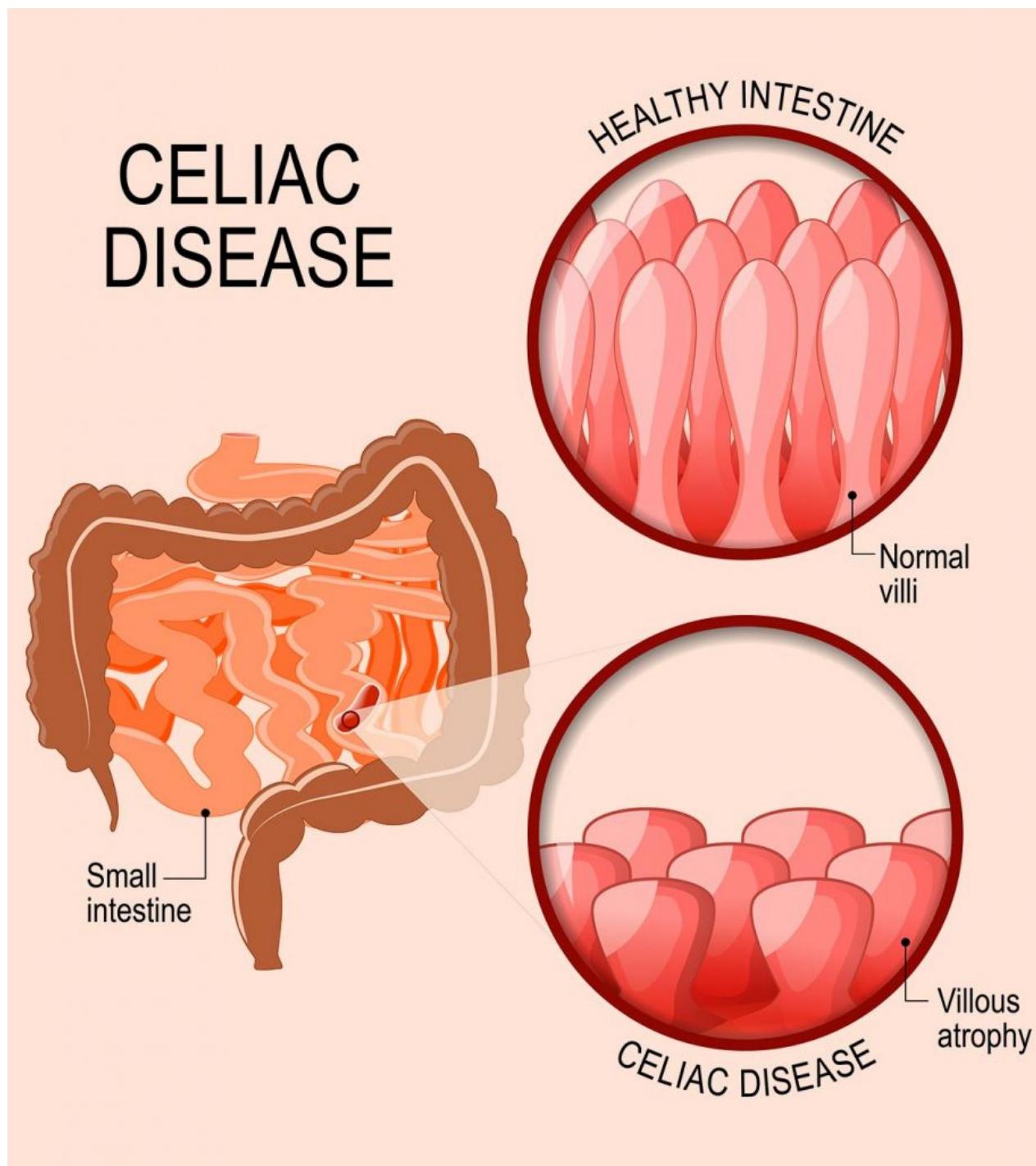
1. Good oral hygiene: fluoride toothpaste **after** eating, flossing, mouthwash (chlorhexidine)
2. Do not over-brush/over-clean teeth
3. Identify medical causes
4. Adjust anti-coagulant doses if causative

Coeliac Disease (Gluten-Sensitive Enteropathy)

[BPAC Be Quick Coeliac Disease Guidelines](#) [Coeliac New Zealand](#)

Description

Celiac disease is a chronic inflammatory disease of the small intestine. It is an immune-mediated reaction to gluten (protein found in wheat, barley, and rye) leading to inflammation and damage/flattening of the villi lining the intestine. This results in malabsorption of nutrients (iron, folic acid, calcium, fat-soluble vitamins) and other medical complications.



Risk Factors

Genetic and environmental (e.g. childhood infections, first exposure to gluten, breastfed infant).

Signs & Symptoms

Asymptomatic, GI problems (diarrhoea, bloating, gas, abdominal pain, N/V), malnutrition-related problems (weight loss, fatigue, anaemia, bone/joint pain, osteoporosis, depression).

Diagnosis

Coeliac Screen

- *Gold-standard* (if patient is still consuming gluten): duodenal biopsy, serology testing (antibodies to TG2 or deaminated gluten peptides)
- If patient is not consuming gluten: gluten challenge
- History, check first degree relatives for coeliac disease

Non-Pharmacological Treatment

- A life-long gluten-free diet is the only effective treatment for people with coeliac disease; such a diet can help manage symptoms and promote intestinal healing — refer to a dietitian and recommend registration with [Coeliac New Zealand](#)
- Pneumococcal vaccination (not funded)
- Optimise bone health: adequate intake of calcium and vitamin D

Treatment Failure

If there is an inadequate response to a gluten-free diet after 12 months and other diagnoses have been excluded, consider non-responsive or refractory coeliac disease; refer the patient to a gastroenterologist for further assessment

Monitoring

Frequency

1. While patient is getting adjusted on a gluten free diet, conduct follow ups every 3-6 months
2. Once symptoms have resolved following establishment of the gluten-free diet, conduct reviews annually

Parameters — See [BPAC Be Quick Coeliac Disease Guidelines](#) for full list

- Monitor growth in children (BMI)
- Lab tests: ferritin, folate, vitamin B₁₂

Lactose Intolerance

[Health Navigator Lactose Intolerance](#),

Description

Lactose intolerance is a common condition in which your body finds it difficult to digest lactose, a sugar found in cows', goats' and sheep milk.

Pathophysiology

Lactose intolerance occurs when your body doesn't produce enough of the enzyme lactase, which breaks down lactose in your gut. Most people with lactose intolerance can tolerate some milk and milk products. You may need to experiment to find what's right for you. There is no way to increase your body's production of lactase. However, many people can avoid the discomfort associated with lactose intolerance by changing their diet.

Risk Factors

1. *Genetics*: Inherited forms of lactase deficiency
2. *Gut damage* e.g. after surgery, stomach infections, coeliac disease, Crohn's disease

Signs & Symptoms

The symptoms of lactose intolerance are usually non-specific and vary between people. You will usually experience symptoms within 30 minutes to 2 hours after eating. These include:

- Flatulence (wind)
- Bloating
- Tummy pain or discomfort
- Nausea (feeling sick)
- Diarrhoea (runny poos)

Complications: osteopenia, osteoporosis, malnutrition from lack of protein/calcium/vitamins from milk

Pharmacological Treatment

[BPAC Diagnosing & Managing Lactose Intolerance](#)



Trial & Error

Completely removing lactose from your diet can actually make symptoms of intolerance worse when you next (intentionally or accidentally) consume milk or milk products. It is important to trial & error to see how much you can tolerate - that is generally the main way to navigate lactose intolerance.

ACID RELATED GI CONDITIONS

Introduction

Before we look into these conditions, it is first important to understand the process of gastric acid secretion. The process is essentially overseen by 3 cells:

Overview of a Gastric Gland

- Stomach Interior -

Goblet Cells
Produce mucus
Lubricates food and protects stomach lining from acid

Parietal Cells
Produce acid (H^+)
Necessary for the digestion and absorption of food

Chief Cells
Produce pepsinogen → pepsin (by H^+)
Stomach enzyme that digests proteins in ingested food

- Stomach Wall -

Modulation of Gastric Acid Secretion

Phase 1 - Cephalic

Sight, smell, taste or though food act as stimuli to initiate the process of acid secretion.

Phase 2 - Gastric

Food stretches stomach wall, which triggers further secretions and eventually aims to reduce acid secretion.

Phase 3 - Intestinal

Once chyme enters the duodenum, this phase activates negative feedback mechanisms to reduce acid secretion.

Gastric Defences Against Acid

1. *Primary*: Lower Oesophageal Sphincter (prevents reflux of acid)
2. *Secondary*: Mucous Layer (prevents damage to stomach lining - prostaglandins stimulate its production)
3. Bicarbonate Secretion (increases pH to prevent acid-related damage)

Protective Factors

Mucus, Bicarbonate, Mucosal Blood Flow, Prostaglandins, Cell Renewal, Growth Factors

Aggressive Factors

Gastric acid, pepsin, NSAIDs, stress, alcohol, H.Pylori, free radicals.

Dyspepsia (Indigestion)

Description

Dyspepsia is the feeling of burning, pain, or discomfort in the digestive tract, that occurs often after eating or drinking. Please note that dyspepsia is not a diagnosis but rather a description of symptoms that may indicate an upper GI tract disease. However, in majority of cases there is no clear pathological cause and many people can manage symptoms themselves without consulting their GP.

Risk Factors

- H.Pylori infection
- *Lifestyle:* dietary factors, smoking, obesity, stress
- *Medicines:* **NSAIDs** e.g. aspirin



Stomach Protection For NSAIDs

Patients who may need NSAIDs long term should be prescribed omeprazole co-currently for stomach protection.

Signs & Symptoms

- Bending over **worsens** symptoms.
- Pain, feeling of fullness, abdominal discomfort
- Bloating, flatulence, N/V, heartburn.

Red Flags

- Anaemia, weight loss, anorexia
- Recent onset of progressive symptoms, black tarry stools (melaena)

Non-Pharmacological Treatment

1. Avoid spicy or fatty foods
2. Smaller and more frequent meals
3. Do not eat quickly, chew well.
4. Avoid eating at night
5. Prop head up on pillow when lying down
6. Weight loss (~ 0.5kg per week)
7. Lower fat diet (reduce sat/trans fats)
8. Alcohol restriction
9. Reduce caffeine intake (tea, coffee, sodas)
10. Smoking Cessation (consider NRT)

Pharmacological Treatment

Enhances Mucosal Defence

1. *Antacids:* Mylanta, Gaviscon, Quick Eze
2. *Prostaglandin Analogues:* Misoprostol

Acid Suppression

3. *Proton Pump Inhibitors (PPI):* Omeprazole

4. *H₂ Receptor Antagonists:* Ranitidine

Note: PPIs show a higher level of efficacy in the treatment of GORD and peptic ulcers than H₂RAs



Drug Interaction Note

All PPI's & H₂RA's will interfere with the absorption of drugs that require an **acidic** environment for optimal absorption (e.g. ketoconazole, itraconazole) — and vice versa.

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Enhance Musocal Defence	[GENERAL SALE] <i>Antacids</i> Mylanta (Al/Mg) Gaviscon (Ca ²⁺ /Na ⁺) Quick Eze Chewable Tablets (Ca ²⁺ /Mg)	Antacids aim to rapidly neutralise excess stomach acid by binding to H ⁺ so it is not available to bind to Cl ⁻	<ul style="list-style-type: none"> Mylanta: Shake bottle (if oral liquid) <p>Antacids combining Al & Mg will be less likely to produce undesirable constipation or diarrhoea because:</p> <ul style="list-style-type: none"> Al, Ca = constipation Mg = diarrhoea 	GI Upset, Bloating, flatulence
	[PHARMACY ONLY] <i>Prostaglandin Analogues</i> Misoprostol (Cytotec)	They mimic endogenous prostaglandins (PGE2 and PDI2) which protect the stomach lining by: <ol style="list-style-type: none"> Reducing gastric acid secretion Stimulating mucous and bicarbonate secretion 	<ul style="list-style-type: none"> Teratogenic - need effective contraception 	
Acid Supression	[PHARMACY ONLY] <i>Proton Pump Inhibitors (PPI)</i> Omeprazole (Losec) Pantoprazole (Panzop) Lansoprazole (Lanzol)	PPIs are prodrugs with enteric coatings that reduce acid secretion. They require activation in acidic environment - this allows them to irreversibly inactivate ATPase pumps (which cause H ⁺ secretion). Acid secretion can only resume when new pumps are synthesised (after 24 - 48 hours)	<ul style="list-style-type: none"> Take before a meal in the morning Swallow, do not crush/chew. Also prescribed for long term NSAID use to prevent gastric ulcers. Do not use prn Caution in hepatic disease Not recommended in breastfeeding 	GI Upset, Bloating, flatulence
	[MULTIPLE] <i>H₂ Antagonists</i> Ranitidine (Zantac) Famotidine (Pepzan)	Competes with histamine and blocks H ₂ receptors on parietal cells, preventing cAMP from entering the pump so acid production is reduced.	<ul style="list-style-type: none"> Swallow the tablets whole with water. Measure the liquid with an oral syringe or measuring spoon. 	

Gastrointestinal Oesophageal Reflux Disease (GORD)

Description

GORD is a chronic acid reflux condition. It occurs when stomach acid flows back into the oesophagus, irritating the lining of the oesophagus. This is caused by a weakened or relaxed lower oesophageal sphincter muscle.

Risk Factors

H.Pylori, dietary factors, smoking, obesity, stress, medicines (NSAIDs, aspirin)

Signs & Symptoms

Same as dyspepsia.

Belching, **heartburn** (burning sensation in chest), nausea, regurgitation

Non-Pharmacological Treatment

Same as dyspepsia.

Pharmacological Treatment

Same as dyspepsia.

Peptic Ulcer (Gastric & Duodenal)

Description

A sore on the lining of the stomach (gastric), small intestine (duodenum), or oesophagus caused by acid, pepsin, bile overwhelm defensive factors of GI mucosa.

Risk Factors

H.Pylori, long term use of NSAIDs

Signs & Symptoms

Stress, spicy foods, alcohol and coffee do **not** cause peptic ulcers, but can **worsen symptoms**.

Constant, annoying, gnawing, burning stomach pain (worse on an empty stomach, between meals, or at night), nausea, **feeling of fullness**, bloating, belching, heartburn.

Red flags: Vomiting, black or tarry stools, unexpected weight loss

Non Pharmacological Treatment

Same as dyspepsia.

Pharmacological Treatment

Same as dyspepsia.

Stress Related Mucosal Injury

Description

Ulcers of the stomach or duodenum caused by illness or trauma, requiring intensive care. Often due to excess acid or mucosal ischaemia.

Pharmacological Treatment

1. IV H₂ blocker
2. IV PPIs
3. Protectant: Sucralfate (sticks to damaged ulcer tissue and protects against acid and enzymes so healing can occur)

Zollinger-Ellison Syndrome

Description

Zollinger-Ellison syndrome is a rare digestive disorder that results in too much gastric acid as a result of **tumours** (gastronomas) in the pancreas or duodenum. This **excess gastric acid** can cause **peptic ulcers** in the stomach and intestine.

Pathophysiology

Gastric-secreting tumours causing the overproduction of acid, resulting in peptic ulcers

Signs & Symptoms

Abdominal pain, diarrhoea, burning, aching, gnawing, heartburn, N/V, weight loss

Pharmacological Treatment

Removal of tumour

MEDICINES-RELATED GI CONDITIONS

Introduction

As we've seen, medications can be the culprits behind many GI conditions, particularly those with anticholinergic activities— this section will focus specifically on medication-induced conditions such as gum bleeding, dry mouth, mucositis, gingival hyperplasia, osteonecrosis of the jaw and developing teeth abnormalities.

Anticholinergic activity of medications

Class	Drugs	Relative anticholinergic potency
Antihistamines	H ₁ receptor antagonists, first-generation: brompheniramine, carboxamine, chlorpheniramine, clemastine, cyproheptadine, dimenhydrinate, diphenhydramine, doxepin, doxylamine, hydroxyzine, meclizine, triprolidine, others	High
	H ₁ receptor antagonists, second-generation: fexofenadine, cetirizine*, loratadine, desloratadine, levocetirizine, others	Low
Antiparkinson	Benztropine, trihexyphenidyl	High
	Amantadine, bromocriptine, entacapone	Low
Analgesic	Opioids: codeine, hydrocodone, fentanyl, meperidine, methadone, morphine, oxycodone, tramadol, others	Low
Antimuscarinic, overactive bladder	Darifenacin, fesoterodine, flavoxate, oxybutynin, solifenacin, tolterodine, trospium	High
Antimuscarinic, spasmolytic	Atropine, belladonna-containing medications, clidinium-chlordiazepoxide, dicyclomine, hyoscamine, glycopyrrolate, homatropine, methscopolamine, propantheline, scopolamine (hyoscine)	High
Antimuscarinic, inhaled bronchodilator	Ipratropium, tiotropium	High (local effect)
Antimuscarinic, ophthalmic drops (mydriatic/cycloplegic)	Atropine, cyclopentolate, homatropine, scopolamine	High (local effect)
Cardiovascular	Disopyramide	Low
Gastrointestinal	Antiemetics (eg, hydroxyzine, meclizine, promethazine, scopolamine); also refer to first-generation antihistamines above	High
	Domperidone, loperamide, prochlorperazine	Low
	H ₂ receptor antagonists (cimetidine, famotidine*)	Low
Muscle relaxant	Orphenadrine, tizanidine	High
	Cyclobenzaprine*, baclofen, methocarbamol	Low
Psychotropic	Antipsychotics, first-generation: chlorpromazine, fluphenazine, loxapine, methotrimeprazine (levomepromazine), thioridazine, trifluoperazine	High
	Antipsychotics, first-generation: haloperidol, perphenazine*, others	Low
	Antipsychotics, second-generation: clozapine	High
	Antipsychotics, second-generation: olanzapine*, quetiapine*, iloperidone, risperidone, others	Low
	Benzodiazepines: chlordiazepoxide, clonazepam, temazepam, triazolam	Low
	Selective serotonin reuptake inhibitor (SSRI) antidepressants: citalopram, fluoxetine, fluvoxamine, paroxetine*	Low
	Tricyclic antidepressants: amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, others	High
Other neurologic	Carbamazepine, lithium, nefazodone, oxcarbazepine, phenelzine, trazodone	Low

Abnormal Bleeding of the Gums

Description

Abnormal bleeding of gums, often presenting when brushing teeth. It can be a very common symptom of gum disease but also other conditions.

Cause

Brushing too hard, ill-fitting dentures, *haemophilia*, *pregnancy*, deficiencies, *leukaemia*, medicines affecting blood clotting (warfarin, dabigatran rivaroxaban, aspirin, clopidogrel, enoxaparin).

Signs & Symptoms

Abnormal bleeding

Pharmacological/Non-Pharmacological Treatment

Dependent on cause

Monitoring (Anti-Coagulants)

1. Warfarin | INR
2. Enoxaparin & Rivaroxaban | anti-Xa levels
3. Dabigatran | Renal Function + aPTT + Tt

Dry Mouth (Xerostomia)

[NZF Drugs that Act on the Oropharynx](#), [Health Navigator Dry Mouth](#)

Description

Saliva is the mouth's natural lubricant and cleanser. Soft tissues of the mouth can become inflamed when the mouth is dry, making it more susceptible to infection (gum disease). Lack of saliva can cause tooth decay and gum disease.

Causes

- Anticholinergics (antimuscarinics, antinicotinics; 3s' = Spit, See, Shit)
- Antihistamines (1st gen)
- Antihypertensives (ACEI, CCBs, Diuretics)
- Antidepressants (TCAs)
- Anti-psychotics
- Decongestants
- Parkinson's Medications
- Opiates
- Radiotherapy or Chemotherapy
- Medical conditions: depression, anxiety, diabetes, Parkinson's

Signs & Symptoms

- Feeling of sticky dryness in your mouth, needing to sip water a lot, bad breath and mouth sores.
- Your mouth is painful, red or swollen, has sore white patches.
- Change in taste
- Symptoms other than dry mouth, eg, dry eyes

Complications: Any problems associated with poor oral hygiene: cavities, ulcers, etc...

Non-Pharmacological Treatment

- Adequate fluid intake (e.g. sipping water regularly)
- Avoid caffeinated drinks (teas, coffee, sodas) and tobacco
- Chewing gum (to stimulate saliva production)

Pharmacological Treatment

- Pilocarpine eye drops used orally (unlicensed/unapproved)
- Artificial saliva

Oral Mucositis (Stomatitis)

Description

This is a painful inflammation and ulceration of the mucous membranes lining the digestive tract (especially mouth and throat)



Cause

Chemotherapy, radiation, smoking, **methotrexate, 5-FU**

Risk Factors

- Pre-existing oral lesions/infections
- Poor dental hygiene/dentures
- Ethnicity (white > black)
- Smoking, alcohol consumption, malnutrition

Complications

- Infections (due to broken skin)
- Nutritional disorders (as painful to swallow)
- Severe pain
- Compromised airway (due to inflammation)
- Tissue necrosis
- Significant bleeding

Signs & Symptoms

Painful, difficulty eating, swelling of mouth

Prevention

- Remove risk factors (e.g. dental therapy)
- Drink adequate water
- Saline and bicarbonate mouth rinse

Non-Pharmacological Treatment

Diet

- Avoid acidic citrus food, hard, spicy, scratchy foods. Eat soft things.
- Stop smoking
- Nutrition: enteral feeding for protection
- Stay hydrated, avoid caffeine, fizzy drinks, alcohol
- Use oral probiotic lozenges and zinc supplements

Oral Care

- Rinse mouth before and after meals and at bedtime with:
 - Normal saline +/- baking soda
 - Chlorhexidine and benzylamine mouthwash
 - Avoid alcohol based mouthwashes
- Use a soft toothbrush with toothpaste that doesn't contain SLS and other irritants
- Floss gently
- Use lip balm to keep lips hydrated

Pharmacological Treatment

Oral Care

- Magic mouth wash
- Saliva substitutes

Pain Relief

- Analgesia (topical lidocaine, topical morphine, oral morphine if severe)
- Morphine infusion

Other

- Folinic acid to counteract methotrexate
- Diarrhoea associated mucositis can be treated with loperamide or octreotide as second line.

Gingival Hyperplasia

Description

Overgrowth of gum tissue around the teeth. Can often look “puffy”



Causes

- Poor oral hygiene
- Drug induced: **anti-epileptics (phenytoin, carbamazepine, lamotrigine, topiramate)**, CCBs (commonly DHP-CCB such as amlodipine), β -blockers, immunosuppressants e.g. ciclosporin ([azithromycin can reverse this](#))

Signs & Symptoms

Bad breath, inflammation, pain

Pharmacological Treatment

Note: if drug-induced, symptoms usually resolve upon the cessation of the drug.

Medication-Related Osteonecrosis of the Jaw (MRONJ)

Description

Osteonecrosis is bone death, caused by distraction of blood flow to the part of a bone

Risk Factors

1. Bisphosphonates (resorption of bone, making it more brittle)
2. Monoclonal antibodies
3. Long term steroids

Signs & Symptoms

Pain in the jaw.

Non-Pharmacological Treatment

- Dental examination prior to starting medication to make sure they do not require extensive dental work
- Good oral hygiene

Medicines and Developing Teeth

Description

Children's adult teeth are forming in the jawbone not long after birth — these are vulnerable to different medications

Risk Factors

1. Tetracycline antibiotics can cause permanent yellow/brown staining of teeth
2. Excessive fluoride can cause fluorosis

Non-Pharmacological Treatment

Fluoride toothpaste for children (adult toothpaste has excess fluoride that can cause fluorosis)



CHAPTER 5

THE HEPATIC SYSTEM

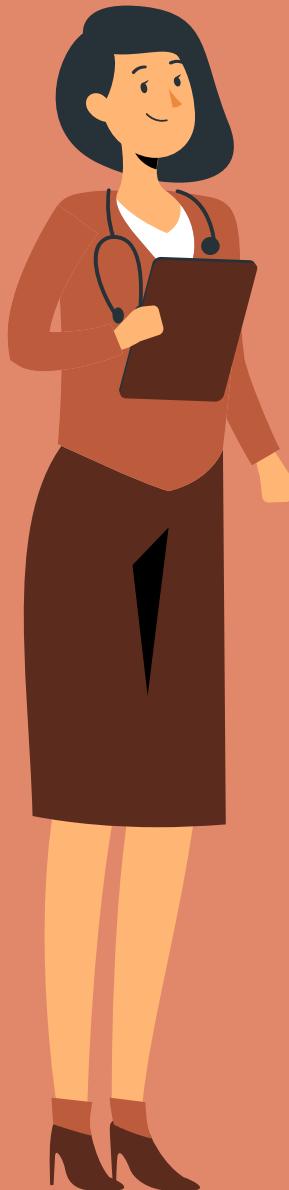


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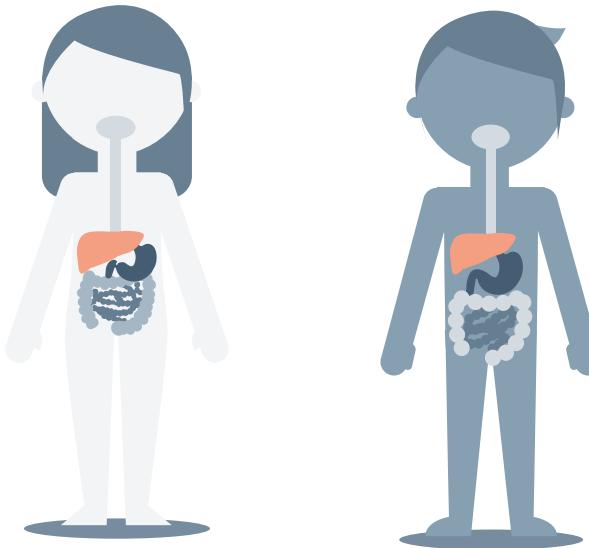
Chapter 5

The Hepatic System

General Overview of Liver Anatomy

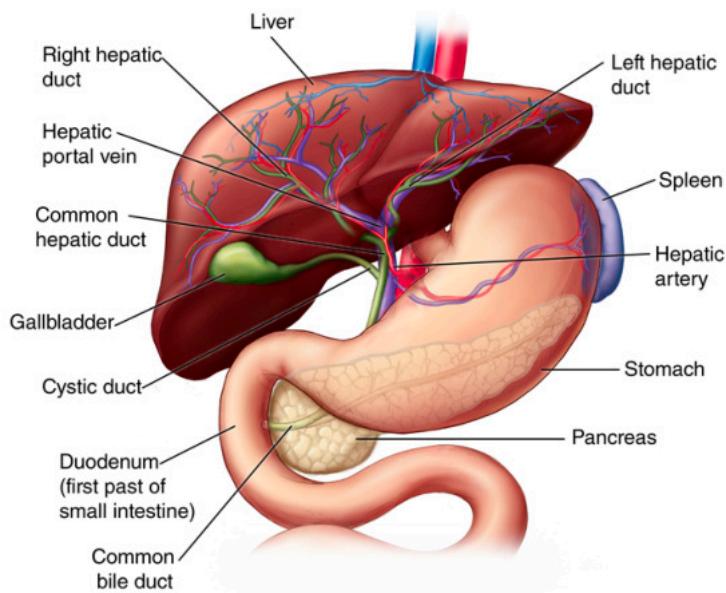
Introduction

The liver is another organ belonging to the digestive system. It is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney, and intestines



Purpose

When the liver has broken down harmful substances, its by-products are excreted into the bile or blood. Bile by-products enter the intestine and leave the body in the form of faeces. Blood by-products are filtered out by the kidneys, and leave the body in the form of urine.



Liver Function Tests (LFTs)

There are three types of tests conducted:

1. Tests for Hepatocyte Integrity (AST, ALT)
2. Tests for Biliary Excretory Function (GGT, ALP, Bilirubin)
3. Tests for Liver Function (Albumin, PT, Proteins, Ammonia)

Hepatocyte Integrity Tests

AST, ALT

Biliary Excretory Function Tests

GGT, Alk Phos, Bilirubin

Liver Function Tests

Albumin, Prothrombin Time, Proteins, Ammonia

Let's start with the Hepatocyte Integrity Tests!

Tests For Hepatocyte Integrity Aminotransferases (AST, ALT)

Individual Elevation

Mild/Moderate AST & ALT elevation (2 - 20x normal)
Non-specific

- Night out at the club,
- Chronic viral hepatitis
- Alcohol hepatitis,
- Drugs (isoniazid, anticonvulsants)

Marked AST & ALT elevation (20 - 1000x normal)

Severe liver injury

- Ischaemic liver injury
- Acute viral hepatitis
- Fulminant necrosis
- Acute drug toxicity

Ratio Elevation

AST/ALT ratio > 2

Alcoholic hepatitis

alcoholics are often malnourished and lack vitamin B6 (used in ALT Formation)

Fluctuating AST & ALT

Hepatitis C

LFTs may be normal however

Aminotransferases ('transaminases') are intracellular enzymes involved in production of amino acids. They are found everywhere in the body but concentrations vary greatly in different tissues. Enzyme-tissue rich tissue leakage is thus often indicated by increased plasma concentrations of this molecule. There are two types of aminotransferases:

1. Alanine Transaminase (ALT)

This enzyme is found in very high concentration in the *liver* compared to organs. Elevations in this enzyme thus suggest specifically suggest **liver injury**

2. Aspartate Transaminase (AST)

This enzyme is found in high concentrations in *several organs*; thus **not specific** for liver injury. High AST could indicate: cardiac muscle injury, skeletal muscle injury, haemolysis, hepatocyte injury, hepatitis, cirrhosis, pancreatitis



How To Remember

Think ALT = Liver Trauma

Tests For Biliary Excretory Function

Alkaline Phosphatase Elevation (ALP)

Mild Elevation

Non-specific

- Hepatic disease (non specific)
- Pregnancy
- Child bone growth

Marked Elevations

Severe cholestatic disease mainly or:

- Cancer
- Bone disease (osteomyelitis, bony metastasis)

ALP & GGT Elevation

GGT & ALP Elevation

Suggests *cholestasis*

Isolated GGT Elevation

Suggests *alcohol abuse*

Bilirubin Elevation (Hyperbilirubinaemia)

Bilirubin elevation can be caused by:

1. Over-production e.g. increased RBC breakdown
2. Decreased clearance
3. Impaired metabolism e.g. rare genetic disorders

The type can indicate the specific cause

1. *Elevated conjugated bilirubin* suggests an obstructive cause (biliary tree blockage, cholelithiasis)
2. *Elevated unconjugated bilirubin* suggests haemolytic anaemia & inflammation (cholangitis).

Bile is a digestive fluid produced by the liver to perform 2 primary functions:

1. To carry away waste.
2. To break down fats during digestion.

Concentrations of three markers are used to understand whether the biliary-excretory function has been impaired.

1. Alkaline Phosphatase (ALP)

ALP is an enzyme that cleaves phosphate from proteins. It is found on the canalicular surface of hepatocytes, bone, kidney, placenta. Thus while elevated concentrations in plasma indicate damage to the biliary tract, it is **not specific** for liver disease. The clinical value of this test is mainly to detect **cholestatic disease**.

2. Gamma Glutamyltranspeptidase (GGT)

This enzyme is found on the canalicular surface of hepatocytes, kidney, pancreas, and gut. Thus it is also not **not specific** for liver disease.

3. Bilirubin

Bilirubin is a metabolic product of red blood cells. Hepatocytes absorb it (unconjugated), and conjugate it so that it can be removed from the biliary tract. If in excess, bilirubin begins to deposit in skin, sclera, mucus membranes - which is dangerous as it causes jaundice.

Tests for Liver Function (Hepatic Synthetic Capacity)

There are two markers that indicate hepatocyte damage: elevated concentrations of PT and reduced albumin may indicate hepatocyte damage. Abnormal LFTs may be present in asymptomatic patients and/or can be extra-hepatic in origin. They do **not** necessarily indicate liver dysfunction.

Drug-Induced LFT Elevations

1. ALT, AST, ALP, GG
2. Mild elevation can be caused by enzyme-inducing drugs (phenytoin, carbamazepine, rifampicin)

Child-Pugh Score

A scoring system used to determine long term survival (prognostic measure for liver disease). Maybe links to drug metabolism. Factors included in the score are albumin, bilirubin, INR, ascites, encephalopathy.

$$INR = \left(\frac{PT_{\text{test}}}{PT_{\text{normal}}} \right)^{ISI}$$

1. Albumin

- Albumin is a protein synthesised by the liver, with a half life of 20-30 days.
- Low albumin: liver disease (cirrhosis), inflammation, malnutrition, protein loss.
- Reduced concentrations can alter vascular oncotic pressure, causing ascites and oedema

2. Prothrombin Time (PT) & International Normalised Ratio (INR):

- Most **clotting factors** are produced in the liver, thus clotting time tests help us understand its function.
- Elevated PT and INR (longer clotting time) occurs due to:
 - Decreased synthesis of clotting factors: **liver disease**, inherited deficiency, warfarin, ↓ vitamin K
 - Decreased activity: thrombin inhibitors (dabigatran)

Classification	ALT	AST	ALP	GGT	Conjugated Bilirubin
Specific Marker For Hepatocyte Damage	Yes	-	-	-	-
Would Suggest Cholestatic Disease	-	-	Yes	Yes	Yes
Mildly Elevated by Enzyme Inducing Drugs (e.g phenytoin)	Yes	Yes	Yes	Yes	-
Marked elevation 2-3 days after a paracetamol overdose	Yes	Yes	Yes	Yes	Yes

Enzyme Interactions

Introduction to CYP Enzymes

Drug interaction: Flockhart Table

Enzymes are involved in the metabolism of drugs for subsequent elimination, particularly cytochrome enzymes which are found at highest concentrations in the liver. Some drugs are enzyme inhibitors and/or inducers, which thereby increase or decrease the drug concentration.

	Substrates	Enzyme inhibitors	Enzyme inducers
CYP1A2	Caffeine, clozapine	Ciprofloxacin	Smoking
CYP2C9	Amitriptyline	Fluconazole, amiodarone	
CYP3A4	Atoravastatin	Macrolides, azole antifungals (itraconazole), diltiazem, verapamil, grapefruit, HIV antivirals	Anticonservants (carbamazepine, phenytoin, phenobarbitone), Rifampicin, HIV antivirals,
CYP2D6		Fluoxetine, paroxetine, bupropion, terbinafine	
CYP2E1			Alcohol
Other:			BBQ foods, st johns wort

HEPATIC INFECTIONS & DAMAGE

Introduction

We will look into only 2 conditions in this chapter: viral hepatitis and paracetamol poisoning

Viral Hepatitis (A, B, C)

[BPAC Introduction to Hepatitis Types](#)

Description

Hepatitis is the inflammation and swelling of the liver. The liver is a vital organ that processes nutrients, filters the blood, and fights infections. When the liver is inflamed or damaged, its function can be affected. Heavy alcohol use, toxins, some medications, and certain medical conditions can cause hepatitis.



Hepatitis A, B and C

Hepatitis A, B, and C are all caused by different viruses. While these three viruses can cause similar symptoms, they differ in several ways, including how they're transmitted and treated. Additionally, hepatitis A only causes an acute illness while hepatitis B and C can become chronic.

Pathophysiology

Viral hepatitis has two main hallmarks:

1. Hepatocyte injury — ‘ballooning degeneration’
2. Hepatocyte death & necrosis

	Hepatitis A	Hepatitis B	Hepatitis C
Family	Family Picornaviridae	Family Hepadnaviridae	Family Flaviridae
Virus	RNA virus	DNA virus	RNA virus
Transmission	<ul style="list-style-type: none">Contaminated food and waterPerson-Person TransmissionNO mother-fœtus transmission	<ul style="list-style-type: none">BloodBodily fluids (not saliva) e.g. sexual contactPerinatal transmission	<ul style="list-style-type: none">BloodBodily fluids (not saliva) e.g. sexual contact
Signs & Symptoms	<i>Acute, self-limiting infection</i> <ul style="list-style-type: none">Malaise, nausea, dark urine, jaundice, hepatomegaly	<i>Acute or chronic, may be self limiting</i> <ul style="list-style-type: none">Asymptomatic ('silent epidemic' but may show symptoms a few <u>decades</u> later)Mild non-specific symptoms (fatigue, joint pain, loss of appetite, nausea, abdominal pain)	<i>Acute or chronic, may be self limiting</i> <ul style="list-style-type: none">Easy bleeding, bruising, fatigue, itchy skin, loss of appetite
Treatment	<ul style="list-style-type: none">None - self-limiting	<ul style="list-style-type: none">Oral Antivirals: Tenovovir, disoproxil, entecavir	<ul style="list-style-type: none">Treatment (curative): DAAs
Vaccine (Prevention)	<ul style="list-style-type: none">Vaccination: Avaxim (HAV), Twinrix (HAV & HBV)	<ul style="list-style-type: none">Vaccination: Infranrix-hexa DTaP-IPV-HepB/Hib vaccine	<ul style="list-style-type: none">No Vaccine

Risk Factors

- Contact with contaminated bodily fluids

- Blood transfusions, dirty needles

Non-Pharmacological Treatment

- Alcohol avoidance
- Monitor medications affecting the liver

Pharmacological Treatment

- Direct Acting Antivirals (DAA): targets the virus
- Indirect Acting Antivirals (IAA): targets the host/host cell processes
- nRTI (nucleoside/nucleotide reverse transcriptase inhibitors): Tenofovir, disoproxil, entecavir

Prevention

- Passive immunisation: IG
- Active immunisation: heat killed vaccines
 - Avaxim (HAV)
 - Twinrix (HAV & HBV)
 - Infanrix-hexa (DTaP-IPV-HepB/Hib)

Vaccine	Vaccine Type	When
Avaxim (HAV)	Inactivated	
Twinrix (HAV & HBV)	Inactivated	Risk groups only
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months

Paracetamol Poisoning

[NZF Paracetamol Poisonding](#) [Starship Hospital Paracetamol Poisoning in Paediatrics](#)

Please visit *Chapter 20 - Fever, Pain & Infections* for more information on Paracetamol

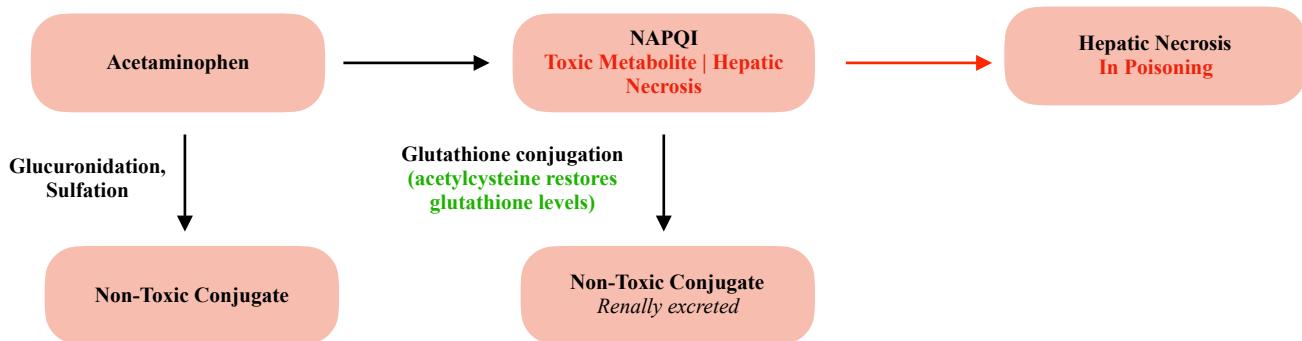
Description

Paracetamol poisoning describes excess concentration of the drug in serum levels. In the body, when paracetamol is metabolised, a toxic metabolite NAPQI is produced via the glucuronidation/sulfation/metabolism pathway via CYP450s. In therapeutic amounts, glutathione is able to detoxify NAPQI, however in overdoses, glutathione levels deplete resulting in the buildup of NAPQI which leads to hepatic necrosis and renal failure. Note that younger children appear to be less susceptible to hepatotoxicity.



Paracetamol Doses

- Usual dose is 3 - 4g daily in adults, and 60mg/kg/day (maximum) in children
- Doses of > 12g or > 150mg/kg carries a significant risk of hepatotoxicity
- Doses of > 20 - 30g carry a very high risk of severe hepatotoxicity
- Unintentional overdose can occur with doses 6 - 10g in susceptible adults e.g. alcoholics, enzyme inducing drugs, nutritionally deplete individuals (frail elderly, eating disorders)



Diagnosis

Use *nomogram* to interpret serum acetaminophen concentration in relation to time ingested

Signs & Symptoms

- Often asymptomatic in the first 24 hours, some will experience anorexia, nausea & vomiting
- LFTs may not usually be elevated until > 18 hours (all LFTs can be elevated)
- Maximum liver damage occurs after 72 - 96 hours
- Liver failure may develop after 3 - 5 days: yellow skin and blood clotting problems

Pharmacological Treatment

1. Activated charcoal (if < 4 hours post ingestion & if tablet or capsule form of paracetamol ingested)
2. N-Acetylcysteine (converts to GSH)
3. Dialysis

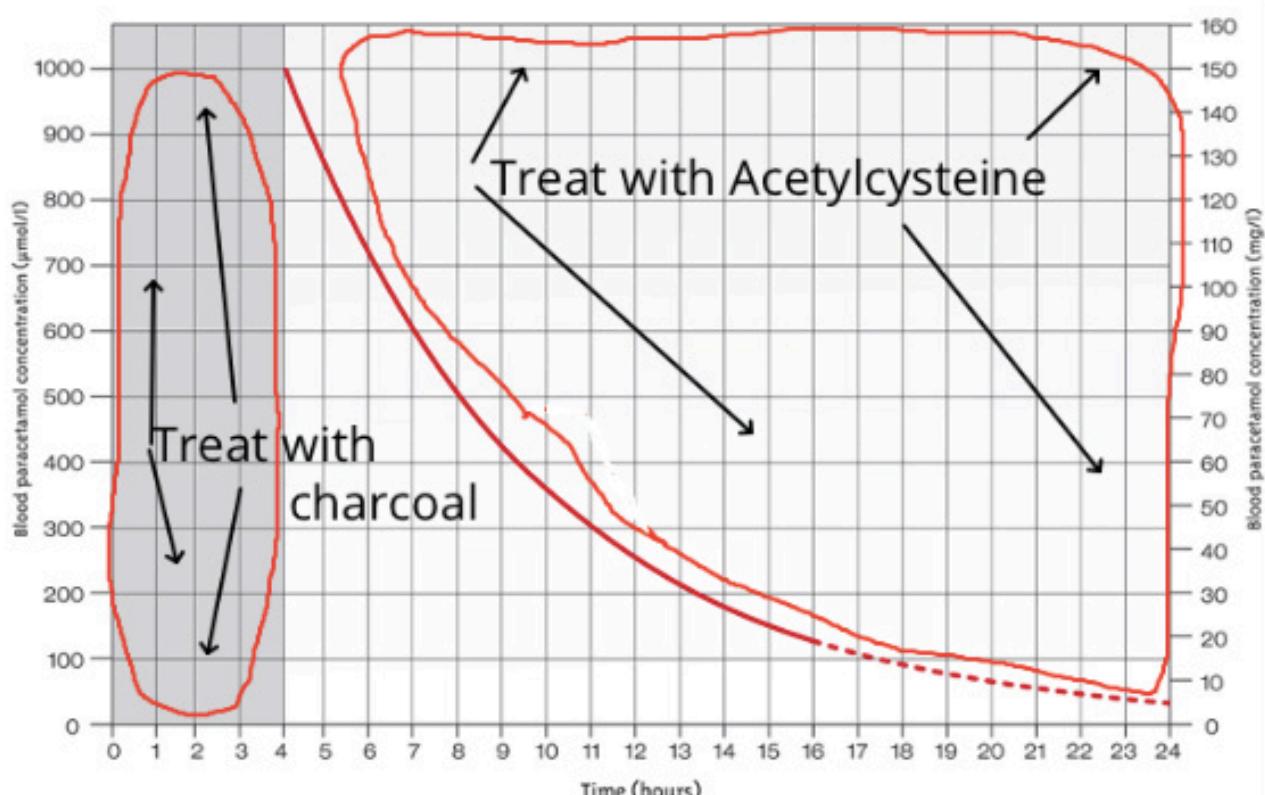
Category	Ingredients	Mechanism of Action	Side Effects
Antidote	N-Acetylcysteine (DBL Acetylcysteine)	<p>Acetylcysteine is thought to act as a sulphhydryl group donor to restore depleted hepatic glutathione levels to prevent the synthesis of toxic paracetamol metabolites, or by acting as an alternative substrate to conjugate with toxic metabolites. These actions reduce hepatic damage in paracetamol poisoning</p> <p>Given as an injection for rapid action. Stop infusion when ALT or AST decreasing, INR < 2.0, and patient is clinically well</p>	N/V/D, constipation, rash
	Activated Charcoal	Charcoal acts as a magnet and aims to prevent absorption of the poison from the stomach into the body	N/V/D, black stools

Monitoring

Acetylcysteine can be ceased if **all** the following criteria have been met:

- Patient is clinically improving
- ALT or AST is decreasing
- INR is improving and < 2
- Acetaminophen (paracetamol) concentration is less than 10 mg/L

Note: Small fluctuations in ALT (e.g. +/- 20 U/L or +/-10%) are common and don't on their own indicate the need for ongoing acetylcysteine.





CHAPTER 6

THE MUSCULOSKELETAL SYSTEM



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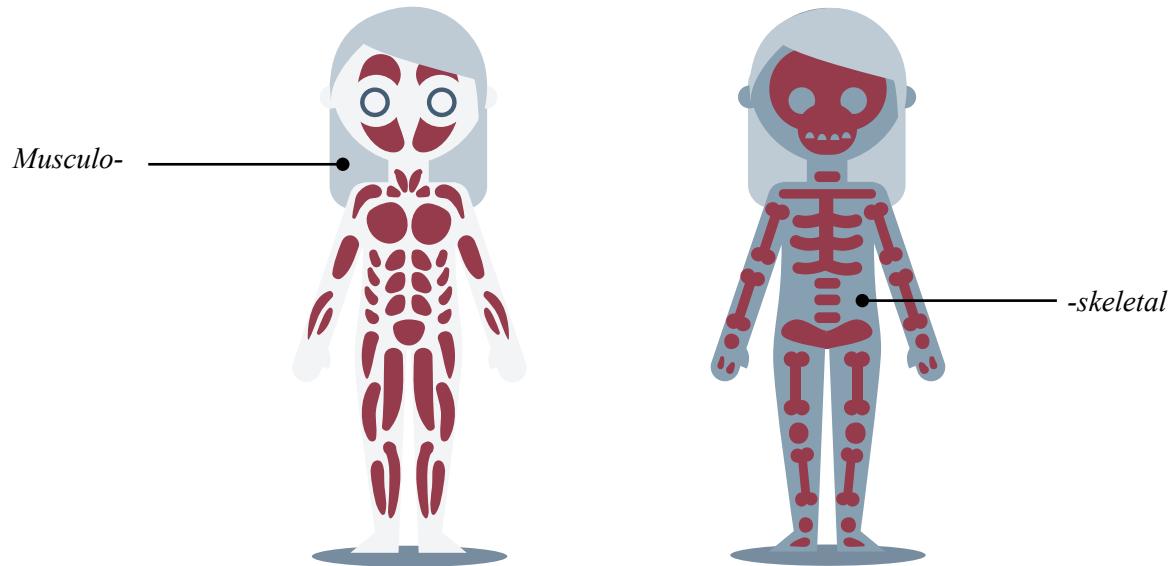
Chapter 6

The Musculoskeletal System

General Overview of Musculoskeletal System Anatomy

Introduction

The musculoskeletal system is a human body system that provides our body with movement, stability, shape, and support. It is *made up of bones, cartilage, ligaments, tendons and muscles*. Tendons, ligaments and fibrous tissue bind the structures together to create stability, with ligaments connecting bone to bone, and tendons connecting muscle to bone.



ARTHRITISES

Introduction

Arthritis is a painful disease that causes inflammation and stiffness of the joints and there are over a 100 types that exist - each with different causes including wear and tear, infections and underlying diseases. Generally, symptoms of arthritis include pain, swelling, reduced range of motion and stiffness and can be improved with medication, physiotherapy and sometimes surgery. We will cover 2 classes of arthritises: infectious and inflammatory ones.

A Note on NSAIDs

You will note that NSAIDs have a prominent role in the management of Arthritises. There is no clear evidence to suggest any one particular NSAID is superior in terms of efficacy for treating patients - the decision as to which NSAID is appropriate should be based on patient response, preferences, risk factors, risk of ADRs and co-morbidities.



Selecting NSAIDs

Please see *Chapter 20 - Fever, Pain & Infection* for more information on how to do this as well as how NSAIDs work. Patients may need to trial more than one NSAID in order to find one which provides sufficient analgesia.

Inflammatory Arthritises

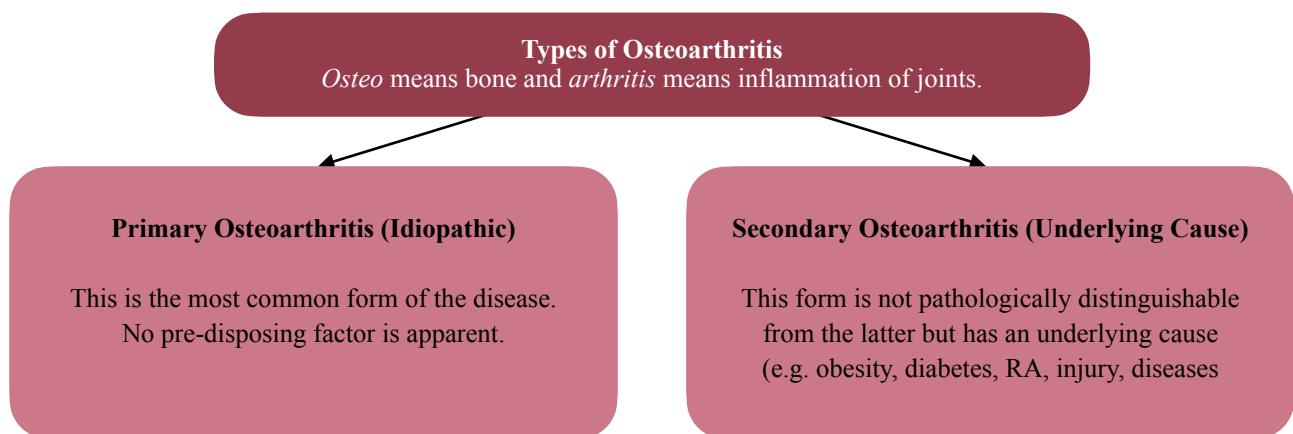
We will cover the following inflammatory arthritises: OA, RA & Gout. Please find a summary below.

Category	Osteoarthritis	Rheumatoid Arthritis	Gout
Cause	Mechanical Wear & Tear	Autoimmune Disease	Hyperuricaemia
Localised Symptoms	Limited to affected joints (non-systemic disease)	No (systemic disease)	Limited to affected joints (non-systemic disease)
Pattern of Affected Joints	OA is unilateral , usually on weight bearing joints or joints closest to fingernails, and eventually progresses to the other side.	RA is peripheral, polyarthritis and symmetrical and often in the smaller joints	Most commonly found at the base of the big toe and unilateral .
Joint Symptoms	Pain increases gradually	Pain increases gradually	Pain appears in acute attacks that reach threshold fast
Pain	Worsens after activity, improves with rest	Worsens after rest, improves with activity	-
Morning Stiffness Duration	< 30 minutes	> 1 hour	-
Radiography Findings	Osteophytes, sclerosis, narrowing of joint space (no correlation with timeline & severity)	Juxta-articular osteopenia, erosions, narrowing of joint space (in late disease)	presence of MSU crystals under polarised microscopy
Laboratory Findings	-	ESR, CRP, anti-CCP, RF	Evidence of Hyperuricaemia
Gender Distribution	Both genders affected depending on location of joint (e.g - men, hip OA women, hand OA)	Women more affected	Men more affected
NSAID of Choice	NSAID: Celecoxib		NSAID: Naproxen

Osteoarthritis (OA)

Description

Also known as Osteoarthrosis or Degenerative Joint Disease, Osteoarthritis is a chronic, mechanical wear & tear joint disease that occurs when the cartilage that cushions the ends of bones in your joints gradually deteriorates - this causes immobility and joint destruction.



Pathophysiology

The pathophysiology of osteoarthritis can be divided into 2 changes: articular, bone & other structures.

Articular Changes

Given it is a mechanical wear & tear disease, the main feature of osteoarthritis that we observe is the progressive degeneration of the **articular cartilage**, that occurs gradually and worsens over time (associated with advancing age). Towards the late stage of OA, the cartilage is generally observed to be hypo-cellular.

Bone Changes

The absence of cartilage means bones begin to rub onto one another - this causes them to grow thicker and harder. This is known as bony sclerosis. As a result of the friction, we also observe the formation of osteophytes - which are bony lumps on the edge of the bone.

Other Structures

Unfortunately this doesn't stop here, with the progression of the disease, we eventually see the the involvement of other structures including the subchondral bone, synovium, ligaments, and neuromuscular tissues.

Signs & Symptoms

1. OA usually affects **distal** joints in a **non-symmetrical manner** (one side of the body)
 - Examples include the knee, hip, hands (thumb base), foot (big toe base), neck, lower back
 - The knee and hands are usually affected in females while in males, it is the hip.
 - Neck/back and foot OA generally occurs equally in both genders
2. It causes joint pain that worsens with activity and improves with rest (**mechanical-wear disease**)
3. Stiffness after inactivity or in the morning lasting **< 30 minutes**
4. Gait abnormalities, reduced range of motion, immobility, muscle weakness, mild swelling
5. Osteophytes, crepitus, tenderness on palpitation, fatigue and sleep disturbances



Joint Pain in Osteoarthritis

As cartilage is *aneural*, joint pain arises from damage of other structures; synovial inflammation, joint capsule inflammation, subchondral bone micro-fractures, stretching of periosteal nerve endings from osteophytes, stretching of ligaments, muscle spasms.

Diagnosis

1. *Radiographic Findings*
 - While these are usually normal in early stage, with time we begin to observe osteophytes, subchondral cysts, narrowing of joint space, bone sclerosis and so forth.
 - However, these often do not keep up with symptoms nor correlate with severity.
2. *Laboratory Tests*
 - There is unfortunately no specific lab test that exists to diagnose OA because **it is not a systemic disease**. Other than the synovial fluid revealing mild leukocytosis, ESR, CBC, urine analysis will all return normal. However:
 - It may help identify an underlying cause in secondary OA e.g. diabetes
 - It is important in excluding other similarly presenting conditions e.g. gout, septic arthritis, RA

Risk Factors

Age, gender, obesity, heredity, injury, occupation, muscle weakness (muscles support joints)

Non-Pharmacological Treatment

1. Weight loss
2. Exercise
3. Joint protection
4. Assistive devices
5. Physiotherapy

Pharmacological Treatment (Analgesics)

BPAC Osteoarthritis Treatment Guidelines

Non pharmacological treatment such as exercise are the mainstay in preserving joint function - however as OA worsens with exercise, pharmacological treatment mainly centres around symptomatic relief using analgesics. See the next few pages for the treatment guidelines flowchart.

First Line

- Paracetamol

Second Line (in <75 years old)

- Capsaicin Cream
- Topical NSAIDs

Third Line

- Oral NSAIDs — **may need gastro-protection**

Alternatives

- Opioids
- Specifically for Knee OA: Duloxetine (SNRI), Intra-articular steroids, Hyaluronic Acid

Analgesics	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
General Analgesics	[GENERAL SALE] <i>1st Line</i> Paracetamol (Pharmacare)	Anti pyretic, analgesic but not anti-inflammatory	<ul style="list-style-type: none"> 1g QID Not helpful in hip/knee OA Do not use with other paracetamol containing products Careful with liver failure and concurrent alcohol use 	Liver Toxicity
	[GENERAL SALE] <i>2nd Line</i> Capsaicin Cream (Zostrix)	Produces burning effect to distract from pain.	<ul style="list-style-type: none"> Maximal effect by 4 weeks Tingling and burning sensation may occur 	Local skin irritation.
NSAIDs	[GENERAL SALE] <i>3rd Line - Topical NSAIDs</i> Diclofenac Gel (Voltaren Emulgel)	Reduces prostaglandin production by inhibiting COX enzymes	<p><i>Topical</i></p> <ul style="list-style-type: none"> Voltaren Emulgel topical - drug of choice. Topical recommended over oral in <75 years old and in Knee/Hand OA (but not Hip) Use 3-4 times daily, maximal effect by 2 weeks Effective if 1-2 joints are affected. 	GIMIRI
	[VARIOUS] <i>3rd Line - Oral NSAIDs + PPI</i> Ibuprofen (Brufen) Naproxen (Noflam, Naprosyn) Celecoxib (Celebrex) Diclofenac (Voltaren)	Reduces prostaglandin production by inhibiting COX enzymes	<p><i>Oral</i></p> <ul style="list-style-type: none"> Celecoxib - drug of choice. Note; all NSAIDs are of similar efficacy If taking long term should be taken with a PPI to prevent gastric ulcers 	GIMIRI
Opioids	[CONTROLLED DRUG] <i>4th Line - Opioids</i> Codeine (Codeine Phosphate) Morphine (M-Eslon/Sevredol) Tramadol (Arrow Tramadol)	Opioid agonists bind to opiate receptors in the brain and spinal cord altering the perception and response to pain.	<ul style="list-style-type: none"> Reserved for patients who cannot tolerate NSAIDs or fail to respond to them. May be prescribed with a laxative. <p>*Tramadol is a weak opioid - not classified as a CD.</p>	Sedation, respiratory depression, cough suppression, constipation, tolerance and dependence.
Alternatives specific for Knee OA	[PRESCRIPTION] <i>Alternative</i> Antidepressants Duloxetine (Duloxetine)	Nerve pain	<ul style="list-style-type: none"> Knee OA approved use Can be used as monotherapy or in combination with the above 	Nausea, Fatigue, Constipation
	[PRESCRIPTION] <i>Alternative</i> Intra-Articular Steroids Triamcinolone acetone, Methylprednisolone acetate	Reduce inflammation	<ul style="list-style-type: none"> Small temporary effect of 4-6 weeks but repeated injections can damage cartilage 	Cartilage damage
	[PRESCRIPTION] <i>Alternative</i> Hyaluronic Acid Injection		<ul style="list-style-type: none"> Reserved for patients who have failed other therapies as costs are high 	

Treatment Guidelines for the Management of Pain in Osteoarthritis

If pain relief is inadequate, move to the next step. If it is adequate, monitor and reduce use.

Step 1 - Non Pharmacological Treatment + Paracetamol
1g QID

Step 2 - Initiate Topical Options

e.g. capsaicin cream or topical NSAID such as diclofenac (voltaren emulgel)

Step 3 - Initiate Oral NSAID

If low risk of GI ADRs and no risk factors

Initiate low-dose non selective NSAID

If moderate risk of GI ADRs with 1-2 risk factors

Initiate low-dose non selective NSAID + Gastroprotection *OR*

Low-dose COX-2 Inhibitor

If high risk of GI ADRs with multiple risk factors

Initiate alternative therapy e.g. local injections, duloxetine, opioids *OR*

Low-dose COX-2 Inhibitor + Gastroprotection

Step 5

Full dose non selective NSAID or COX-2 Inhibitor +/- Gastroprotection

Supplement with local injections, duloxetine or opioids



Step 6

Surgery

Rheumatoid Arthritis (RA)

Description

Rheumatoid Arthritis is a chronic **autoimmune** inflammatory disorder that attacks the joints leading to their destruction, deformity, and loss of function.

Pathophysiology

Although the exact cause is uncertain, it can generally be traced back to a genetically susceptible host being exposed to an unknown antigen. This triggers a systemic immune response which not only induces an inflammatory cascade in the joints, but ends up affecting the whole body.

Thus, the pathology of this type of arthritis can thus be divided into two parts:

- 1) Joint Inflammation
- 2) Joint Destruction

Risk Factors

1. Genetic Factors e.g. certain alleles)
2. Environment Factors e.g. cigarette smoke, infectious agents, occupational exposures

Signs & Symptoms

Given that RA is a **systemic** disease, it has articular and extra-articular manifestations.

1. *Articular Manifestations*
 - Usually **symmetrical** and **polyarthritic** joints are affected e.g. hands, wrists, feet, elbows, shoulders, knees, ankles. Distal joints are usually spared.
 - Joint pain that **worsens with rest** and improves with exercise
 - Morning stiffness that can last **> 1 hour**
 - Reduced range of motion and grip strength
2. *Extra-Articular manifestations*
 - Cutaneous, ocular, pulmonary, cardiac, neuromuscular, haematological, musculoskeletal
 - Fatigue, anorexia, weakness, low-grade fever
 - Vague musculoskeletal symptoms (muscle pain, joint soreness)

Diagnosis

No specific test exists to diagnose RA.

1. *Radiographic Findings*
 - This evaluation becomes useful only in later disease - later stages show loss of cartilage, bone erosions, juxta-articular osteopenia and narrowing of joint space.

2. *Laboratory Tests*

- Non-specific: Rheumatoid Factor (RF), ESR, CRP, WBCs
- More specific: Anti-citrullinated protein antibodies (ACPA), WBCs in synovial fluid analysis

Non-Pharmacological Treatment

1. Exercise

Goals of Treatment

1. Achieve rapid/effective pain relief and provide cost effective therapy
2. Achieve disease remission & control
3. Improve QoL and maintain joint function
4. Prevent disease complications as well as treatment related adverse effects

Pharmacological Treatment

There is **no cure** and treatment aims to slow the progression of the disease.

1. NSAIDs: **Celecoxib**
2. Corticosteroids: Prednisone
3. DMARDs
 - Traditional DMARDs: MTX (first line), SSZ, HCQ, LEF
 - Biological DMARDs: TNF inhibitors, Abatacept, Rituximab, Tocilizumab, Fostamatinib
 - Targeted DMARDs: JAK Inhibitors

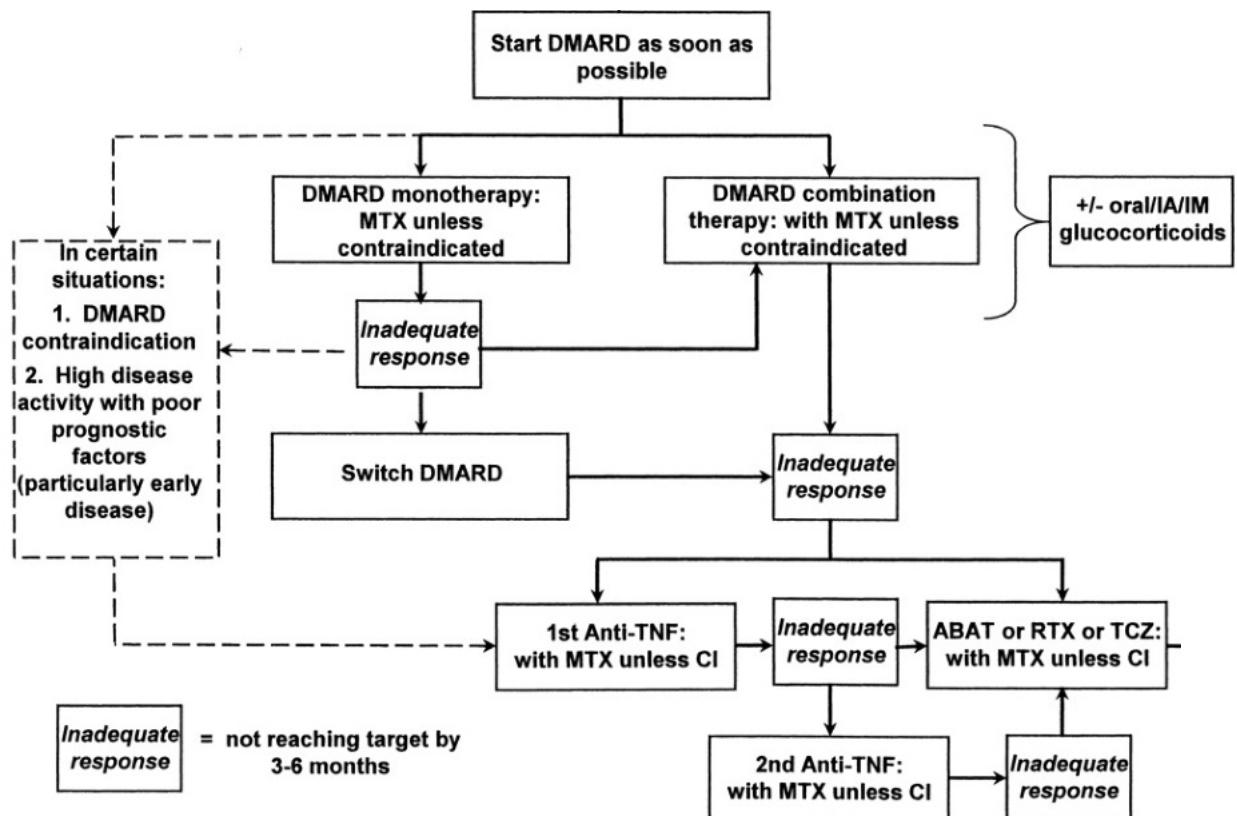


Old Paradigm vs New Paradigm

In the past, patients with RA would begin treatment with analgesics and slowly progress their way up to DMARDs - however this meant that patients would be given truly effective therapy too late. Thus the new paradigm in place suggests that patients diagnosed with RA should start treatment with a DMARD as soon as possible to improve treatment outcomes

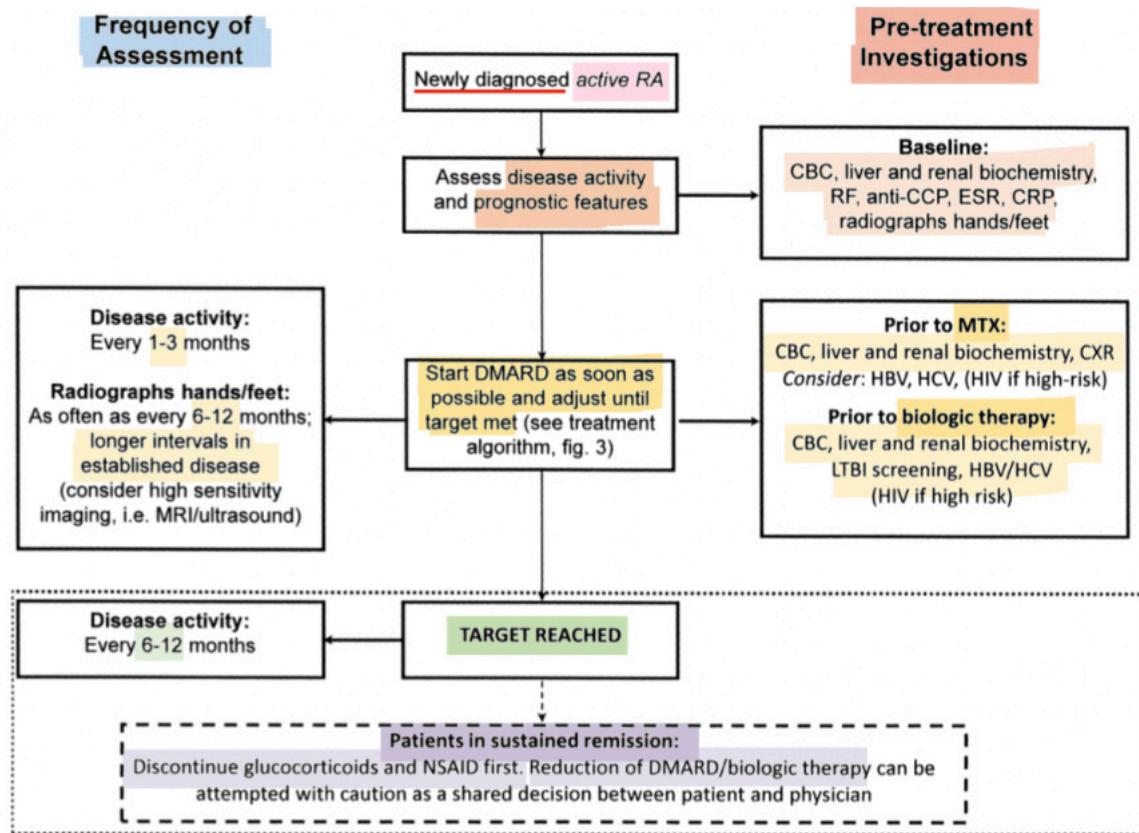
Category	Ingredients	Important Points	Mechanism of Action	Side Effects
Analgesics	[VARIOUS] <i>Oral or Topical NSAIDS</i> Celecoxib, Ibuprofen, Naproxen, Diclofenac Gel	<ul style="list-style-type: none"> NSAIDs in RA relieve pain and reduce inflammation. Celecoxib is the NSAID of choice to treat OA and RA but cannot be used in conjunction with MTX. 	Selectively inhibits COX Enzymes which reduce prostaglandin production, resulting in analgesic, anti-inflammatory and anti-pyretic effects.	GIMIRI
	[PRESCRIPTION] <i>Corticosteroids</i> (Prednisone)	<ul style="list-style-type: none"> Corticosteroids reduce inflammation and slow joint damage. 	Decrease inflammation by reducing production of inflammatory proteins	Thinning of bones, weight gain, HPA axis suppression and diabetes.
Traditional DMARDs tDMARDs mainly target inflammation by reaching therapeutic concentrations in joint capsules without reaching toxic levels in the serum.	[PRESCRIPTION] <i>1st Line - MTX</i> Methotrexate + Folic Acid (Trexate)	Onset of Action: 2-3 weeks PO/SC: MTX has weekly dosing (MTX Mondays, Folic Acid Fridays) MTX is an antimetabolite, cytotoxic and immunosupressing drug that is a folic acid antagonist. It inhibits DNA and RNA synthesis required for normal cell division. For this reason - folic acid supplementation is necessary.		Teratogenic Blood dyscrasias, Hepatotoxicity Stomatitis Thrombocytopenia
	[PRESCRIPTION] <i>2nd Line - SSZ</i> Sulfasalazine (Salazopryn)	Onset of Action: 8 weeks PO SSZ is an IBD drug - the sulfapyridine component is rumoured to have anti-rheumatic properties.		May turn skin and urine yellow/orange. Bleeding Ok in pregnancy
	[PRESCRIPTION] <i>2nd/3rd Line - HCQ</i> Hydroxychloroquine (Plaquenil)	Onset of Action: 6 weeks PO Anti-malarial drug that is a very weak DMARD. Proposed to have: Suppression of T-cells, Inhibition of leukocyte chemotaxis and Inhibition of DNA and RNA synthesis		HCQ has ocular toxicities Okay to use in pregnancy
	[PRESCRIPTION] <i>Last Line - LEF</i> Leflunomide (APO-Leflunomide)	Onset of Action: 6 weeks PO Anti-inflammatory properties are the result of immune regulation. LEF is the <i>last resort</i> treatment for rheumatoid arthritis if the other treatments have failed.		Teratogenic
Biological DMARDs Biologics are genetically engineered to block inflammation through highly specific action. A particular target is TNF-alpha. Combining MTX with TNF inhibitors makes them more useful.	[PRESCRIPTION] <i>TNF Inhibitors</i> (Etanercept, Infliximab, Adalimumab, Golimumab)	TNF Inhibitors are either monoclonal antibodies or soluble TNF receptor antagonists. Both bind to soluble and membrane bound TNF Onset of Action Etanercept: 1 - 4 Weeks Human fusion protein Onset of Action Infliximab: days - weeks Chimeric monoclonal antibody Onset of Action Adalimumab & Golimumab: days - months Fully human monoclonal antibody		Note: bDMARDs cause immunosuppression, therefore: <ol style="list-style-type: none"> Be careful of infections and live vaccines with biologics! Do not combine biologics! Be careful of red flags such as signs of infections e.g. opportunistic, bacterial or fungal infections, URTIs, CNS demyelinating syndrome → stop biologic immediately
	[PRESCRIPTION] <i>T cells</i> Abatacept <i>B cells CD20</i> Rituximab <i>IL-1</i> Tocilizumab <i>Syk Kinase</i> Fostamatinib	Onset of Action Abacept: 2 months Fully human fusion protein Onset of Action Rituximab: 2 months Chimeric monoclonal antibody Onset of Action Tocilizumab: 3 months Humanised monoclonal antibody with partial mouse protein.		
Targeted Synthetic DMARDs	[PRESCRIPTION] <i>JAK Inhibitors</i> (Tofacitinib)	N/A	N/A	N/A

Treatment Guidelines of Rheumatoid Arthritis



Monitoring

- Adjust therapy if no improvement at 3 months or target has not been reached by 6 months
- Monitor: active disease (every 1-3 months), remission (every 3-6 months), target reached (every 6-12 months)



OSCE Points — see [MTX RheumInfo](#)

- MTX takes 6-8 weeks to work
- Recommend birth control if there are chances patient could get pregnant
- Can be taken with food and/or in the evening to minimise stomach upset
- MTX Mondays, Folic Acid Fridays (folic acid decreases MTX side effects - always check patients understand the need to take folic acid and are adherent)
- Contact prescriber if SoB, mouth sores or signs of infection develop
- Avoid or limit alcohol to 1-2 standard drinks to prevent liver damage
- Minimise exposure to sunlight and increase sun protection measures.
- Emphasise on the importance of getting blood work done while on MTX (every 4-8 weeks)
- Do not take sulpha antibiotics or NSAIDs while on this medication.

Gout

Description

Gout is a chronic disease, and the most common form of *inflammatory* arthritis that exists. It is the result of monosodium uric acid crystals (MSU) depositing in peripheral joint spaces and peri-articular tissues, causing pain and discomfort. It usually affects the first metatarsophalangeal joint, ankle, knee, and elbow.

Pathophysiology

Uric acid is a resulting waste product of the natural bodily process of purine breakdown. It is excreted by the kidneys as the human body cannot break it down since we do not have a uricase enzyme. There are thus 2 things that cause hyperuricaemia:

1) Increased Uric Acid Production | 10%

- *Genetics*
- *Lifestyle*: alcohol, high purine diet (drinks with corn syrup e.g. soft drinks, red meat, seafood)
- *Medical Conditions*: lymphoproliferative & myeloproliferative disorders
- *Medicines*: warfarin, chemotherapy

2) Decreased Renal Clearance | 90%

- *Genetic*: GLUT 9 Polymorphism
- *Medical Conditions*: HTN, dyslipidaemia, CKD, obesity, T2/T1DM, hypo/hyperthyroidism
- *Medicines*: Diuretics, calcineurin inhibitors, laxative abuse, anti-TB, levodopa, **low dose aspirin**

Once hyperuricaemia occurs, factors such as low temperature or nocturnal articular dehydration can lead to the crystallisation, growth and deposition of MSU crystals in joint spaces and other extra-articular sites. It is the phagocytosis of those very MSU crystals that triggers an acute gout flare attack.

Signs & Symptoms

- Red, warm, swollen joints. Mild fever and tophi is usually associated with advanced disease
- Acute attacks last **7-10 days**. Pain and swelling may intensify within 6-12 hours

Complications: If left untreated, damage to **kidneys** and joints may occur over time - for this reason, gout is associated with diabetes and other cardiovascular disease.

Risk Factors

Men are 3x more affected than women.

Diagnosis

- Hyperuricaemia levels are $> 0.36 \text{ mmol/L}$ in women, $> 0.42 \text{ mmol/L}$ in men



A Note on Serum Urate Levels

Be careful when interpreting serum urate levels as these tend to be **normal** during gout flares.

- MSU crystals can be detected under polarised microscopy (gold standard)
- Main clinical features present
- Joint aspiration

Differential Diagnosis (SA & PG)

1. *Septic Arthritis*: SA joint pain is monoarticular accompanied with systemic symptoms and an underlying joint condition such as OA or immunosuppressive medicines. SA is treated with antibiotics.
2. *Pseudo Gout*: PG is a type of acute calcium pyrophosphate di-hydrate crystal arthritis (CPPD) and it is strongly associated with previous joint damage. It is treated via symptom relief only as no CPPD lowering medicines exist.

Non-Pharmacological Treatment (Adjunctive Role Only)

1. Rest and elevate affected joint, cold compress to reduce pain and swelling
2. Regular exercise to reduce weight
3. Smoking cessation
4. Diet: hydration, low-fat dairy products, vegetables; avoid red meats, alcohol, sweetened beverages

Pharmacological Treatment — [BPAC Gout Part 1](#) [BPAC Gout Part 2](#)

Symptomatic/Prophylactic Pain Relief

1. *NSAIDs*: Naproxen (+/- PPI)
2. *Corticosteroids*: Prednisone, triamcinolone (intra-articular)
3. *Anti-Mitotic*: Colchicine (unapproved indication)

Urate Lowering Therapy (ULT): Long Term Prevention

1. *Xanthine-Oxidase Inhibitors*: Allopurinol (first line), Febuxostat
2. *Uricosurics*: Probenecid (first line), Benzbromarone (discontinuing)
3. *Urate Oxidase*: Rasburicase



Indication of Pain Relief in Gout (please note that doses differ depending on this — see NZF)

Acute Treatment of a Gout Attack: pain relief is required **until the pain has settled**

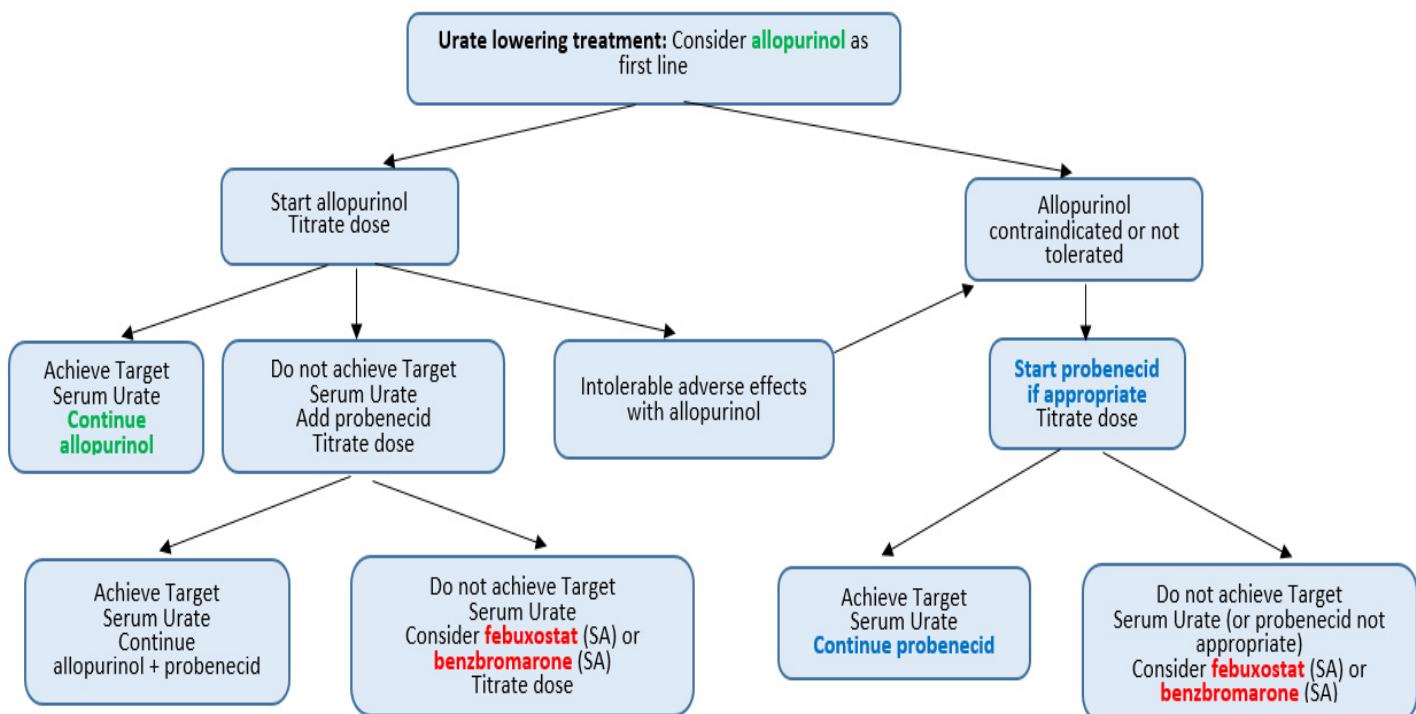
Prophylaxis of Gout Flares during ULT initiation: prophylaxis required for at least **6 months**

Criteria for Urate Lowering Therapy (ULT)

Gout Diagnosis + at least 1 of the following:

- > 2 attacks/year,
- > CKD Stage 2 Tophi
- Kidney stones (urolithiasis)

Category	Ingredients	Mechanism of Action	Side Effects
First Line Pain Relief for Acute Attacks/ Flares	[PRESCRIPTION] <i>1st Line</i> NSAIDs + PPI Naproxen (Naprosyn, Noflam) Indomethacin (Indomethacin) Sulindac (Sulindac)	NSAIDs reduce prostaglandin production by inhibiting cyclooxygenase, resulting in analgesic, anti-inflammatory, and anti-pyretic effects. For acute flares, most effective when given within 24 hours of pain onset . Naproxen is the preferred NSAID.	GI - Bleeding MI - Myocardial RI - Renal
	[PRESCRIPTION] <i>Alternative</i> Oral/Intra-articular Glucocorticoids Prednisone, Triamcinolone	Decreases inflammation by reducing production of inflammatory proteins. It is the preferred analgesic in renal impairment. Remember to taper off	Thinning of bones, weight gain, HPA axis suppression, infections and diabetes.
	[PRESCRIPTION] <i>Alternative</i> Colchicine (Colgout)	Most effective when given within 12 hours of pain onset. Anti-mitotic activity on <i>immune cells</i> which results in a decreased inflammatory response to the crystals. Colchicine does not decrease urate production OR increase renal urate excretion OR possess any analgesic properties. It is solely used to treat the inflammation (no effect on uric acid)	Reversal Agent: Activated Charcoal Narrow therapeutic index. Be careful of colchicine toxicity signs: N/V/D, abdominal pain Be careful of renal impairment.
Long Term Prevention with ULT	[PRESCRIPTION] <i>1st Line ULT</i> Xanthine-Oxidase Inhibitors Allopurinol (Allopurinol) Febuxostat (Adenuric)	Purines are metabolised by Xanthine Oxidase → Uric Acid which is 100% filtered through the glomerulus but 99% reabsorbed in undersecretors. Inhibition prevents conversion of uric acid. Febuxostat to only be considered if Allopurinol + Probenecid is ineffective.	Note: Allopurinol increases risk of flare in the first few months Rash, N/V/D, DRESS hypersensitivity (Take Allopurinol with food)
	[PRESCRIPTION] <i>2nd Line ULT</i> Uricosurics Probenecid (Probenecid) Benzbromarone (Narcarinic)	Act on URAT-1 (renal tubular transporter) to prevent reabsorption of uric acid and increase its excretion . Preferred treatment if the patient is an under-excretor.	N/V/D
	[PRESCRIPTION] <i>Urate Oxidase</i> Rasburicase (Fasturfec)	Converts uric acid into allantoin which is more soluble. Rasburicase is a recombinant version of urate oxidase. Given by IV	Fever



Monitoring

1. Adherence: ULT medicines are to be taken everyday and lifelong for prophylaxis. Titrate medicines to lowest effective dose.
 - **Target serum uric acid: <0.36mmol/L or <0.30mmol/L for patients with severe gout, e.g. those with tophi, chronic gouty arthritis or frequent flares**
2. Prevention of flares: number of flares per year
 - Note: Serum urate levels are normal during flares (do not test) — ULT can be initiated during flares with caution
3. Serum urate: every **4 weeks** when titrating ULT until target has been reached. Then every **6-12 monthly** for monitoring
4. Symptoms review at 3 month interval during the 6 month prophylaxis period
5. Renal function: every 6-12 monthly, dose adjustments with allopurinol
6. X-rays: tophi or erosions

Infectious Arthritis

We will cover these three types of infectious arthritises in detail below.

Category	Osteomyelitis	Septic Arthritis	Reactive Arthritis
Affected Area	Bone	Joint	Joint
Common Pathogens	Staph, others depending on patient factors	Staph, others depending on patient factors	Enteric, genitourinary
Diagnosis	Patient factors, imaging	Aspiration, patient factors	Patient factors, gene testing
Treatment Duration	3-12 weeks +	4 weeks +	Depends on response, may not need treatment

Osteomyelitis (OM)

Description

Osteomyelitis describes the inflammation of the **bone** due to **infection** (often bacterial e.g. *s.aureus*) that can be chronic or acute.

Two broad categories exist:

1. *Haematogenous Osteomyelitis*
 - A bone infection where the original pathogen (single pathogenic infection) spread through the **blood**, commonly affecting the femur and tibia of children, and vertebra of elderly.
2. *Contagious Osteomyelitis*
 - A bone infection that occurs when micro-organisms (multiple pathogenic infection) are introduced to the bone via contamination from a proximal source of infection.
 - a) Vascular insufficiency: Trauma, surgery, beside soft tissue infection → any bone involvement
 - b) Non-Vascular insufficiency: Common in diabetics, peripheral vascular disease (PWD) → lower extremity bones, more severe disease

Risk Factors

Normally bones are resistant to infection, however can become susceptible due to certain conditions:

- Indwelling catheters, IV drug use
- Poor vascularity
- Immunocompromised, Age < 5
- Sickle cell disease
- Trauma

Symptoms

Pain and tenderness over the affected bone, local inflammation, erythema, oedema, high-grade fever, malaise, warmth at site of infection, loss range of motion.

Complications: inflammatory response can then lead to bone necrosis and chronic infections.

Diagnosis

- *Gold Standard:* bone biopsy
- Symptoms, lab tests (WBC, ESR, CPR), cultures, imaging (x-ray, MRI, CT), bone scan

Pharmacological Treatment

1. *Acute (3 - 8 weeks):* Surgical debridement, empiric IV Antibiotics (e.g. flucloxacillin — **cover s.aureus**), deescalate therapy when sensitivities are returned.
2. *Chronic (6 - 12+ weeks):* Surgical intervention, antibiotics **in** the joint space

Monitoring

- Improvement of signs & symptoms
- Microbiology (culture) and imaging — *be careful as the sample may not grow during an active antibiotic therapy even if the infection is still going*
- Lab tests returned to baseline

Septic Arthritis (SA)

Description

Inflammation of the **joint** due to **infection** (often bacterial — *s.aureus*, strep). Inflammatory cells can cause cartilage breakdown and bone loss.

Cause

- Haematogenous spread from blood
- Bites, trauma
- Direct inoculation during joint surgery
- Pre-existing infection in joint space

Risk Factors

- Age >80 years
- Pre-existing arthritic disease, diabetes
- Prosthetic joints, recent surgery
- Prior intra-articular corticosteroids, injecting drug use
- Alcoholism

Symptoms

Pain and tenderness over the affected joint (usually single joint involvement), inflammation, erythema, warmth, oedema, fever, restricted movement

Diagnosis

- Clinical symptoms
- Synovial fluid aspiration and culture — *Aspirate before starting empiric antibiotics*

Treatment

- Empiric antibiotics
- Drainage of affected joint

Monitoring

- *Same as osteomyelitis.*

Reactive Arthritis

Description

Inflammation of the **joint** that develops soon after or during an infection somewhere else in the body (usually GIT, genitourinary tract infection). Often caused by gram -ve bacteria (food poisoning, STIs) and may be associated with the HLA-B27 gene. The microorganism cannot be recovered from the joint i.e. the joint is still sterile.

Signs & Symptoms

- Often 1 - 4 weeks after precipitating infection
- Peripheral arthritis, enthesitis, dactylyis, back pain
- Pain and tenderness over the affected joint, inflammation, erythema, oedema, extra-articular symptoms (ocular, genitourinary tract, GI, oral lesions, skin changes, nail changes, cardiac issues)

Pharmacological Treatment

1. *Treat the underlying infection if needed*
 - Antibiotics
2. *Treat the arthritis*
 - Acute: NSAIDs, intra-articular glucocorticoids, systemic glucocorticoids
 - Chronic (>6 months): DMARD, TNP inhibitors
3. *Treat extra-articular symptoms if needed*
 - Usual disease duration is 3-5 months??

OTHER MSK CONDITIONS

Introduction

We will look into two conditions here: osteoporosis and sprains/strains.

Osteoporosis

Description

Osteoporosis is a condition in which there is a reduction in the density and quality of the bone, making them weak, brittle, and more likely to fracture. Unsurprisingly, osteoporosis usually goes undiagnosed until a fragility fracture occurs.

Pathophysiology

Before we go into how osteoporosis develops, it is first important to understand the metabolic processes of bones.



Did You Know?

Bone is a structure so rich in calcium that 99% of our body's calcium stores can be found in bone.

Tissue Arrangement

Bone is made of connective tissue regardless of its shape. The different arrangement of connective tissue within the bone is what creates two types: cancellous (20%) and compact (80%) bone.

Hormones

Daily turnover of bone minerals (mainly calcium) means that plasma calcium concentration levels are regulated by:

- PTH, Calcitonin, Vitamin D,
- Oestrogen, Growth Hormone,
- Steroids, Cytokines.

Bone has an extracellular and an intracellular component:

Extracellular Composition

1. Organic (33%): made of collagen. Functions to resist tension.
2. Inorganic (67%): made of hydroxyapatite. Functions to resist compression and provide hardness.

Cellular Composition

Osteogenic stem cells differentiate to the following bone cells:

1. Osteoblasts (OB): bone-forming cells, build the ECM by adding lamellae on the outside
2. Osteocytes (Oc): in the lacunae of mature cells, important for communication between OBs and OCs

- Osteoclasts (OC): shape the medullary cavity by breaking down the ECM

In Osteoporosis

A balance exists between these cells to maintain the continuous remodelling of the skeleton throughout life. However, in osteoporosis, there is an imbalance (OC > OB) - resulting in a greater breakdown than there is formation.

- Early in life: Bone loss due to increased OC activity (mainly affecting spongy bone)
- Later in life: Bone loss due to decreased OB activity (mainly affecting compact bone)

Risk Factors

- Diet:* nutritional deficiencies
- Physical factors:* exercise, loading
- Age:* > 30 years, menopause, castration
- Medical Conditions:* Hypothyroidism, Cushing's Syndrome
- Medicines:* glucocorticoids, thyroxine

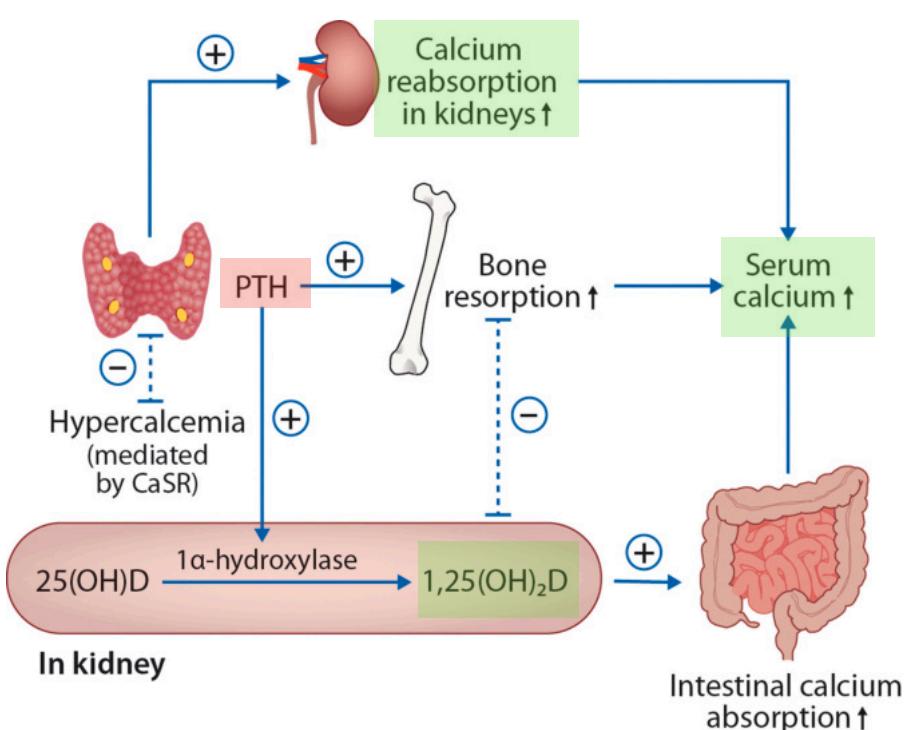


Glucocorticoids:

Physiological concentrations allow for OB differentiation (decreases Ca^{2+}). However, excessive concentrations (Cushing's Syndrome) inhibits this process and may stimulate OC action and increase plasma Ca^{2+} , leading to osteoporosis

Thyroxine:

Stimulates OC action, reducing bone density, and increases plasma Ca^{2+} . Caution as osteoporosis occurs in association with hypothyroidism



Signs & Symptoms

Bone loss and fracture

Non-Pharmacological Treatment

Good diet, no drinking or smoking, exercise

Pharmacological Treatment

BPAC Biphosphonates

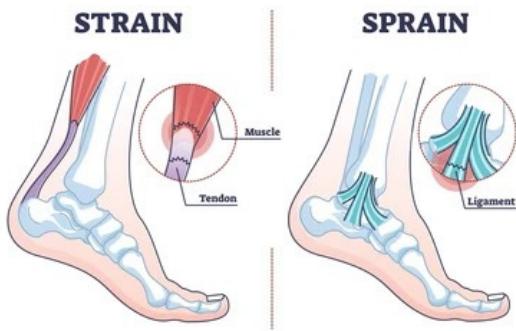
1. *Bisphosphonates*: Alendronic acid, zoledronic acid (IV), risedronate
2. *Estrogen*: SERMs, HRT, Raloxifene
3. *Vitamin D*: Cholecalciferol, calcitriol
4. *Parathyroid hormone*: Teriparatide
5. *Calcitonin*

Category	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
<i>1st Line</i> Bisphosphonates (IV or Oral)	[PRESCRIPTION] <i>Ist Line</i> Alendronic Acid (Fosamax) Risedronate (Risedronate) Zoledronic Acid IV (Aclasta)	Decreases plasma $[Ca^{2+}]$ Bisphosphonates are adsorbed onto the bone, <i>reducing OC bone resorption</i> and therefore reducing the rate of bone turnover <i>Note:</i> Fosamax Plus contains Alendronic Acid + Colecalciferol <i>Note:</i> Oral bisphosphonates is once weekly , IV bisphosphonates is once a year.	<ul style="list-style-type: none"> Due to its acidic properties, it may irritate the oesophagus (stay upright for 30 minutes after taking). Low Bioavailability (take on an empty stomach) 	Oesophageal reactions , abdominal pain, dyspepsia, nausea, N/V/D Osteonecrosis of the Jaw Takes a while to see the effects due to the slow turnover of bone.
 Estrogen Therapy	[PRESCRIPTION] <i>Alternative</i> (SERMs, HRT, Raloxifene)	Decreases plasma $[Ca^{2+}]$ Loss of oestrogen during menopause can lead to osteoporosis. 1. <i>Bone</i> : inhibit OC recruitment and mobilises PTH action while promoting osteoblast proliferation.	First line for women within 10 years of menopause. HRT can ameliorate osteoporosis caused by the decline in oestrogen in post-menopausal women	Hot flushes, leg cramps, teratogenic
 Vitamin D (Cholecalciferol converted to Calcitriol)	[PRESCRIPTION] <i>Alternative</i> Calcitriol, Cholecalciferol (Vitamin D Multichem)	Increases plasma $[Ca^{2+}]$ Lipophilic pre-hormone converted into a number of active metabolites that functions as hormones (this doesn't happen in kidney or liver impairment) and maintain plasma calcium concentrations by acting on: 1. <i>Bone</i> : Mobilises calcium from bone by increasing OC activity + decreasing osteoblast activity. 2. <i>Kidney</i> : Prevents its excretion 3. <i>GI Tract</i> : Promotes calcium absorption from the intestine Calcitriol is the active form of Vitamin D. Its synthesis is regulated by PTH.	<i>Paradoxical Effect</i> : when given to patients that are vitamin D deficient, it restores bone formation.	N/V/D Excessive vitamin D intake causes hypercalcaemia, which can cause kidney stones.
 Parathyroid Hormone Peptides (PTH)	[PRESCRIPTION] <i>Alternative</i> Teriparatide (Forteo)	Increases plasma $[Ca^{2+}]$ and lowers phosphate levels. PTH increases plasma calcium by acting on: 1. <i>Bone</i> : Mobilises calcium from bone by increasing OC activity. 2. <i>Kidney</i> : Promotes its reabsorption by the kidney, stimulates calcitriol (Vit D) synthesis 3. <i>GI Tract</i> : Promotes calcium absorption from the intestine	<i>Paradoxical Effect</i> : Drug that mimics PTH. Although PTH promotes bone resorption, small doses paradoxically stimulate OB activity to enhance bone formation.	Dizziness, Headache & Arthralgias. Give a biphosphonate at the end of the course of teriparatide to prevent bone loss from its withdrawal.
 Calcitonin	[PRESCRIPTION] <i>Severe Osteoporosis</i> Calcitonin Salmon (Myacalcic)	Decreases plasma $[Ca^{2+}]$ Peptide hormone secreted by specialised C cells found in thyroid follicles. Feedback regulated by sensing how much calcium is entering blood stream. 1. <i>Bone</i> : inhibits osteoclasts to decrease bone resorption 2. <i>Kidney</i> : decreases calcium and phosphate reabsorption	Only women least five years past menopause can take calcitonin. Patients with severe osteoporosis seem to do the best with this drug.	

Sprains & Strains (RICE)

Description

Sprains are due to forcing a **joint** into an abnormal position that overstretches or twists **ligaments**. Strains involve tearing **muscle** fibres and are usually a result of overexertion when the muscles are stretched beyond its usual limits. These are often caused by sports injuries.



Signs & Symptoms

Marked swelling, bruising, pain, reduced range of motion.

Red Flags: Refer children as bones are softer and therefore more prone to greenstick fractures (fractures of the outer part of the bone)

Non-Pharmacological Treatment

1. RICE: Rest, Ice, Compression, Elevation
2. Avoid HARM: Heat, Alcohol, Running, Massage

Note: Use cold <72h, heat can be used >72h of injury

Pharmacological Treatment

1. NSAIDs (for 7 days)
2. Paracetamol

The RICE guide provides four steps for initial injury management:

- R**: Rest the injured area for 48 hours.
- I**: Ice for 20 minutes at a time, 4 to 8 times per day.
- C**: Compress to help reduce swelling.
- E**: Elevate the injured limb 6 to 10 inches above the heart.

verywell

For the first few days after an injury, prevent further damage by avoiding **HARM**.

The HARM guide lists four activities to avoid:

- H**: Heat - Don't have hot baths, showers or saunas and avoid using heat rubs or packs after an injury.
- A**: Alcohol - Avoid alcohol as it can slow down your recovery and increase your chances of hurting yourself again.
- R**: Running - Don't run or do other types of moderate activity as this may cause further damage.
- M**: Massage - Massaging the injured area can cause more swelling and bruising, so avoid this for the first day or two.

Bupa



CHAPTER 7

THE RESPIRATORY SYSTEM



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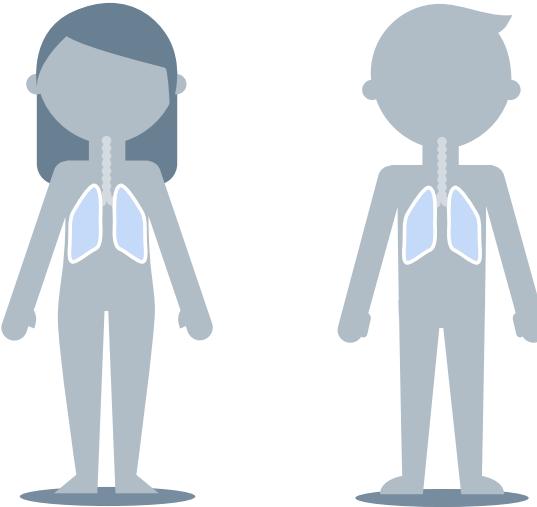
Chapter 7

The Respiratory System

General Overview of Respiratory Structures

Introduction

The lungs are the centre of the respiratory (breathing) system which function to oxygenate blood via gaseous exchange. The respiratory system is divided into the upper and lower respiratory tract, and is lined with a mucous membrane in which the mucous traps small particles like pollen or smoke.



The Upper Respiratory Tract (URT)

The upper respiratory tract (URT) involves the following structures:

1. Oral Cavity (mouth): Air enters and leaves the lungs through the mouth and nostrils
2. Nasal cavity (nose/nostrils): Air passes from the nose into the nasal cavity, and then the lungs
3. Pharynx (throat): Air from the mouth is sent to the lungs via the throat
4. Larynx (voice box): Helps air pass into the lungs and keeps out food and drink

The Lower Respiratory Tract (LRT)

The lower respiratory tract (LRT) involves the larger airways - therefore infections are usually more serious:

1. Trachea (windpipe)
2. Bronchi, bronchioles, alveoli
3. Lungs

Understanding Gas Exchange

Components

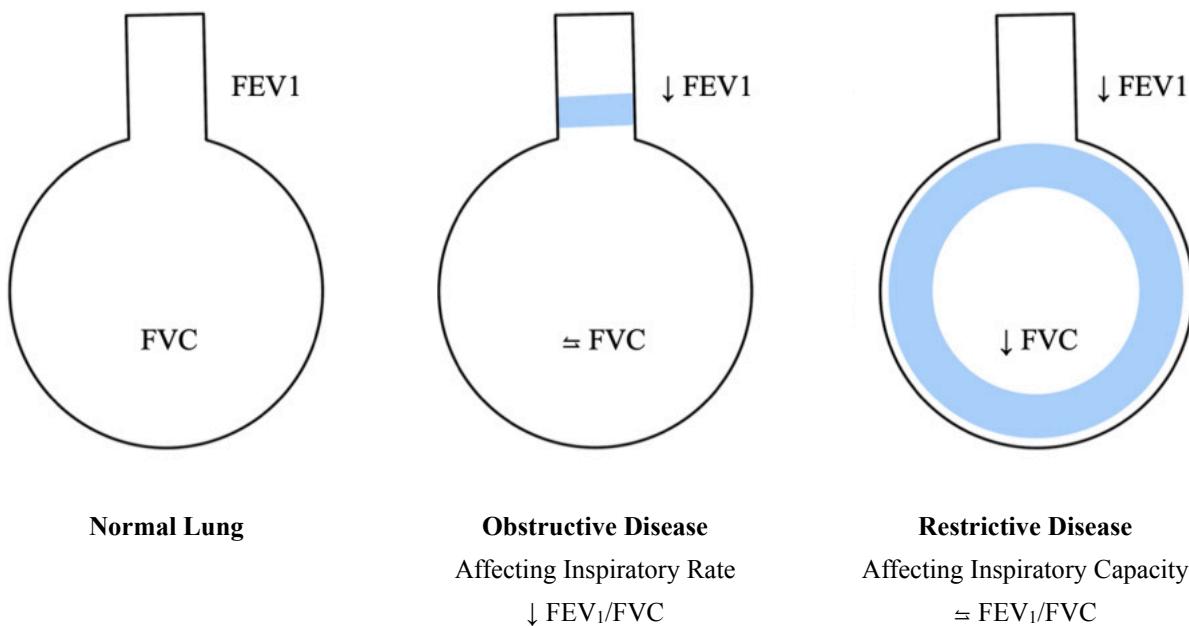
Gas exchange has 4 components - which diseases can affect in different ways.

Component	Description	Measuring This Component	Diseases That Affect This Component
Ventilation	Ventilation describes the movement of air in and out of the lung	<ul style="list-style-type: none"> FEV₁ (L/s): (<80% will cause symptoms) FVC (L): FEV₁:FVC is usually 0.8 PEFR (L/min) 	<ul style="list-style-type: none"> Obstructive diseases affects inspiratory rate (asthma, COPD, bronchitis) — evidence of reversibility Restrictive diseases affects inspiratory capacity (pulmonary fibrosis, pneumonia, end stage COPD)
Diffusion of Gases	Oxygen must reach the alveolar space and diffuse into the capillary blood flow while carbon dioxide must do the opposite for an efficient exchange.	<ul style="list-style-type: none"> PaO₂: 100mmHg (< 60mmHg will cause symptoms) PaCO₂: 40mmHg (> 50mmHg will cause symptoms) 	<ul style="list-style-type: none"> Pneumonia (prevents air from getting to the alveolar space) Tumour (affects alveoli function) HF (reduced perfusion)
Capillary Blood Flow	In order for gas exchange to occur, an adequate blood flow is required.	<ul style="list-style-type: none"> pH: 7.4 (< 7.35 is acidosis due to excess CO₂, < 7.0 is life threatening) Hb (< 80 g/L will cause symptoms) 	<ul style="list-style-type: none"> Pulmonary embolism (PE): blood clot affects alveolar side Right ventricular dysfunction
Carriage of Gases by Blood	Oxygen is then carried by Haemoglobin and released by a pressure gradient.	<ul style="list-style-type: none"> SaO₂: > 95-98 % (< 90% will cause symptoms) CaO₂: 16-20 mL/100mL 	<ul style="list-style-type: none"> Hb (anaemia, blood loss) Binding of O₂ to Hb (arterial pH, carbon monoxide)

Obstructive/Restrictive Diseases & FEV₁/FVC

Many students find it difficult to grasp the concept of how obstructive/restrictive diseases affect FEV₁ and FVC - this lung analogy may help simplify this.

Lung ‘Analogy’



FEV₁ & FVC

- FEV₁ is a measure of the *rate* at which air can be expelled from the lungs in one second
- FVC is a measure of the viral *capacity*

Obstructive Diseases

- Obstructive diseases affect the *inspiratory rate* - think of them as a ‘wine cork’ in your lungs. It doesn’t affect how much air you can hold (FVC), but it does affect the rate at which you can breathe out (FEV₁)
- This means FEV₁ is reduced, FVC is unaffected and overall FEV₁ / FVC goes down.

Restrictive Diseases

- Restrictive diseases affect the inspiratory capacity - think of them thick tubes that narrow the space available in your lungs. They would not only affect the rate at which you can breathe out (FEV₁) but also how much air you can hold (FVC).
- This means FEV₁ and FVC is reduced, resulting the the overall FEV₁ / FVC remaining the same.

COMMON RESPIRATORY SYMPTOMS

Introduction

Let's start off this chapter with some easy, simple and straightforward symptoms: blocked noses, runny noses, difficulty sleeping because of cold symptoms and dry/chesty coughs.



Children & Cough/Colds Medicines

Cough & Cold medicines should not be given in children under 6 years old. Supply to 6-11 years old should only be done on the advice of medical practitioners and nurses. Herbal products such as English ivy leaf extract (*Hedera helix*) can be used in children 2-6.

Blocked Nose

Description

A stuffy or congested nose occurs when the tissue lining becomes swollen due to inflamed blood vessels.

Non-Pharmacological Treatment

- Steam, warm compress, saline spray, vicks

Pharmacological Treatment

- Topical decongestants (*first line*)
- Systemic decongestants
- Intranasal corticosteroids
- Intranasal anticholinergics

	Medicine	Cautions/ Contraindications	Pregnancy	Breastfeeding	Child	ADRs
Systemic Sympathomimetics	Phenylephrine & Pseudoephedrine Hydrochloride (Capsule) Dimetapp Nasal Decongestant (Tablet) Codral Decongestant, Maxiclear Sinus Relief Sudafed Nasal Decongestant Multichem	<i>Cautions:</i> Heart problems, high BP, diabetes, prostate problems, glaucoma, overactive thyroid	No	Yes	≥12 years	
	Oxymetazoline (Nasal Spray) Drixine, Mucinex Sinus, Sudafed, Medco Blocked Nose Relief, Vicks, Sinex Extrafresh	<i>Contraindications</i> • A degree of systemic absorption is possible, especially when using drops, <small>as a small quantity</small>	No	Yes		Fast heart rate, changes in heart rhythm, palpitations, high blood pressure, headache <small>Red flags: signs of</small>

Topical Sympathomimetics	Xylometazoline (Nasal Drops) Otrivin (Nasal Spray) Otrivin, Maxiclear, Sudafed	as a small quantity might be swallowed. They should therefore be avoided in patients taking MAOIs. Caution • CV disease, diabetics, and elderly, Note: Avoid prolonged use — risk of rebound congestion	No	No	≥6 years	Red flags, signs of anaphylaxis
Intranasal Anti-inflammatory	Corticosteroids Fluticasone Nasal Spray (Flixonase), Budesonide (StereoClear)		Yes	Yes	≥12 years	<ul style="list-style-type: none"> Burning, stinging, dryness and crusting of the nostrils Nose bleed
Intranasal Anticholinergic	Anticholinergics Ipratropium bromide (Univent)		Yes	Yes	≥12 years	<ul style="list-style-type: none"> Discomfort and mild nosebleeds Dry or irritated nose or throat Headache

A Focus on Otrivin Products (Nasal Decongestants)

Otrivin Product Range

Main active ingredients: Xylometazoline, (ipratropium)

BLOCKED NOSES WITH OTRIVIN							
	Otrivin Adult	Otrivin Menthol	Otrivin Plus	Otrivin Junior	Otrivin Baby & Kids	Otrivin Seawater	Otrivin Breathe Clean
Product Image							
Indicate	Clears blocked nose	Clears blocked nose	Clears blocked nose + stops runny nose	Clears blocked nose	Clears blocked nose naturally by washing away irritants + moisturises	Clears blocked nose naturally by washing away irritants + moisturises	Isotonic natural solution that washes away impurities in the nose.
Ingredient	Xylometazoline	Xylometazoline	Xylometazoline + Ipratropium	Xylometazoline	Saline	Seawater	Seawater, Water, Aloe vera
Decongestant	Yes	Yes	Yes	Yes	Yes	Yes	No
Applicator Format	Nasal Spray or Drop	Nasal Spray	Nasal Spray	Nasal Spray or Drop	Nasal Spray	Nasal Spray	Nasal Spray
Dosage	12 & Over 1 spray per nostril 2-3 times daily pm	12 & Over 1 spray per nostril 2-3 times daily pm	18 & Over 1 spray per nostril up to 3 times daily pm	6-11 2 sprays per nostril 2-3 times daily as necessary	2 & Over 1-2 spray per nostril 2-4 times daily pm	6 & Over 1 spray per nostril up to 6 times daily pm	6 & Over 1-2 sprays in each nostril as required.
Precautions	Do not use more often than every 8-10 hours Do not exceed recommended dosage Do not share the nasal spray for hygienic reasons	Do not use more often than every 6 hours Do not exceed recommended dosage Do not share the nasal spray for hygienic reasons	Do not use more often than every 8-10 hours Do not exceed recommended dosage Do not share the nasal spray for hygienic reasons	Do not use more often than every 8-10 hours Do not exceed recommended dosage Do not share the nasal spray for hygienic reasons	Seek medical advice before using it on an infant less than 2 weeks old. Adult supervision is needed for children below 11 years. Do not share.	Adult supervision is needed for children below 11 years. Do not share.	

Runny Nose (Rhinorrhoea/Rhinitis) & Difficulty Sleeping

Description

A runny nose is mucous dripping or ‘running’ out of the nose. They can also cause difficult in sleeping — many medicates thus have the added benefit of sleepiness. When a cold virus or an allergen such as pollen or dust first enters your body, it irritates the lining of your nose and sinuses and your nose starts to make a lot of clear mucus. This mucus traps the bacteria, virus or allergens and helps flush them out of your nose and sinuses.

Non-Pharmacological

- Rest
- Drink plenty of fluids, especially water
- Use a saline nasal spray to help relieve symptoms. Limit the use of decongestant nasal sprays to no longer than a few days, as instructed on package labels.
- A cool-mist humidifier at your bedside can combat congestion worsened by dry winter air.

Pharmacological Treatment

- **Antihistamines - both help with runny noses, 1st gen have the added benefit of drowsiness**
- Intranasal antimuscarinic
- Intranasal corticosteroids
- Decongestants

Medicine	Cautions/Contraindications	ADRs	Pregnancy	Breastfeeding	Child
Brompheniramine + Phenylephrine (Oral Liquid) Dimetapp, Dimetapp Cold & Allergy					
Chlorpheniramine Histafen	1st Generation Antihistamines - aid with sleep and runny nose	1st Generation Antihistamines (crosses BBB) Anticholinergic side effects: Spit, See, Shit Increased HR, increased BP	Yes, caution with 1st gen use	Yes	>2y or if diphenhydramine> 12y (with exceptions)
Chlorpheniramine + Phenylephrine (Oral Liquid) Demazin Cold Relief					
Diphenhydramine (Capsule) Unisom					
Ipratropium Bromide (Nasal Spray) Univent		Dry mouth, GI motility disorder, constipation, diarrhoea, cough, headache, sinusitis	Yes	Yes	≥12y
Corticosteroids Fluticasone Nasal Spray (Flixonase) Budesonide (StereoClear)		• Burning, stinging, dryness and crusting of the nostrils • Nose bleed	Yes	Yes	≥12 years

Cough (Dry or Chesty)

Description

A cough is the body's way of clearing the lungs and airways of irritants so you can breathe better. Coughs can be dry or chesty in nature; dry coughs are tickly and unproductive so we aim to suppress them while chesty coughs are productive so we aim to aid the excretion of phlegm. Extremely persistent coughs can also be treated with a reliever inhaler such as Salbutamol.

Coughs are either classified as acute or chronic:

- Acute: lasts less than 2 weeks
- Protracted acute (children): 2–4 weeks
- Chronic (children): more than 4 weeks
- Chronic persistent (adults): more than 8 weeks

The duration of the cough can indicate the possible cause:

- *3 days*: URTI
- *3 weeks*: acute or chronic bronchitis
- *3 months*: conditions such as chronic bronchitis, tuberculosis, and carcinoma

Pathophysiology

- *Dry*: May come after a cold, flu, or COVID-19. As you forcefully expel **air** to clear the tickling sensation in the throat by coughing, your throat can become irritated and dry and may develop a sore throat. Other conditions such as GORD, heart failure, or lung cancer can cause chronic dry coughs.
- *Chesty*: Illness affecting the respiratory system

Signs & Symptoms

- *Dry*: Tickly, unproductive, sore throat, chest tightness, chest pain (strained lung or chest muscles)
- *Chesty*: Productive, SoB

Note: Persistent coughing can cause blood to be present in mucus — this is often a one-off event and does not require referral

Risk Factors

Smokers (more prone to chronic and recurrent coughs)

Non-Pharmacological Treatment

- Demulcent Linctus: good for < 1 month old, pregnant women, those with polypharmacy, elderly
- Lifting head with a pillow when sleeping at night to encourage downwards drainage of phlegm
- Stay hydrated
- Suck on cough drops or hard candies
- Spoonful of honey (**do not give to children under 1 — in babies, honey can cause botulism**)
- Humidifier

Pharmacological Treatment

Dry coughs

Dextromethorphan (first line), Pholcodine (second line), Codeine/Dihydrocodeine (third line) and Anti-Histamines (last line) are the mainstay of anti-tussive treatment. Antihistamines **should not be used routinely** unless night-time sedation is perceived as beneficial to aid sleep.

DRY COUGH					
Medicine (Cough Supressants)	Cautions/Contraindications	ADRs	Pregnancy	Breastfeeding	Child
Dextromethorphan (Capsule) Robitussin Dry Cough (Lozenge) Vicks Cough (Oral Liquid) Vicks Formula 44 Bisolvon Dry Benadryl Dry Forte	<i>Contraindications:</i> <ul style="list-style-type: none">Use of monoamine oxidase inhibitor (MAOI) within 14 daysChronic obstructive pulmonary disease <i>Cautions:</i> <ul style="list-style-type: none">respiratory failure; asthma; bronchitis, emphysema; dependence and misuse has been reported; serotonin syndrome	Sedation, constipation - increased with alcohol, opioid analgesics, anxiolytics, hypnotics and antidepressants. Respiratory depression	Yes	Yes	> 12
Pholcodine (Oral Liquid) Duro-Tuss Dry Cough Pholcodine (AFT)	<i>Contraindications:</i> <ul style="list-style-type: none">Pregnant/breastfeedingChronic bronchitis, COPD, Bronchiectasis, Patients at risk of respiratory failure,Severe hepatic or renal impairment,Conditions associated with raised intracranial pressure, acute head injury <i>Cautions:</i> <ul style="list-style-type: none">Asthma		No	No	> 12
Codeine Codeine Linctus 5mg/3ml or 15mg/5ml	<i>Contraindications</i> <ul style="list-style-type: none">Children under 12		No	No	> 12

Chesty coughs

Bromhexine & Guaifenesin are the mainstay in the treatment of chesty coughs.

CHESTY (PRODUCTIVE COUGH)					
Medicines (Expectorants or Mucolytics)	Cautions/Contraindications	ADRs	Pregnancy	Breastfeeding	Child
Bromhexine Mucolytic (Oral Liquid) Duro Tuss Chesty Cough (Tablet) Bisolvon	<i>Cautions:</i> <ul style="list-style-type: none">Severe liver disease and severe renal failure.	Nausea, vomiting, diarrhoea	No	No	≥6y
Guaifenesin Expectorant (Oral Liquid) Codral, Lemsip, Robitussin Chesty Cough, Vicks (Tablet) Mucinex	<i>Cautions:</i> <ul style="list-style-type: none">Asthma, bronchitis, COPD	Nausea, vomiting, GI discomfort (uncommon)	Yes	Yes	≥12y

A Focus on Duro-Tuss Products

Duro-Tuss Product Range

Main active ingredients: Bromhexine, guaifenesin, pholcodine

COUGH WITH DURO-TUSS													
	Chesty Cough				In Between		Dry Cough				Natural Range		
	Heavy Cough		Stubborn Heavy Cough	Cough & Nasal Congestion	Cough & Sore Throat (on the go)	Dry Cough & Phlegm	Cough	Stubborn Cough	Cough & Nasal Congestion	Cough & Sore Throat (on the go)	Clears Airways (Day)	Clears Airways (Night)	Lingering Chest
Product Image													
Name & Size	Duro-Tuss Chesty Cough Liquid - (200ml)	Duro-Tuss Chesty Cough Liquid - (24 tablets)	Duro-Tuss Chesty Double Strength Cough (200ml)	Duro-Tuss Chesty Cough + Nasal Decongestant (200ml)	Duro-Tuss Chesty Cough Lozenge (24 lozenges)	Duro-Tuss Expectorant (200ml)	Duro-Tuss Dry Cough Liquid (200ml)	Duro-Tuss Dry Cough Liquid Forte (200ml)	Duro-Tuss Chesty Cough + Nasal Decongestant (200ml)	Duro-Tuss Dry Cough Lozenges (24 Lozenges)	Duro-Tuss Children's Liquid Nighttime (200ml)	Duro-Tuss Children's Liquid Nightime (200ml)	Duro-Tuss Lingering Chest + Immune Support (200ml)
Indication	Dark green = Heavy Mucus Double action: mucolytic & expectorant 1) Breaks down mucus 2) Clears it from chest		Purple = Stubborn Congestion Mucolytic	Red = Ask Mucolytic Reduces chesty cough and a blocked/runny nose	Anti-bacterial Clears chest congestion and associated sore throats	Green = Light Mucus Double action: mucolytic & cough suppressant	White = no mucus Cough Suppressant & Decongestant	Orange = dry cough Cough Supressant (highest strength)	Pink = Ask Cough Supressant & Decongestant Relieves stubborn dry coughs and sooths irritation of the throat	Antibacteri al Relieves dry cough and associated sore throats	Baby Pink: Day Mucolytic & Non Drowsy	Baby Pink; Night Soothes chest, clears airways and boosts immunity	White: Lingering ills & chills Calms, settles and clears air wards and supports healthy immune system.
Ingredients	Bromhexine Guaifenesin		Bromhexine	Bromhexine Phenylephrine	Bromhexin e Cetylpyrid ium	Bromhexin e Pholcodine	Pholcodine	Pholcodine Sorbitol	Pholcodine Phenylephrin e	Pholcodine Cetylpyridi um	Hedera Helix Sorbitol	Hedera Helix Sorbitol Chamomile	Hedera Helix Sorbitol Althaea Officinalis
Age Indication	6 & Over	12 & Over	6 & Over	6 & Over	6 & Over	6 & Over	6 & Over	12 & Over	6 & Over	6 & Over	2 & Over	3 & Over	6 & Over
Sugar Free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Suitable for Diabetes	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Lactose Free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Gluten Free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Alcohol Free	✓	✓	✓	✓	✓	✓	✓				✓	✓	✓
Artificial Colouring Free	✓	✓	✓	✓			✓				✓	✓	✓
Non Drowsy	✓	✓	✓	✓	✓						✓	✓	✓
Doses/Directions	Max 4 times per day Over 12 10 ml q6h prn 6-12 5ml q6h	Over 12 1t q4-6h prn (max 4 a day) Over 12 5-10ml q8h prn 6-12 5ml q8h prn	Max 3 times per day Over 12 5-10ml q8h prn 6-12 7.5ml q6h	Max 4 times per day Over 12 15ml q6h 6-12 1 lozenge q8h prn (max 3 a day)	Over 12 2 lozenges (max 6 a day) 6-12 5-10ml q6h prn	Max 4 times per day Over 12 10-15ml q6h prn 6-12 5-10ml q6h prn	Max 4 times per day Over 12 5ml q6h prn (max 4 times a day) 6-12 5-10ml q6h prn	Max 4 times a day Over 12 10-15ml q6h prn 6-12 5-10ml q6h prn	Max 4 times a day Over 12 5ml q6h prn (max 4 times a day) 6-12 5-10ml q6h prn	Over 12 Dissolve 1 every 3 hours prn (max 12 per day) 6-12 Dissolve 1 every 3 hours prn 9max 6 per day)	Max 3 times per day Over 12 10ml q8h prn 1-11 7.5ml q8h prn 2-5 5ml q8h prn	Max 3 times per day Over 12 15ml q8h prn 3-11 10ml q8h prn	Max 3 times per day Over 12 10ml q8h prn 6-12 5ml q8h prn
Pregnancy Category	A	A	A	B2	A	A	A	A	B2	A	Consult HCP		

A Focus on Codral Products

Main ingredients: Paracetamol, guaifenesin, phenylephrine, (chlorphenamine)

COUGH WITH CODRAL												
	Cold & Flu Tablets/Capsules					Hot Drinks (Sachets)		Liquids		Sore Throat Lozenges		
	Cold & Flu	Cold & Flu + Mucus Cough	Decongestant	Night & Day	Cold & Flu	Cold & Flu	Cold & Flu + Mucus Cough	Mucus Cough	Mucus Cough + Cold Liquid	DuoRelief Sore Throat Lozenges Lime & Lemon	Sore Throat Lozenges Honey & Lemon	Sore Throat Lozenges Menthol
Product Image												
Name & Size	Codral Cold & Flu (24 Tablets)	Codral Cold & Flu + Mucus Cough (18 Capsules)	Codral Decongestant (20 tablets)	Codral Day & Night (18 day/ 6 night Tablets)	Codral Night	Codral Cold & Flu (Max Strength) (10 Sachets)	Codral Cold & Flu + Mucus Cough (Max Strength) (10 Sachets)	Codral Mucus Cough (150ml)	Codral Mucus Cough + Cold Liquid (200ml)	DuoRelief Sore Throat Lozenges (16 Lozenges)	Sore Throat Lozenges (16 Lozenges)	
Indication	Headaches, fever, blocked/runny nose, body aches and pain	Headaches, fever, body aches and pain, blocked/runny nose, sore throat, chesty cough	Relief of blocker and runny nose	Headaches, fever, blocked/runny nose, body aches and pain	Headaches, fever, blocked/runny nose, body aches and pain, sneezing/watery eyes	Headaches, fever, blocked/runny nose, body aches and pain, sore throat	Headaches, fever, blocked/runny nose, body aches and pain, sore throat, chesty cough	Chest congestion, chesty cough	Heavy and chesty coughs, blocked/runny nose	Sore throat (Antibacterial + Anaesthetic)	Sore throat (Antibacterial)	
Ingredients	Paracetamol 500mg Phenylephrine hydrochloride 5mg	Paracetamol 500mg Guaifenesin 100mg Phenylephrine hydrochloride 6.1mg	Phenylephrin e hydrochloride 10mg	Day: Paracetamol 500mg, Phenylephrine hydrochloride 5mg Night: Paracetamol 500mg, Phenylephrine hydrochloride 5mg, Chlorphenamine maleate 2mg	Paracetamol 500mg Phenylephri ne hydrochlori de 5mg Chlorphen a mine maleate 2mg	Paracetamol 1000mg Phenylephrin e hydrochlorid e 12.2mg	Paracetamol 1000mg Guaifenesin 200mg Phenylephrin e hydrochlorid e 12.2mg	Guaifenesin 100mg/5mL	Guaifenesin 100mg/5mL Phenylephri ne hydrochlori de 5mg/ 5mL	Benzocaine 10mg Cetylpyridini um chloride 1.47mg	Enzy alcohol 6.5mg Etylpypyridium chloride 1.47mg	Benzyl alcohol 6.5mg Cetylpyridiu m chloride 1.47mg
Age Indication	12 & Over				12 & Over			6 & Over	12 & Over	6 & Over	6 & Over	12 & Over
Doses/ Directions	2 tablets every 4-6 hours prn. Maximum 8 capsules in 24 hours	2 capsules every 4-6 hours prn. Maximum 8 capsules in 24 hours	1 tablet every 4 hours prn. Maximum 6 tablets in 24 hours	2 day tablets every 4-6 hours prn. Maximum 6 tablets in 24 hours	2 tablets every 4-6 hours prn. Maximum 8 tablets in 24 hours	Dissolve contents of one sachet in hot (not boiling) water. Stir until dissolved and drink.	1 sachet every 4-6 hours prn. Maximum 4 sachets in 24 hours	6-12 years: 5-10 mL Adults Over 12: 10-20 mL	10 mL every 4 hours prn. Maximum 6 doses in 24 hours.	Dissolve 1 lozenge slowly in the mouth.	Dissolve 1 lozenge slowly in the mouth.	Every 2-3 hours prn. Maximum 8 lozenges in 24 hours
Precautions	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Adults: Stop after 3 days Children: Stop after 48 hours	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)	Do not take longer than a few days (48h hours in children)

OSCE Points

Sputum colour

- Clear suggests no infection while yellow, green or brown suggests the opposite (usually viral)

Onset of cough

- A cough that is worse in the morning may suggest chronic bronchitis
- A cough that is worse at night and accompanied by chest tightness/wheeze may indicate asthma. Please note unproductive coughs are the most common presentation of asthma in children at the pharmacy.
- Certain medications such as ACEI can produce dry coughs.

UPPER RESPIRATORY TRACT CONDITIONS

Description

The major passages and structures of the upper respiratory tract include the nose or nostrils, nasal cavity, mouth, throat (pharynx), and voice box (larynx). The respiratory system is lined with a mucous membrane that secretes mucus.

Allergic Rhinitis (Hayfever)

Description

Rhinitis describes the inflammation of the mucous membranes of the nose. While many kinds of rhinitis exist, the most common kind is allergic in nature - a good example of this is hayfever

Type	Cause
Allergic Rhinitis	<ul style="list-style-type: none">Pollen
Infective Rhinitis	<ul style="list-style-type: none">Viral Infection
Non-Allergic	<ul style="list-style-type: none"><i>Intrinsic:</i> no apparent cause<i>Vasomotor:</i> overactive parasympathetic or hypoactive sympathetic NS response to irritants (eg. dry air, pollutants, strong odours)
Rhinitis of pregnancy	<ul style="list-style-type: none">Hormonal Changes
Medicine-induced	<ul style="list-style-type: none">ACEI, NSAIDs, α-blockers, sildenafil, chlorpromazine, OC, aspirin<i>Rebound congestion:</i> prolonged use of nasal decongestants

Pathophysiology

Similar to asthma (as we will see later on), rhinitis involves a sensitisation period and a re-exposure period.

- Sensitisation:* First presentation of the antigen activates DCs, which move to lymph nodes to activate and proliferate T and B cells - the latter begin to produce IgE. These go on to coat mast cells.
- Re-Exposure:* Subsequent presentation of antigen causes IgE-coated (sensitised) mast cells to degranulate, releasing inflammatory mediators such as histamine. Histamine binds to H₁ receptor on blood vessels (vasodilation/leaky), goblet cells (watery mucous), sensory nerves (itching, sneezing) to cause the symptoms we observe.

A Note on Histamines

Histamines are mediators of allergic and inflammatory conditions - they also have a role in gastric secretion and function both as a neurotransmitter and neuromodulator. Most histamines are stored in granules within mast cells or basophils. When a stimuli causes degranulation, histamine exerts its effects.

Receptor Subtype	Distribution
H1	<ul style="list-style-type: none">Smooth muscle, mast cells, endothelium, brain
H2	<ul style="list-style-type: none">Gastric mucosa, cardiac muscle, neutrophils
H3	<ul style="list-style-type: none">Brain, Mysenteric, Plexus, Other Neurons
H4	<ul style="list-style-type: none">Eosinophils, Neutrophils, CD4 T cells

Signs & Symptoms

Allergic Rhinitis causes cold-like signs and symptoms including runny nose, itchy eyes, congestion, sneezing, and sinus pressure.

1. *Early phase (minutes)*: sneezing, nasal itching, rhinorrhoea, nasal congestion, watery/swollen/itchy eyes (can lead to allergic conjunctivitis)
2. *Late (6-12 hours)*: nasal congestion/obstruction, nasal hyperactivity

Risk Factors

The cause of allergic rhinitis can be traced back using the frequency of the symptoms:

1. *Seasonal Symptoms*: <4 days/week for <4 weeks
 - Outdoor allergens (worse in the morning due to peak pollen levels)
2. *Persistent (perennial)*: ≥4 days/week for ≥4 weeks i.e. all year round
 - Indoor allergens (dust mites, animal/pet dander) causing sleep disturbance, impairment of daily activities, and troublesome symptoms.
3. *Mix: Seasonal + Perennial*
 - Many people are allergic to both indoor and outdoor allergens; their symptoms are **perennial with seasonal exacerbations**.

Diagnosis

- Skin prick test

Differential Diagnosis

1. *From asthma*: no wheezing or breathlessness
2. *From common cold*: no cough

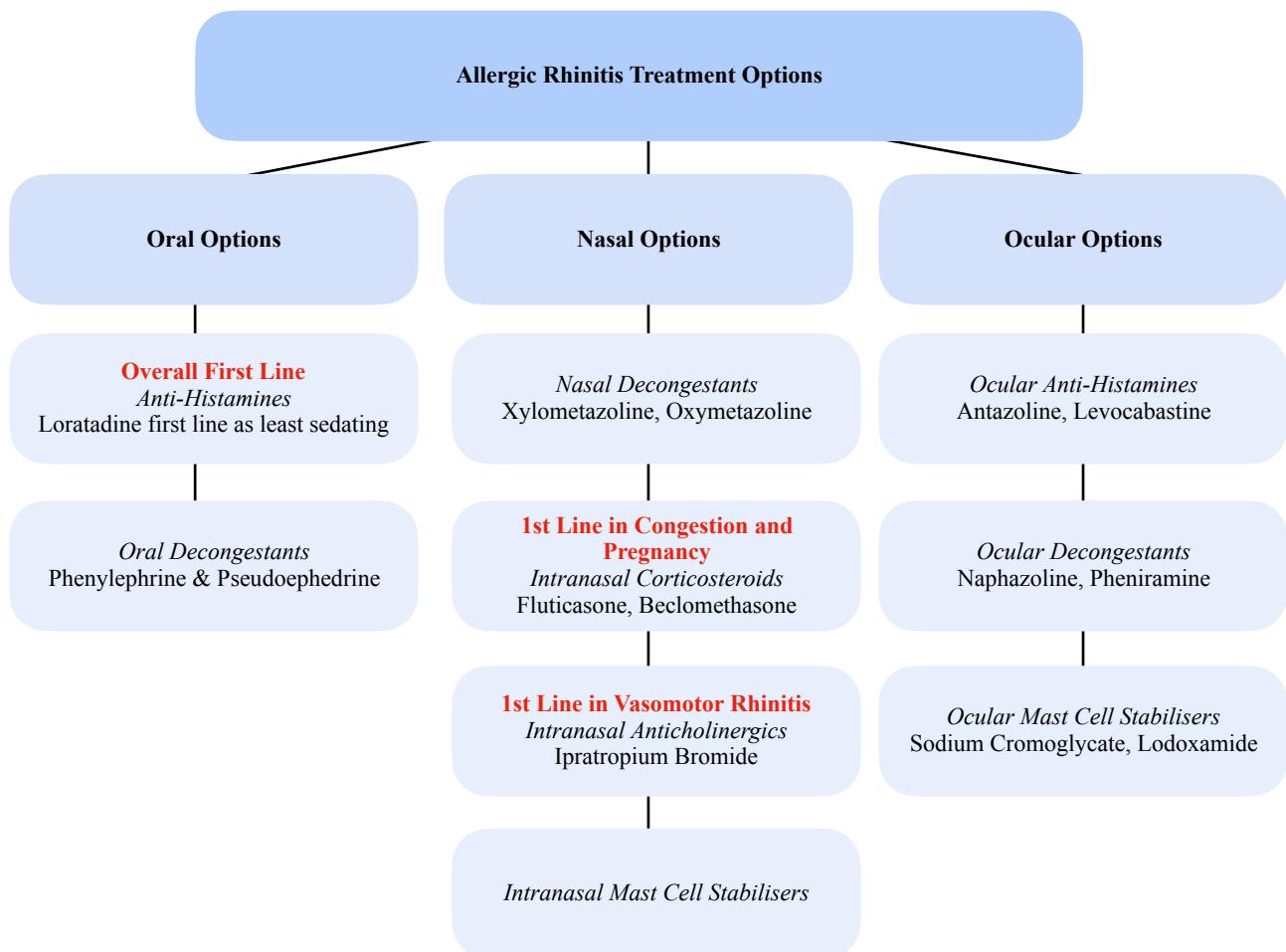
Non-Pharmacological Treatment

1. Avoid exposure to the allergen (although may not always be practicable)
2. Saline spray/drops

Allergen	Advice
Animal Dander	Keep pets out of the bedroom and off carpet/furniture
Dust Mites	Wash bedding weekly, keep humidity low and good house ventilation, replace carpet with wood or vinyl flooring.
Food Allergies	Keep a diary of what you eat to help identify your allergens.
Insect Bites & Stings	Covered clothing, insect repellents
Pollen	Shower and wash hair at night to wash away any pollen stay indoor during high pollen count, wear a mask
Skin Allergies	Avoid strong soaps, perfumes, products that may irritate

Pharmacological Treatment

Mainly surrounding symptomatic relief - which can be targeted to the most affected area.



A Note on Antihistamines

2 generations exist - with the first one having poor H1 selectivity and high BBB permeability (resulting in sedation)

Sedating Antihistamines (1st Gen)	
Active Pharmaceutical Ingredient	Brand Name
Promethazine hydrochloride (more sedative)	Phenergan, Allersoothe
Chlorpheniramine maleate	Histafen
Pheniramine maleate	Naphcon (with naphazoline)
<i>Diphenhydramine</i>	Benadryl, Unisom [sleep]
<i>Cyclizine</i>	<i>Nausicalm [N/V]</i>
Non-Sedating Antihistamines (2nd Gen)	
Active Pharmaceutical Ingredient	Brand Name
Bilastine	Labixten
Cetirizine	Histaclear, Hayzone, Zyrtec, Zista, Razene, Zetop
Levocetirizine (isomer of cetirizine)	Levoclear, Levrix, Elerhin, Selct
Fexofenadine (active metabolite of terfenadine)	Telfast, Fexaclear, Fexofast
Loratadine (least sedating)	Haylor, Lorfast, Lorafix
Desloratadine (active metabolite of loratadine)	Aerius

Category	Ingredients	Indication	Patient Counselling	Mechanism of Action	Side Effects
Oral	[NON PRESCRIPTION] <u>1st Generation</u> Promethazine (Allersothe) <u>2nd Generation</u> Loratadine (Lorafax) Cetirizine (Zista) Fenofexadine (Fexaclear)	Onset: 1 hour Duration: 12-24 hours Rhinorrhoea Sneezing Itching Allergic conjunctivitis Nasal congestion	<ul style="list-style-type: none"> First line for mild - intermittent symptoms in early phase Interacts with MAOI Children must be at least 1 years old. Commence preventative therapy BEFORE allergen exposure. 	Block histamine binding to receptors. However, as they have no effect on histamine release from storage sight, they are more effective if given prophylactically.	<ul style="list-style-type: none"> Anti-cholinergic effects (blurred vision, dry mouth, GI disturbances, urinary retention, sedation) Safe for long term use
	[NON PRESCRIPTION] <i>Oral Nasal Decongestants</i> Phenylephrine Hydrochloride Pseudoephedrine Hydrochloride	Onset: 5-15 minutes Duration: 3-6 hours Nasal Congestion Sinusitis	<ul style="list-style-type: none"> Best for nasal congestion and intermittent symptoms Often given to provide relief until corticosteroids kick in 	Reduce swelling of the blood vessels in your nose, throat and sinuses.	<ul style="list-style-type: none"> Short term only
Nasal	[NON PRESCRIPTION] <i>Nasal Decongestants</i> Xylometazoline (Otrivin), Oxymetazoline	Onset: 5-15 minutes Duration: 3-6 hours Nasal Congestion Sinusitis	<ul style="list-style-type: none"> Best for nasal congestion and intermittent symptoms Often given to provide relief until corticosteroids kick in 	Reduce swelling of the blood vessels in your nose, throat and sinuses.	<ul style="list-style-type: none"> Short term only — Rebound congestion
	[NON PRESCRIPTION] <i>Intranasal Corticosteroids</i> Fluticasone propionate, Beclomethasone dipropionate	Onset: 12 hours Duration: 12-48 hours Rhinorrhoea Sneezing Itching Nasal Congestion Allergic conjunctivitis Sinusitis	<ul style="list-style-type: none"> First line in moderate-severe intermittent symptoms or persistent allergic rhinitis and pregnant women Shake before use May take a few days for maximum relief. Best for late phase symptoms 	Reduce the influx of inflammatory cells into the nasal mucosa in response to allergic stimuli.	<ul style="list-style-type: none"> Safe for long term use
	[NON PRESCRIPTION] <i>Intranasal Anticholinergics</i> Ipratropium Bromide + Xylometazoline	Onset: 10-20 minutes Duration: 4-12 hours Rhinorrhoea	<ul style="list-style-type: none"> Recommended for vasomotor rhinitis 	Acetylcholine antagonist via blockade of muscarinic cholinergic receptors	Nasal dryness, irritation, nose bleed
	[NON PRESCRIPTION] <i>Intranasal Mast Cell Stabilisers</i>	(Less effective than nasal steroids) Rhinorrhoea Sneezing Nasal Congestion	Less effective than steroids	Prevents degranulation of mast cells	
Ocular	[NON PRESCRIPTION] <i>Ocular Antihistamines</i> Olopatadine (Olopatadine) Antazoline + Naphazoline (Albacon-A), Levocabastine (Livostin), Ketotifen (Zaditen)	Rhinorrhoea Sneezing Nasal Congestion		Blocks histamine binding	
	[NON PRESCRIPTION] <i>Ocular Decongestant</i> Naphazoline (Naphcon Forte) Pheniramine + Naphazoline (Naphcon-A)	Allergy symptoms			Irritation
	[NON PRESCRIPTION] <i>Ocular Mast Cell Stabilisers</i> Sodium Cromoglycate (Cromo-Fresh, Rexacrom) Lodoxamide	Onset: 10 days Allergy symptoms		Narrow blood vessels in the eye	

Drug		Runny Nose	Sneezing	Congestion	Sinusitis	Nasal Polyps	Allergic Conjunctivitis	Urticaria
Oral	Antihistamines	++	++	+/-			+/-	++
	Oral Decongestants			++	++			
Nasal	Intranasal Decongestants			++				
	Intranasal Corticosteroids	++	++	++	++	++	+/-	
	Intranasal Intracholinergics	++						
	Intranasal Mast Cell stabilisers	++	++	++				
Ocular	Ocular Antihistamines						++	
	Ocular Mast Cell Stabilisers						++	

Sinusitis (Rhinosinusitis)

Description

Rhinosinusitis, or more simply sinusitis, is the inflammation of one or more of the paranasal sinuses (air-filled spaces located in your cheeks, forehead, and around your eyes that drain into the nasal cavity).

Following a cold, sinus air spaces can become filled with nasal secretions, which *stagnate* due to reduced ciliary function of the cells lining the sinuses.

Viruses (most commonly) or bacteria, such as *Streptococcus* and *Haemophilus*, can then secondarily infect these stagnant secretions. For this reason, inflammation from acute sinusitis is often accompanied by an *infection*. Sinusitis can be:

- Acute: up to 4 weeks
- Sub-acute: 1-3 months
- Chronic: > 3 months

Signs & Symptoms

Heavy, full feeling/pressure in your head that can be painful and uncomfortable (**worse when leaning forward**), often feels like a cold that won't go away, congestion, **toothache**

Red flags: swelling around the eyes, severe headache, high fever.

Risk Factors

May develop as a complication of a viral URTI, hayfever, or allergy.

Non-Pharmacological Treatment

1. Sinus Rinses

Pharmacological Treatment

[BPAC Antibiotic Guidelines for Sinusitis](#)

1. Analgesics: Paracetamol, NSAIDs
2. Corticosteroid Nasal Spray: fluticasone, budesonide
3. Oral Sympathomimetics/Decongestants
4. Nasal Sympathomimetics/Decongestants
5. Antibiotics: Amoxicillin is first line (although antibiotics are typically not needed in sinusitis)
6. Antihistamines

Classifications	Ingredients	Patient Counselling	Mechanism of Action	Side Effects
Analgesics	[GENERAL SALE] NSAIDs, Paracetamol	<ul style="list-style-type: none"> Anti-inflammatory, antipyretic, analgesics Can reduce pain and discomfort 	<ul style="list-style-type: none"> Careful of Reye's syndrome - do not give Aspirin in <16y 	GIMIRI
Anti-Inflammatory	[PHARMACY ONLY] <i>Corticosteroid Nasal Spray</i> Betamethasone, Budesonide, Fluticasone, Triamcinolone (BecloCLEAR, Butacort, Flixonase, Telnase)	<ul style="list-style-type: none"> Shake the bottle before use. Gently blow your nose before use. Tilt your head slightly forward when using the spray It takes a few days to 2 weeks for a steroid spray to build up to its full effect (you won't get an immediate relief of symptoms) 	<ul style="list-style-type: none"> Reduce inflammation of the nasal mucosa The long term use of steroid nasal sprays is thought to be safe. 	Burning, stinging, dryness of the nostrils, nose bleed may occur.
Nasal Decongestants	[GENERAL SALE/ PHARMACY ONLY] <i>Xylometazoline</i> Otrivin, Maxiclear, Sudafed <i>Oxymetazoline</i> Drixine, Mucinex Sinus, Sudafed Nasal Spray, Vicks <i>Anti-Cholinergics:</i> <i>Ipratropium Bromide (+/-)</i> <i>Xyometazoline</i> Univent, Otrivin Plus <i>Sodium Chloride</i> Otrivin Saline	<ul style="list-style-type: none"> Rebound congestion possible so use is limited to 3-5/5-7 days Rebound congestion describes the swelling of blood vessels as a response to the medication wearing off. It is much harder to treat than normal congestion. 	<ul style="list-style-type: none"> Contraindications: issues with heart, kidneys, blood pressure, diabetes, glaucoma, thyroid gland, prostate. 	Local irritation
Oral Decongestants	Please see NZF Link above for full list of products containing these.	<ul style="list-style-type: none"> Note: Nasal decongestants for administration by mouth may not be as effective as preparations for local application but they do not give rise to rebound nasal congestion on withdrawal. 	<ul style="list-style-type: none"> Nasal decongestants reduce congestion and swelling. 	
Antibiotics	[PRESCRIPTION] <i>Amoxicillin (first line)</i> <i>Phenoxy-methylpenicillin, Amoxicillin-Clavulanic acid</i> <i>Doxycycline, Clarithromycin</i>	<ul style="list-style-type: none"> Take until finished Take with food if stomach upset <p>Antibiotics are seldom required as sinusitis is often viral in nature. These would be trialled if symptoms last for longer than 10 days, symptoms are severe or there is evidence of a skin infection.</p>	<ul style="list-style-type: none"> Given if the infection fails to resolve on its own. 	Hypersensitivity reactions, GI effects
Antihistamines	[GENERAL SALE] <i>1st Gen: Promethazine</i> <i>2nd Gen: Cetirizine, Loratadine, Fexofenadine</i>	<ul style="list-style-type: none"> If the sinusitis is the result of an allergic cause, antihistamines can help dry up nasal secretions and relieve post nasal drip. 1st gen can help onset of sleep. 	<ul style="list-style-type: none"> Some doctors advise against using antihistamines during a sinus infection because they can cause excessive drying and slow the drainage process. 	Drowsiness, dizziness

Sore Throat (Pharyngitis, Tonsilitis, Laryngitis)

Description

A sore throat is the feeling of pain, scratchiness or irritation in your throat that often worsens when you swallow. Sore throats often accompany infections such as the cold or flu and thus, are mostly viral in nature.

Incidence	Cause
Most Likely (70-90%)	Viral Infection
Likely	Streptococcal Infection
Unlikely	Glandular Fever, Trauma
Very Unlikely	Carcinoma, Medicines

However, a small percentage (~30%) of sore throats end up being bacterial. Knowing how to differentiate them is important!

BACTERIAL VS VIRAL SORE THROAT					
Incidence	Age	Tonsillar/Pharyngeal Exudate	Duration	Cough	Other Symptoms
Viral Infections	Any age	Possible but generally limited	3-7 days	Common	Low grade fever, headache
Bacterial Infections	School Children	Often present and can be substantial		Rare	High grade fever (>38 degrees, possible rash, swollen lymph nodes)

Any structure of the upper respiratory tract can cause a sore throat, for example: the pharynx (pharyngitis), the tonsils (tonsillitis) and the larynx (laryngitis).

	Pharyngitis	Tonsilitis	Laryngitis
Description	Inflammation of the pharynx, causing rapid onset of sore throat.	Inflammation of the tonsils in the upper part of the throat.	Inflammation of the larynx
Cause/Risk Factors	<ul style="list-style-type: none"> Viral: rhinovirus, coronavirus, adenovirus, (para)influenza, Epstein-Barr Bacterial: streptococcus (GAS) 	<ul style="list-style-type: none"> Viral infection Bacterial infection 	<ul style="list-style-type: none"> Viral, bacterial, fungal infection (antibiotics use, ICS) Inflammation: reflux laryngitis, trauma (coughing, overuse of voice, burn from hot food, dry mouth, smoking)
Symptoms	Sore throat	<ul style="list-style-type: none"> Sore throat, cold symptoms, difficulty or painful swallowing, bad breath, systemic symptoms, swollen and tender tonsils with spots of white/yellow pus Tonsillar/pharyngeal exudate (if bacterial) 	<ul style="list-style-type: none"> Hoarseness, feeling of lump in throat, pain and discomfort in neck Cough, headache
Treatment	<ul style="list-style-type: none"> Self-limiting (symptomatic relief) Antibiotics (if bacterial) 	<ul style="list-style-type: none"> Paracetamol, NSAIDs Throat lozenges Corticosteroids (if difficulty swallowing or breathing) Antibiotics (if bacterial) 	<ul style="list-style-type: none"> Self-limiting (symptomatic relief) Antibiotics (if bacterial)

Complications: Bacterial infection can lead to heart, kidney failure, abscess, and rheumatic fever

Red Flags: >2 weeks duration, marked tonsillar exudate with high fever and swollen glands, dysphagia and dysphonia (different from normal pain), high risk groups

Diagnosis

1. Visual examination: mouth, glands
2. If bacterial: throat culture

Primary Prevention - Rheumatic Fever

[BPAC Antibiotic Guideline: Sore Throat & RF Risk](#) [Heart Foundation - Sore Throat Algorithm](#)

As only a small proportion of sore throats are bacterial in nature (~30%) - caution needs to be exercised around prescribing antibiotics. Even in the event that the sore throat is bacterial - antibiotics will not make much of a difference as the immune system clears the infection within a few days. There is however one exception to this rule.

Group A Streptococcal, also known as GAS A, is a particular type of bacteria that can cause sore throats. While most GAS infections are superficial, in a small number of cases (1-3%) it can lead to severe complications such as Rheumatic Fever (RF). In order to avoid it from developing, prompt screening and treatment of susceptible individuals is required:

1. Patients that are at high risk of RF should have a **throat swab** taken **AND** have **empiric antibiotic treatment** initiated at the same time
2. If throat swabs come back negative for GAS, individuals are welcome to discontinue antibiotic use.



Patients At Risk of Rheumatic Fever

Personal, family or household history and 2+ of the following:

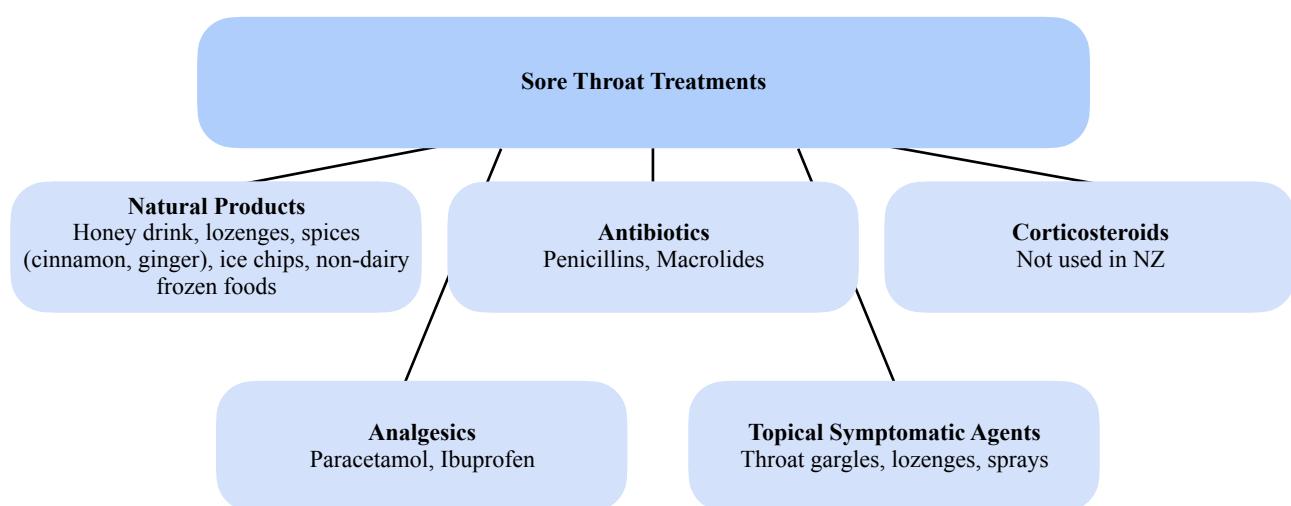
- A. Māori or Pacific ethnicity
- B. Aged 3-35 years
- C. Living in crowded circumstances or lower socioeconomic areas

Non-Pharmacological Treatment

1. Rest & fluids
2. Natural products: honey drink, lozenges, spices (cinnamon, ginger), ice chips, non-dairy frozen foods
 - Lack of evidence for alcohol based drinks, lemon drinks, apple cider vinegar
 - Dairy products can induce production of mucus which causes irritation

Pharmacological Treatment

1. *Symptomatic relief:* analgesics, throat gargles/lozenges/sprays
2. *Antibiotics:* if bacterial infection, severe inflammation, abscess, swallowing difficulty, systemically unwell, co-morbidities, a risk of complications (pneumonia)



Classifications		Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Bacterial	Antibiotics	[PRESCRIPTION] <i>1st Line</i> Penicillin V, Amoxicillin <i>Alternatives</i> Erythromycin, Roxithromycin	<ul style="list-style-type: none"> Penicillins are antibiotics that attach to penicillin binding proteins to interrupt cell wall biosynthesis, leading to bacterial cell lysis and death 	<ul style="list-style-type: none"> Recommended in high risk of rheumatic fever 10 day course. Take until finished Take with food if stomach upset, or take probiotics following the antibiotic 	<ul style="list-style-type: none"> Hypersensitivity reactions, GI effects.
	Topical Antibacterial Agents	[GENERAL SALE, PHARMACY ONLY] Chlorhexidine (Sava/Rivacol) Benzalkonium chloride + Cetylpyridinium (Cepacaine Mouthwash)	<ul style="list-style-type: none"> Topical antibacterial agents 	N/A	N/A
Bacterial & Viral	Local anaesthetics	[VARIOUS] <i>Lidocaine/Lignocaine</i> <i>Benzocaine + Cetylpyridinium Chloride</i> Codral Duo Relief Sore Throat Lozenges Strepsils Sore Throat Lozenges	<ul style="list-style-type: none"> Numb the throat 	<ul style="list-style-type: none"> <i>Codral:</i> Not suitable for children under 12 years <i>Strepsils:</i> Not suitable for children under 6 years 	<ul style="list-style-type: none"> Careful when drinking hot drinks due to altered perception of heat.
		[GENERAL SALE] <i>Benzydamine</i> Difflam Mouth Wash, Oral Spray			Mouth wash can sting a bit - dilute if needed
	Anti-Inflammatory Topical Symptomatic Therapy (e.g. Spray/Lozenges/Gargles)	[PHARMACY ONLY] <i>Flurbiprofen</i> Strepfen Intensive Lozenges	<ul style="list-style-type: none"> Numbs the throat 	<ul style="list-style-type: none"> Place in oral cavity and slowly let dissolve. Throat sprays are effective for night time due to fast action and ease of taking (no need to suck on a lozenge). 	<ul style="list-style-type: none"> Taste disturbances, mouth ulcers (move lozenge around the mouth) Careful of Hypersensitivity to aspirin or any other NSAIDs. GIMIRI.
		[GENERAL SALE] <i>Povidone Iodine</i> Betadine Ready to Use Sore Throat Gargle	<ul style="list-style-type: none"> Topical antiseptic 	<ul style="list-style-type: none"> Avoid regular use in patients with thyroid problems or on lithium therapy, avoid application on large open wounds (can cause metabolic acidosis) 	
		[PRESCRIPTION] <i>Corticosteroids</i> <i>(Not used in NZ)</i>	<ul style="list-style-type: none"> Anti-inflammatory 	<ul style="list-style-type: none"> Weak recommendation, may help. 	Unlikely harm from a single dose.
	Analgesics	[GENERAL SALE] Paracetamol, Ibuprofen, Aspirin Gargle	<ul style="list-style-type: none"> Anti-inflammatory, antipyretic, analgesics 	<ul style="list-style-type: none"> For Aspirin, careful of Reye's syndrome - do not give in <16y 	GIMIRI
	Probiotics	[GENERAL SALE] <i>Probiotic Lozenges</i> Blis Throat Guard	<ul style="list-style-type: none"> Contains killed bacteria or pathogens often found in colds and chills. 	N/A	N/A

A Focus on Difflam Products

Difflam Product Range

SORE THROATS WITH DIFFLAM										
	Natural Lozenges	Lozenges			Sprays		Gargles			Mouth Gel
Symptom	Mild Throat Irritation	Moderate Sore Throat	Painful Sore Throat	Sore Throat + Unproductive Cough	Painful Sore Throat	Sore Throat	Sore Throat	Sore Throat/Mouth	Sore Throat/Mouth	Sore Mouth/Gums
Product Image										
Product Name & Size	Difflam Natural Soothing Drops (20 Drops)	Difflam Sore Throat Lozenges (16 Lozenges)	Difflam Plus Anaesthetic Sore Throat Lozenges (16 Lozenges)	Difflam Plus Sore Throat + Cough Lozenges (24 Lozenges)	Difflam Sore Throat Spray Forte (15ml)	Difflam Ready to Use Sore Throat Gargle With Iodine (200ml)	Difflam Sore Throat Gargle & Mouth Solution Anti-Inflammatory (500ml)	Difflam-C Ready to Use Sore Throat Gargle & Mouth Solution (100ml/200ml)	Difflam Anti-Inflammatory + Antibacterial Mouth Gel (10g)	
Indication	Helps sore throat + supports immune system	Fast relief of sore throat/mouth	Rapid relief within 90 minutes. Has extra numbing effects.	Relieves dry cough and sore throat.	Targeted pain relief	Targeted pain relief	Aids in treatment of sore throat	Fast pain relief	Dual action - has added antiseptic	Fast relief of painful inflamed condition of the mouth
Ingredients	Wellmune Manuka Honey Sucralose	Benzydamine Cetylpyridinium Saccharin Sucralose	Lignocaine Dichlobenzyl	Benzydamine Cetylpyridinium Saccharin Phocodine	Benzydamine Alcohol Saccharin	Benzydamine Alcohol Saccharin	Iodine Saccharin	Benzydamine Saccharin	Benzydamine Chlorhexidine	Benzydamine Cetylpyridinium Saccharin
Age Indication	6 & Over	6 & Over	6 & Over	6 & Over	6 & Over	6 & Over	12 and Over	6 & Over	6 & Over	6 & Over
Sugar Free	X	✓	✓	✓	✓	✓	✓	✓	✓	✓
Suitable for Diabetes	X	✓	✓	✓	✓	✓	✓	✓	✓	Mouth Ulcers in Diabetes should be checked up
Lactose Free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Gluten Free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Alcohol Free	✓	✓	✓	✓	X	X	X	X	X	✓
Artificial Colouring Free	✓	X	X	X	✓	✓	✓	X	X	✓
Doses/Directions	Over 6 Dissolve 1 drop as required. Excess consumption may have a laxative effect.	Over 6 Dissolve 1 lozenge as required every 3 hours (at most every 1-2 hours). Max of 12 lozenges per day.	Over 6 Dissolve 1 lozenge as required every 3 hours (at most every 1-2 hours). Max of 12 lozenges per day.	Over 12 1 lozenge every 3 hours as required. Max 12 a day 6-12 1 lozenge every 3 hours as required. Max 8 lozenges.	Over 12 Spray 2-4 times directly on sore area and swallow gently. Repeat every 1/2 to 3 hours as required. 6-12 Spray 2 times directly on sore area and swallow gently. Repeat every 1/2 to 3 hours as required. 2 times	Over 12 Spray 4-8 times directly on sore area and swallow gently. Repeat every 1/2 to 3 hours as required. 6-12 Spray 4 times directly on sore area and swallow gently. Repeat every 1/2 to 3 hours as required. 2 times	Over 12 Using measuring cup provided, gargle 15ml for 30 seconds and expel from mouth. Repeat every 3-4 hours as necessary. Do not swallow	Over 6 Using measuring cup provided, gargle 15ml for 30 seconds and expel from mouth. Repeat every 3-4 hours as necessary. Do not swallow	Over 6 Using measuring cup provided, gargle 15ml for 30 seconds and expel from mouth. Repeat every 3-4 hours as necessary. Do not swallow	Over 6 Gently message approximately 1cm into sore area with a clean finger tip every 2-3 hours as required (max of 12 times per day). Do not eat or drink for 15 minutes after application.
Pregnancy Category	-	B2	B2	B2	B2	B2	-	B2	B2	B2

Rheumatic Fever (RF) & Rheumatic Heart Disease (RHD)

Description

Rheumatic fever is a non-contagious, autoimmune disease that causes inflammation of the heart, joints, brain, and skin. It can develop if a GAS infection such as a strep sore throat is not treated properly. And as we've established earlier, while most GAS infections are superficial, they can cause issues only in a small number of cases (1-3%) - which is why prompt screening and treatment of susceptible individuals with sore throats should be done.



JONES Criteria

Joints (Arthritis 60-80%)

Heart (Carditis, EchOcardiogram 30-45%)

Skin (Nodules, Erythema 1-8%)

CNS (Sydenham's Chorea/Neurological symptoms 10%)

Pathophysiology

In RF, the damage is not caused by the bacteria but instead, the immune response to it. Although the body produces the correct anti-GAS antibody, it begins to cross-react with self-tissues given certain structural similarities the GAS pathogen shares with our own cells. This triggers the autoimmune response we observe.

Signs & Symptoms

Please note the below resolve without therapy with no lasting damage.

JONES CRITERIA	Mechanism of Action
Polyarthritis Joint	Antibody cross-reacts with synovial proteins resulting in the influx of inflammatory cells
Carditis Heart	Antibody response against heart valve proteins and VCAM-1
Skin Nodules & Erythema Skin	Antibody cross reacts with keratin
Sydenham's Chorea CNS	Antibody cross-reacts with neuronal proteins which results in altered signalling which presents as involuntary movements that affect trunk, limbs, face (grimaces, frowns). Not life-threatening.

Complications

This disease can progress to chronic Rheumatic Heart Disease (RHD) which can cause damage to the heart valves.

Risk Factors

ARF (5 - 14y) / RHD (20 - 30y)

- *Ethnicity:* Higher in Māori/Pasifika populations
- *Socio-economic:* Living in a crowded environment, poverty
- *Age:* 3-35 years
- *Genetic*

Diagnosis

There is **no** definitive test. But correct diagnosis is important to avoid:

- Unnecessary antibiotic treatment (monthly injection for years!)
- Cardiac damage & reduced lifespan

Generally RF often requires hospitalisation for investigation (inflammatory markers, throat swab, anti-GAS serology, ECG, echocardiogram, chest x-ray)

Prevention

Primordial Prevention

- Increase awareness of rheumatic fever (what causes it, how to prevent it)
- Reduce household crowding and therefore reduce household transmission of GAS
- Improve access to timely and effective treatment for strep throat infections in priority communities – school based sore throat swab service

Primary Prevention

- Throat swabs in schools with kids with sore throats

Secondary Prevention

- Antibiotic Course - see pharmacological treatment

Non-Pharmacological Treatment

Strict bed rest may be recommended for a few weeks to a few months - especially if the heart is affected.

Pharmacological Treatment

[RF & RHD Heart Foundation Treatment Guidelines](#) and see [NZF](#) for dosing guidelines

1. *Antibiotics (for treatment of current infection + secondary prevention):* Oral Penicillin V, amoxicillin
2. *Arthritis:* Paracetamol, Naproxen (or any other anti-inflammatories)
3. *Chorea:* Valproic acid, carbamazepine — ONLY if necessary
4. *Cardiac:* Cardiac drugs and/or surgery — treat as necessary

Classifications	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Antibiotics	<p>[PRESCRIPTION] <i>1st Line</i> Penicillin V, Amoxicillin</p> <p><i>Alternatives</i> Erythromycin, Roxithromycin</p>	<ul style="list-style-type: none"> Penicillins are antibacterials that attach to penicillin binding proteins to interrupt cell wall biosynthesis, leading to bacterial cell lysis and death 	<ul style="list-style-type: none"> Recommended in high risk of rheumatic fever 10 day course. Take until finished Take with food if stomach upset 	
Secondary Prevention Antibiotics	<p>[PRESCRIPTION] <i>1st Line</i> Benzathine Penicillin</p> <p><i>Second Line</i> Penicillin V</p> <p><i>Alternatives</i> Erythromycin</p>		Benzathine Penicillin (IM every 4 weeks for 10 years) for prevention	Hypersensitivity reactions, GI effects
Arthritis	<p>[VARIOUS] <i>NSAIDS</i> Paracetamol, Naproxen</p>	<ul style="list-style-type: none"> Anti-inflammatory, antipyretic, analgesics 	<ul style="list-style-type: none"> Careful of Reye's syndrome with aspirin - do not give in <16y 	GIMIRI
Chorea	<p>[PRESCRIPTION] <i>Anti-Epileptics</i> Valproic Acid, Carbamazepine</p>	<ul style="list-style-type: none"> Altering electrical activity in neurons by affecting ion (sodium, potassium, calcium, chloride) channels in the cell membrane 	N/A	dizziness, drowsiness, and mental slowing
Heart	[PRESCRIPTION] Cardiac drugs & Surgery			

Common Cold

Description

The common cold is a self limiting **viral** illness of the respiratory system lasting from 2 days to 2 weeks, causing a sore throat and nasal discharge. These occur due to the body's defence attempt to clear the airways of foreign bodies and particulate matter. This is supplemented by the mucociliary escalator.

Signs & Symptoms

Productive (chesty) **or** nonproductive (dry, tight, tickly) cough, sore throat, fatigue, weakness, sneezing, stuffy nose. Many patients will say they are not producing sputum, although they may say they 'can feel it on their chest'. In these cases, the cough is probably productive in nature and should be treated as such.

Complications: Pneumonia or asthma really only occur in the elderly, young, or immunocompromised.

Risk Factors

1. Virus (Rhinoviruses, coronaviruses, parainfluenza, RSV, adenoviruses, enteroviruses)

Non-Pharmacological Treatment

1. Rest & fluids
2. Saline irrigation (safely used in infants but may cause minor irritation)
3. Vapour inhalation
4. Demulcents: simple linctus, honey
5. Vitamin C, Echinacea, Black elderberry, garlic
6. Limit viral spread by using disposable tissues and washing hands frequently

Pharmacological Treatment — See Common Respiratory Symptoms

BPAC Coughs & Colds Medicines

Given that it is a viral illness, the infection is self limiting (7-10 days) and treatment is mainly surrounding symptomatic relief with non-prescription cough and cold medicines. Medsafe advises that most oral cough and cold medicines are **not used in children under 6 years.**

- Buccaline Tablets (Oral vaccine)
- Topical Sympathomimetics / Decongestants (Nasal Sprays/Drops)
- Systemic Sympathomimetics / Decongestants
- Cough Suppressants
- Cough Expectorant
- Mucolytics
- Sedating Anti-Histamines

Classifications	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Antibacterial Oral Vaccine (Tablet)	[PHARMACIST ONLY] <i>Oral Vaccine</i> Buccaline Tablets	<ul style="list-style-type: none"> Contains killed bacteria or pathogens often found in colds and chills. 	<ul style="list-style-type: none"> Will not offer protection against viral coughs or cold. Does not replace flu vaccine 	<ul style="list-style-type: none"> N/A
Topical Sympathomimetics/ Decongestant (Nasal Spray & Drops)	[PHARMACY ONLY] <i>Xylometazoline</i> Otrivin, Otrivin Plus <i>Oxymetazoline</i> Sudafed Nasal Spray, Vicks	<ul style="list-style-type: none"> Nasal decongestants reduce congestion and swelling. <p>Do not use in CVD risk</p>	<ul style="list-style-type: none"> Rebound congestion possible so use is limited to 3-5/5-7 days 	<ul style="list-style-type: none"> Local nasal irritation
Systemic Sympathomimetics/ Decongestant	[VARIOUS] <i>Phenylephrine</i> Sudafed, Lemsip (+ Paracetamol + Caffeine) [CONTROLLED DRUG] <i>Pseudoephedrine - C3</i> Sudafed	<ul style="list-style-type: none"> Activate adrenergic receptors which act to ease vascular constriction and a reduction of nasal blood supply. <p>Do not use in CVD risk</p>	<ul style="list-style-type: none"> Rebound congestion possible so use is limited to 3-5/5-7 days Do not take dose (children) before bedtime as their mild stimulant action can disturb sleep. 	<ul style="list-style-type: none"> Sleepiness, insomnia, restlessness, tachycardia. Caution in HTN, CV, T1/T2DM, thyroid, prostatic hypertrophy, pregnancy.
Cough Suppressants (antitussives)	[PHARMACIST ONLY] <i>(Opiate Derivatives)</i> Dextromethorphan Pholcodine, Codeine	<ul style="list-style-type: none"> Suppresses unproductive (dry) coughs by acting directly on the cough centre to depress the cough reflex. 	<ul style="list-style-type: none"> Do not use dextromethorphan with other serotonin modulation drugs (risk of serotonin syndrome): SSRIs, MAOI 	<ul style="list-style-type: none"> Sedation
Cough Expectorants	[GENERAL SALE] <i>Guaifenesin</i> Robitussin, Mucinex, Lemsip chesty cough (+ Paracetamol)	<ul style="list-style-type: none"> Increases volume and decreases viscosity of secretions of productive (wet) coughs to assist removal of sputum. 	<ul style="list-style-type: none"> Lemsip contains paracetamol — make sure patients are not taking excessive doses unknowingly 	<ul style="list-style-type: none"> Gastric irritation
Mucolytics	[PHARMACIST ONLY] <i>Bromhexine</i>	<ul style="list-style-type: none"> Supports the body's mechanisms for clearing mucous from the respiratory tract (thins and breaks down mucous) 	<ul style="list-style-type: none"> Do not oversuse 	<ul style="list-style-type: none"> GI effects
1st Generation Sedating Antihistamines	[PHARMACIST ONLY] <i>Chlorphenamine (Histafen)</i> <i>Diphenhydramine (Unisom)</i>	<ul style="list-style-type: none"> Anticholinergic drying action on mucous membranes (i.e. to dry up nasal secretions) and not via histamine. Sedative effects help promote sleep 	<ul style="list-style-type: none"> Careful of driving or operating heavy machinery 	<ul style="list-style-type: none"> Sedation, dry mouth, constipation Avoid in closed-angle glaucoma and prostate enlargement because it could lead to increased intraocular pressure and precipitation of urinary retention.
Intranasal Anticholinergics	[PHARMACY ONLY] <i>Ipratropium bromide</i> (Univent, Atrovent)	<ul style="list-style-type: none"> Anticholinergic 		
Demulcents	[VARIOUS] Simple Linctus, Honey	<ul style="list-style-type: none"> Reduce irritation by coating the pharynx and thus prevent coughing. 	<ul style="list-style-type: none"> Safe to use in any patient group 	
Saline Irrigation Nasal Spray	[GENERAL SALE] Fess Sinus Cleanse	<ul style="list-style-type: none"> Cleanses sinuses 	<ul style="list-style-type: none"> Safe to use in any patient group, but may cause minor irritation 	

Osce Points

- Check for sinus infection e.g. pain that is worse when leaning forward
- Check of middle ear involvement e.g. ear pain

Influenza (Flu)

Description

Influenza, also known as the flu, is a common viral infection (RNA virus) affecting the nose, throat, and lungs. It is more severe and abrupt than a cold and spreads quickly from person to person via droplets/secretions, particularly during the flu season (May to October). The flu may be life-threatening especially in high-risk groups — mortality is usually due to **secondary bacterial pneumonia**.

Individuals can get infected multiple times due to virus continuously mutating (seasonal vs epidemic/pandemic variants).

SYMPTOMS OF COLD



SYMPTOMS OF FLU



Pathophysiology

- The virus has 2 major surface glycoproteins; haemagglutinin (HA) and neuraminidase (NA). HA allows the host cell to be infected and NA allows the virus to leave the cell to infect other cells.
- There are three types of influenza (A, B, C). However, only A and B causes disease in human; A causes epidemics and pandemics.

Signs & Symptoms

These are present 4 days after exposure and last a week:

- Fever, sore throat, fatigue, weakness, chills, muscle aches, SoB, dry cough (> 2 weeks duration), congestion, runny nose, headache, malaise, insomnia, loss of appetite

Red Flags: worsening fever, altered mental status, O₂ saturation < 94%

Complications: Pneumonia, COPD, severe lung inflammation causing respiratory failure, congestive HF

Differential Diagnosis

Although the flu and the common cold share many symptoms such as fever, cough, shortness of breath, and a sore throat, the flu differs in the fact that it has more severe symptoms such as difficulty breathing, chest pain and confusion. The flu also has a more abrupt onset and lasts longer.

SIGNS AND SYMPTOMS	COLD	FLU
Symptom onset	Gradual	Abrupt
Fever	Rare	Usual
Aches	Slight	Usual
Chills	Uncommon	Fairly common
Fatigue, weakness	Sometimes	Usual
Sneezing	Common	Sometimes
Chest discomfort, cough	Mild to moderate	Common
Stuffy nose	Common	Sometimes
Sore throat	Common	Sometimes
Headache	Rare	Common

Non-Pharmacological Treatment

- Prevention via good hand hygiene
- Cover mouth, nose, face
- Ventilation, oxygenation
- Rest
- Fluids/ Hydration

Prevention

- Seasonal flu vaccine

Vaccine	Vaccine Type	When	Eligibility Criteria
<ul style="list-style-type: none"> • Afluria Quad • Afluria Quad Junior • Flud Quad • Fluquadri 	Inactivated quadrivalent subunit vaccine	Influenza immunisation programme: 1st April - 31st December	<ol style="list-style-type: none"> 1. ≥ 65 years 2. 55 - 64 years (if Māori or Pacifica) 3. ≤ 65 years with CVD, chronic respiratory disease, diabetes, CKD, cancer (<i>excluding</i> non-cancerous skin cancers), autoimmune conditions, Down-syndrome, immune deficiency... 4. Pregnant women (any trimester) 5. Children aged 3 to 12 years inclusive 6. Children ≤ 4 years old who have been hospitalised for respiratory illness or have a history of significant respiratory illness.

Pharmacological Treatment

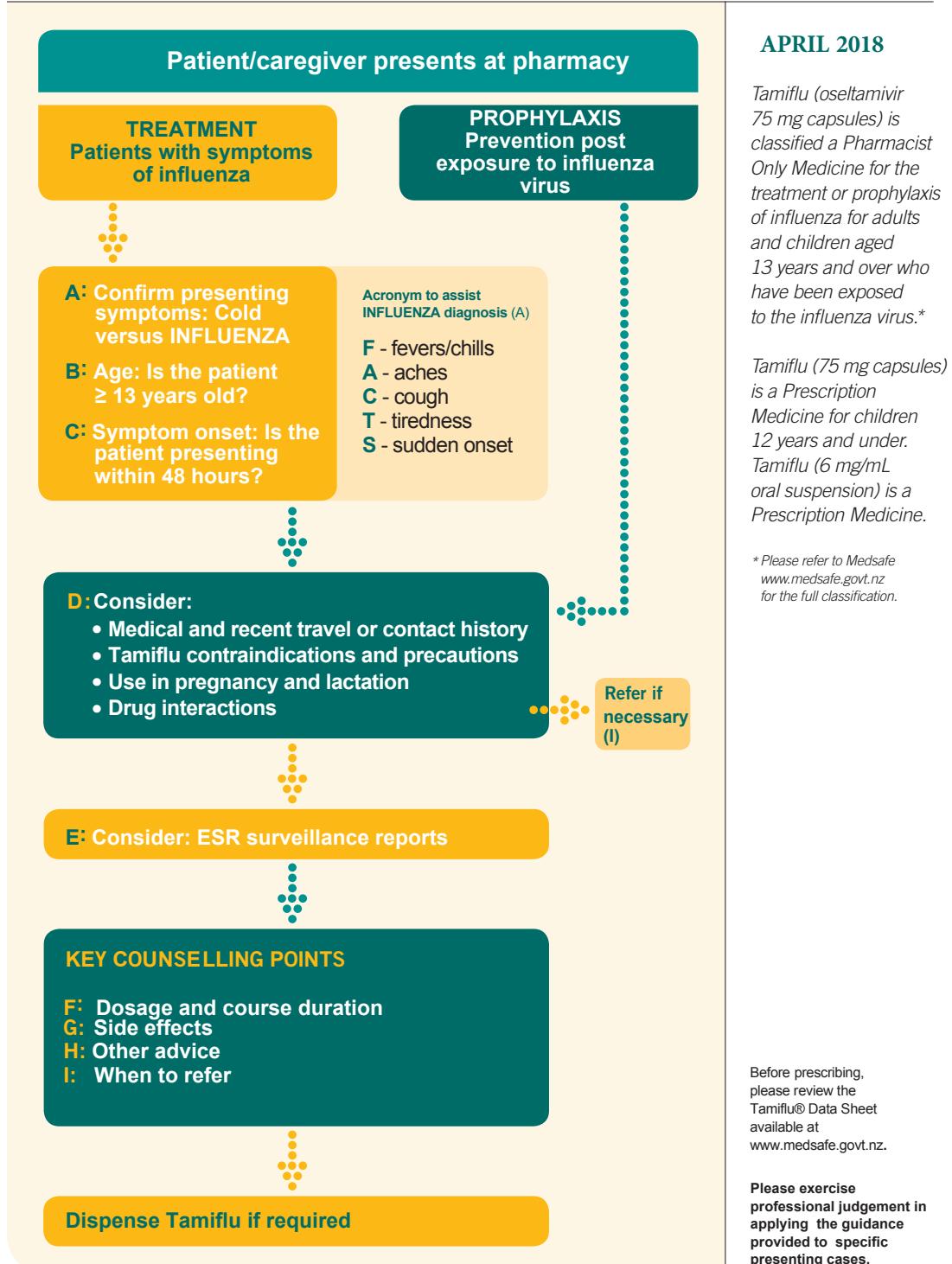
Symptomatic relief as the disease is self-limiting (~2 weeks) — *See Colds Treatment*

1. *Neuraminidase inhibitors:* Oseltamivir (Tamiflu), Zanamivir (Relenza)
2. *Analgesia/Antipyretics:* Paracetamol, NSAIDs
3. *Oral/Nasal Sympathomimetics/Decongestants:* Oxymetazoline, xylometazoline, pseudoephedrine
4. *Intranasal Anticholinergics:* Ipratropium
5. *Others:* Zinc lozenges, Vitamin C, (Methanol) Vapour inhalation, Saline sprays

Classifications	Ingredients	Mechanism of Action	Patient Counselling	Side Effects
Antiviral	[PHARMACIST ONLY] <i>Oseltamivir</i> Tamiflu <i>Zanamivir</i> Relenza	Oseltamivir reduces replication of influenza A and B viruses by inhibiting viral neuraminidase.	<i>Oseltamivir</i> Treatment: 75mg BD for 5 days (best started early, but can be effective for 48 hours after onset) Prevention: 75mg OD for 10 days (start within 48 hours of coming into contact with someone with the flu). We cannot sell it as a prophylaxis to people who haven't been exposed .	N/V/D, headache, abdominal pain, conjunctivitis
Analgesics	[VARIOUS] NSAIDs, Paracetamol	Helps treat headache, fever, sore throat pain, muscle aches, chills, sinus pain, ear ache	Do not take any other paracetamol containing products with paracetamol.	GIMIRI
1st Generation Antihistamines	[PHARMACIST ONLY] <i>Chlorphenamine</i> (Histafen) <i>Diphenhydramine</i> (Unisom)	Helps treat runny nose, sneezing, coughing	May make you sleepy. Limit alcohol	Sedation
Oral/Nasal Sympathomimetics (Decongestants)	[VARIOUS] <i>Xylometazoline</i> Otrivin, Otrivin Plus <i>Oxymetazoline</i> Sudafed Nasal Spray, Vicks <i>Pseudoephedrine, phenylephrine</i> Sudafed, Lemsip	Nasal decongestants reduce congestion and swelling.	<ul style="list-style-type: none"> • Shake before use • Rebound congestion possible so use is limited to 3-5/5-7 days 	Local irritation, headache, nausea
Intranasal Anticholinergics	[PHARMACY ONLY] <i>Ipratropium</i> Univent Nasal Spray	Helps treat runny nose due to anticholinergic activity	These medications help to relieve the symptoms of nasal allergies that lead to inflammation and infections. However, some doctors advise against using antihistamines during a sinus infection because they can cause excessive drying and slow the drainage process.	Nasal dryness, irritation, nose bleed



Tamiflu® (oseltamivir) Pharmacist Protocol



APPENDIX B: ELIGIBLE CONDITIONS FOR FUNDED INFLUENZA VACCINATION

Funded influenza vaccine is available each year for people who meet the following criteria set by PHARMAC:^{*}

1. All people 65 years of age and over; or
2. Māori and Pacific peoples aged 55 to 64 years; or
3. People under 65 years of age who:
 - have any of the following cardiovascular diseases:
 - ischaemic heart disease, or
 - congestive heart failure, or
 - rheumatic heart disease, or
 - congenital heart disease, or
 - cerebrovascular disease; or
 - have either of the following chronic respiratory diseases:
 - asthma, if on a regular preventative therapy, or
 - other chronic respiratory disease with impaired lung function;^a or
 - have diabetes; or
 - have chronic renal disease; or
 - have any cancer, excluding basal and squamous skin cancers if not invasive; or
 - have any of the following other conditions:
 - autoimmune disease,^b or
 - immune suppression or immune deficiency, or
 - HIV, or
 - transplant recipient, or
 - neuromuscular or CNS disease/disorder,^c or
 - haemoglobinopathy,^d or
 - children on long-term aspirin, or
 - a cochlear implant, or
 - error of metabolism at risk of major metabolic decompensation, or
 - pre- or post-splenectomy, or
 - Down syndrome, or
 - are pregnant (any trimester); or
4. Children aged 4 years or under who have been hospitalised for respiratory illness or have a history of significant respiratory illness.

Unless also meeting the previous criteria, the following conditions are excluded from funding:

- asthma not requiring regular preventative therapy
- hypertension and/or dyslipidaemia without evidence of end-organ disease

^{*}New Zealand Pharmaceutical Schedule at schedule.pharmac.govt.nz/ScheduleOnline.php

^a Chronic respiratory diseases include chronic bronchitis, chronic obstructive pulmonary disease, cystic fibrosis, emphysema.

^b Autoimmune diseases may include coeliac disease, Crohn's disease, Grave's disease, Hashimoto's thyroiditis, lupus, rheumatoid arthritis. Immune suppression or immune deficiency includes disease modifying anti-rheumatic drugs (DMARDs) or targeted biologic therapies.

^c Neuromuscular and CNS diseases/disorders include cerebral palsy, congenital myopathy, epilepsy, hydrocephaly, motor neurone disease, multiple sclerosis, muscular dystrophy, myasthenia gravis, Parkinson's disease, spinal cord injury.

^d Haemoglobinopathies include sickle cell anaemia, thalassemia.

Whooping Cough (Pertussis)

Description

Whooping cough is a highly infectious disease caused by the Gram- bacteria, *Bordetella pertussis*. It is spread by coughing and sneezing, and causes airway inflammation, oedema, and airway cell death with a 7-10 day incubation. It can be life-threatening and infants are often more at risk.

Signs & Symptoms

Mainly: Fever, sneezing, runny nose, dry cough

- *Stage 1 (1 week)*: malaise, low grade fever, sneezing, runny nose, dry cough
- *Stage 2 (4 weeks)*: short bursts of extreme paroxysmal coughing, vomiting, feeling of choking as the body cannot remove the mucus, ‘whooping’ between coughing fits
- *Stage 3 (6 weeks-months)*: recovery

Complications: Pneumonia, convulsions, brain damage, and death

Pharmacological Treatment

[BPAC Whooping Cough \(Pertussis\) Antibiotic Guidelines](#)

Symptomatic relief as the disease is self-limiting (2 weeks)

1. Analgesia/Antipyretics
2. Decongestants
3. Antibiotics at stage 1 (to decrease severity of stage 2) — **may also need to treat contacts**

Prevention

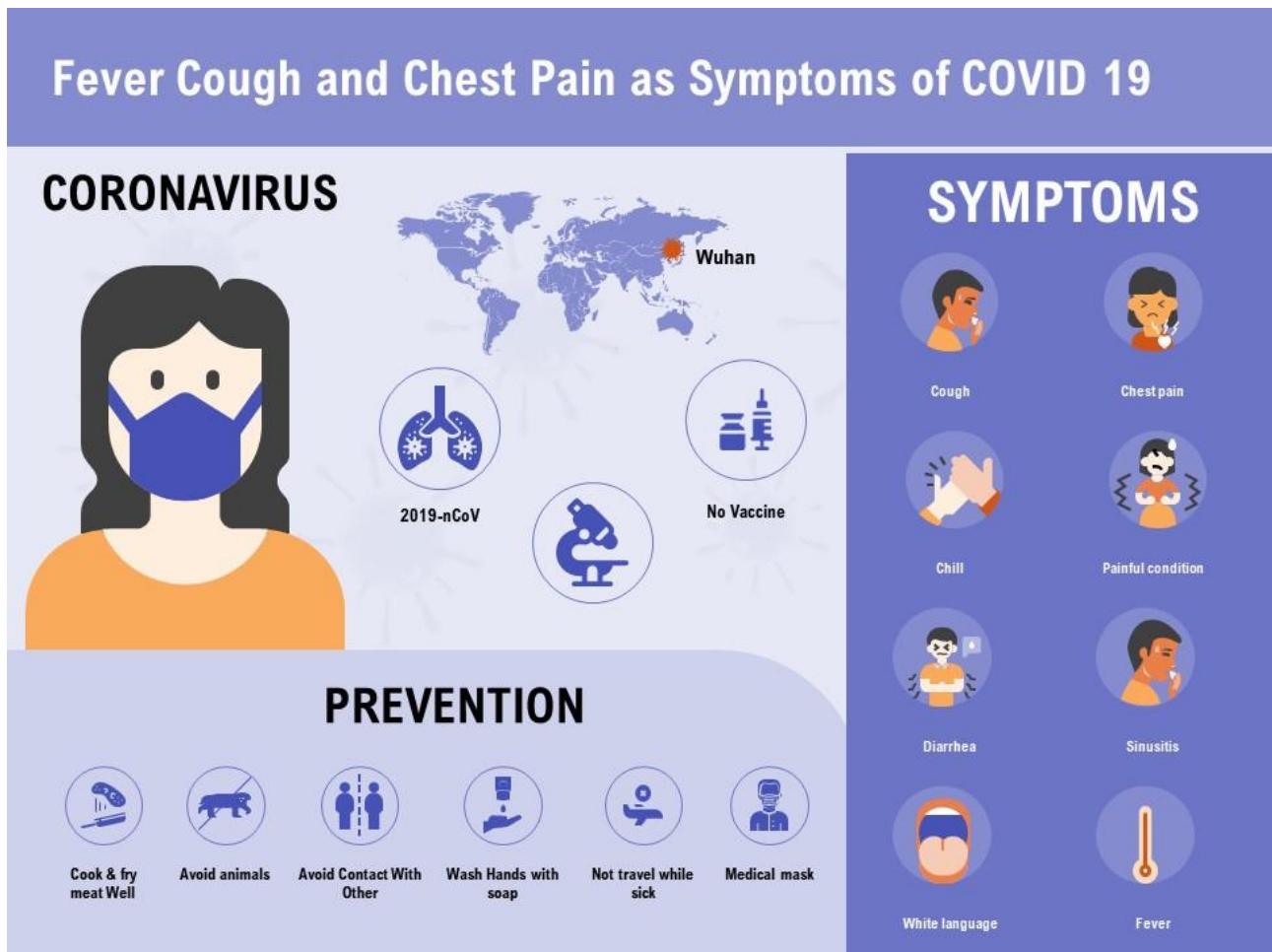
1. TDaP vaccine at 6w, 3m, 5m, 4y, 11y, and 16 weeks gestation of pregnancy
 - Infanrix-hexa (DTaP-IPV-HepB/Hib)
 - Infanrix-IPV (DTaP, polio) booster
 - Boostrix (DTaP) booster
2. At-risk infants will need to be **cocooned** by immunising all adults around them

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Infanrix-IPV booster (DTaP, polio)	IPV is inactivated or whole killed	4 years
Boostrix booster (DTaP)	Inactive	11 or 12 years Unfunded at 45y, 65y, pregnant

Coronavirus (COVID-19)

Description

COVID-19 is a viral respiratory disease caused by a coronavirus named SARS-CoV-2 that can affect your lungs, airways, and other organs. It is transmitted via droplets and with each mutation, the virus becomes more transmissible but less deadly.



Pathophysiology

Coronaviruses are a large and diverse family of viruses which cause illnesses (both in animals and humans) such as the common cold. Spike protein binds to ACE-2 receptors which are largely present in the lungs. The virus has a 4-5 day incubation and symptoms usually appear 2-5 days after being infected.

Risk Factors

The following are at risk for severe disease (see [complete list](#)) — this informs the [antiviral eligibility criteria](#)

- Māori and Pacific peoples
- Pregnancy
- Compromised immunity
- People with disability
- Age (>70 years, those in aged-care facilities, infants, premature babies)

- Smokers
- Mental health conditions and addiction
- High risk medical conditions e.g. lung disease, serious cardiac conditions, diabetes, hypertension, CKD, liver disease, cancer, obesity...

Signs & Symptoms

Usually appear 2-5 days after infection.

General symptoms: cough, sneezing, runny nose, fever, fatigue/tiredness, sore throat, SOB, temporary loss of smell or altered sense of taste, respiratory failure, cytokine storm.

Stages of symptoms

1. *Asymptomatic/pre-symptomatic* with a positive test
2. *Mild*: fever, sore throat, headache, aches (with **no** SOB, dyspnoea)
3. *Moderate*: evidence of lower respiratory disease, O₂ sat > 94%
4. *Severe*: evidence of lung infiltrates, O₂ sat < 94%, RR > 30
5. *Critical*: respiratory failure, septic shock, and/or multiple organ failure

Prevention

1. Isolation
2. Public health measures
3. mRNA vaccine and boosters



COVID-19 & Myocarditis

Risk of myocarditis is prevalent with this vaccine, but 10x higher if you contract COVID.

Vaccine	Vaccine Type	When
Pfizer-BioNTech (Comirnaty)	mRNA	2 doses (3-8 weeks apart) Booster (5 months after 2nd dose) 2nd Booster for > 50 years (4 months after 1st booster)
Moderna	mRNA	
Janssen/Johnson & Johnson	Vector	
AstraZeneca	Vector	<i>Discontinued in NZ</i>
Novavax	Protein subunit	

Pharmacological Treatment - Anti-Viral Treatment

[Paxlovid Health Navigator Information Sheet](#), [Molnupiravir Health Navigator Information Sheet](#)

Although only 1% of cases in NZ lead to hospitalisation, the purpose of antiviral treatment is to reduce the chances of this — therefore the eligibility criteria is informed by populations who are at much higher risk of developing severe disease (see risk section).

Prophylaxis

Prevent COVID disease prior to infection: public health measures i.e. close contacts

Community (mild/moderate disease) — Pharmacist Role

Management of mild/moderate disease & prevent progression to severe disease/hospitalisation

Treatment (mainly antivirals):

Paxlovid, molnupiravir, remdesivir, (Ronapreve in immunocompromised patients)

Hospital (hospitalised patients)

Management of hospitalised patients & prevent progression to ICU/Critical Disease

Treatment:

Dexamethasone, remdesivir, Ronapreve, tocilizumab, baricitinib, budesonide



ICU (severe/critical disease)

Management of severe/critical disease: characterised by an excessive immune response (cytokine storm)

Treatment:

Ronapreve, tocilizumab, baricitinib, ventilation, O₂, vascular support

Two types of oral antivirals are available in New Zealand to treat people who have COVID-19 in the community. [Paxlovid](#) and [Molnupiravir](#) are indicated for the treatment of mild-to-moderate COVID-19 infection in the community for adults aged 18 and older (do not require initiation of supplemental oxygen or at a high risk of disease progression to severe illness, hospitalisation, or death).

These antivirals can be supplied through a prescription from a GP or as pharmacist-only medicine. Patients must meet the PHARMAC eligibility criteria to be supplied these medicines.

ANTIVIRAL TREATMENT OPTIONS		
Drug	Mechanism of Action	Side Effects
First Line <i>Paxlovid</i> (Nirmatrelvir + Ritonavir)	<ul style="list-style-type: none"> <i>Nirmatrelvir</i>: Protease inhibitor in the pathway required for viral replication. Combined with ritonavir in efforts to improve systemic exposure as it has very poor oral bioavailability due to pre-systematic metabolism and possible efflux by P-glycoprotein. <i>Ritonavir</i>: Viral protease and anti-retroviral but not active against SARS-CoV-2. Substantially reduces nirmatrelvir metabolism and allows its eliminations mainly as an unchanged drug renally. 	Diarrhoea, vomiting, dysgesia (taste disturbance), headache. Less common: hypertension, myalgia.
<i>Lagevrio</i> (Molnupiravir)	Molnupiravir Viral ribonucleoside analogue - inhibits viral replication by causing errors in the genome. Is a prodrug and has good bioavailability. <i>Missed doses:</i> <ul style="list-style-type: none"> Within 10 hours: take dose and carry on More than 10 hours: skip and carry on (do not double doses to make up for missed doses) 	Common: diarrhoea, nausea, dizziness, hypersensitivity, angioedema, erythema, rash, urticaria.
<i>Remdesivir</i>	-	
<i>Ronapreve</i> (Casirivimab / imdevimab)	<ul style="list-style-type: none"> Use in immunocompromised patients 	

PHARMACIST SUPPLY OF ANTIVIRAL TREATMENT		
Introduction	<p>Supply Cost</p> <ul style="list-style-type: none"> Distribution and supply: PHARMAC Funding: MoH (taxpayers) Therefore, there is no cost to NZ Hospitals, pharmacies, and patients. (No special authority needed) <p>Paxlovid & Molnupiravir are approved for pharmacist supply if:</p> <ol style="list-style-type: none"> Eligibility criteria is met Willing to undergo a clinical assessment (6 steps) Antiviral treatment is not contraindicated 	
Step 1: Assess Antiviral Eligibility Criteria	<p>Eligibility Criteria — PHARMAC Eligibility Criteria for COVID-19 Antiviral Treatment</p> <ol style="list-style-type: none"> Confirmed/(probable) COVID case Symptoms within the last 5 (Paxlovid, Molnupiravir) or 7 days (Remdesivir) Patient does not require oxygen Patient is: <ul style="list-style-type: none"> Immunocompromised, Down's syndrome, sickle cell disease, previous COVID ICU admission ≥ 65 years of age (≥ 50 years if: Māori/Pacific or have not completed a primary vaccination course) ≥ 3 high-risk medical conditions 	
1. Assess Patient Symptoms	<p>Clinical Assessment Pathway (For Pharmacist Only Supply)</p> After having met the eligibility criteria, patient must have: <ol style="list-style-type: none"> Positive COVID test Mild-moderate symptoms Manageable in the community Cannot be attributed to another issue <p>Refer if: difficulty breathing at rest, blue face & lips, unable to talk in short sentences, dizzy, faint, fever >40°C, profound exhaustion, confusion, cold clammy pale skin, dehydration, blood in sputum, unexplained HR > 100</p>	
2. Pregnancy/Breastfeeding	<p>No data</p> <ul style="list-style-type: none"> Antivirals are not recommended in pregnancy/breastfeeding/child-bearing age without contraception. Stop breastfeeding during treatment & for 7 days after last dose if possible <p>Paxlovid (Nirmatrelvir + Ritonavir)</p> <ul style="list-style-type: none"> <i>Child-bearing age</i>: contraceptive AND extra precautions recommended during & for 4 days after <i>Males with partners of childbearing age</i>: contraceptive AND extra precautions recommended during & for 3 months after 	

Step 2: Clinical Assessment Pathway	3. Assess Renal function	<p>Assess current eGFR eGFR ideally within last 3-6 months (no older than 12 months). Refer if not available.</p> <p>Paxlovid (adjustment of nirmatrelvir can be done by pharmacist)</p> <ul style="list-style-type: none"> • GFR ≥ 60ml/min: No adjustment needed • GFR 30-60ml/min: Adjust nirmatrelvir to 1x 150mg • GFR <30ml/min: Contraindicated. Consider molnupiravir or refer 	Molnupiravir No adjustment needed
	4. Assess Liver Function	<p>Assess liver function by lab tests Refer if information is not available.</p> <p>Paxlovid Contraindicated in severe liver disease (Child-Pugh C score of 10-15 — total bilirubin, serum albumin, PT, INR, ascites, hepatic encephalopathy)</p>	Molnupiravir Can be used in severe liver disease
	5. Review Medication History & Identify Potential Drug Interactions	<ul style="list-style-type: none"> • Consider OTC, herbal therapies, traditional therapies • University of Liverpool Interaction Checker (NZF or medsafe may not be current) • Ontario Science Brief Table 3 <p>Note: Cannot use with St John's Wort</p>	Molnupiravir No identified drug interactions
	6. Establish management strategy for important drug interactions	<p>Paxlovid (Risk:benefit analysis)</p> <ol style="list-style-type: none"> 1. Green: No interactions 2. Amber: Dose adjustment OR withhold interacting medicine for 8 days (monitor!) — discuss with GP 3. Red: Possible contraindication 	
	<p>Paxlovid is the first choice oral antiviral medicine.</p> <p>Dose: 300 mg nirmatrelvir (2x 150 mg tablets) AND 100 mg ritonavir (1x 100 mg tablet) taken together orally every 12 hours for 5 days.</p> <p>Contraindications to Paxlovid <i>Relative Contraindications/insufficient data</i></p> <ul style="list-style-type: none"> • Patients < 18 years old • Severe liver impairment (child-pugh class C) • Severe renal impairment (eGFR < 30ml/min) • Pregnancy/Breastfeeding <p>Absolute Contraindications</p> <ul style="list-style-type: none"> • Hypersensitivity to drug or tablet components • Use with CYP3A4 substrates (serious or life threatening interactions) <ul style="list-style-type: none"> • E.g. Amiodarone, flecainide, colchicine, statins, cyclosporin, non-DHP CCBs, anti-HIV, diazepam, sildenafil, NOAC anticoagulants • Use with CYP3A4 inducers (loss of antiviral effect) <ul style="list-style-type: none"> • E.g. Anti-epileptics (carbamazepine, phenytoin, phenobarbitone), rifampicin, St john's wort • Unable to swallow tablets (no IV or NG formulation) 	Molnupiravir should only be supplied if Paxlovid is contraindicated. Dose: 4 capsules BD (every 12 hours) for 5 days.	
	<p>Step 3: Antiviral Treatment is not contraindicated</p>		

PAXLOVID VS MOLNUPIRAVIR

	PAXLOVID	MOLNUPIRAVIR
Pregnancy/ Breastfeeding	Not recommended - if suitable, discontinue breastfeeding while on treatment	
Contraceptive Requirements	During treatment and 1 week after	Females: during treatment and 4 days after Males: during treatment and 3 months after
Renal Function	Dose Adjustment	Consider this antiviral if eGFR < 30ml/min
Liver Function	Cannot be used in severe liver disease	Can be used in severe liver disease
Drug Interactions	Dose adjustment or withholding	No identified interactions

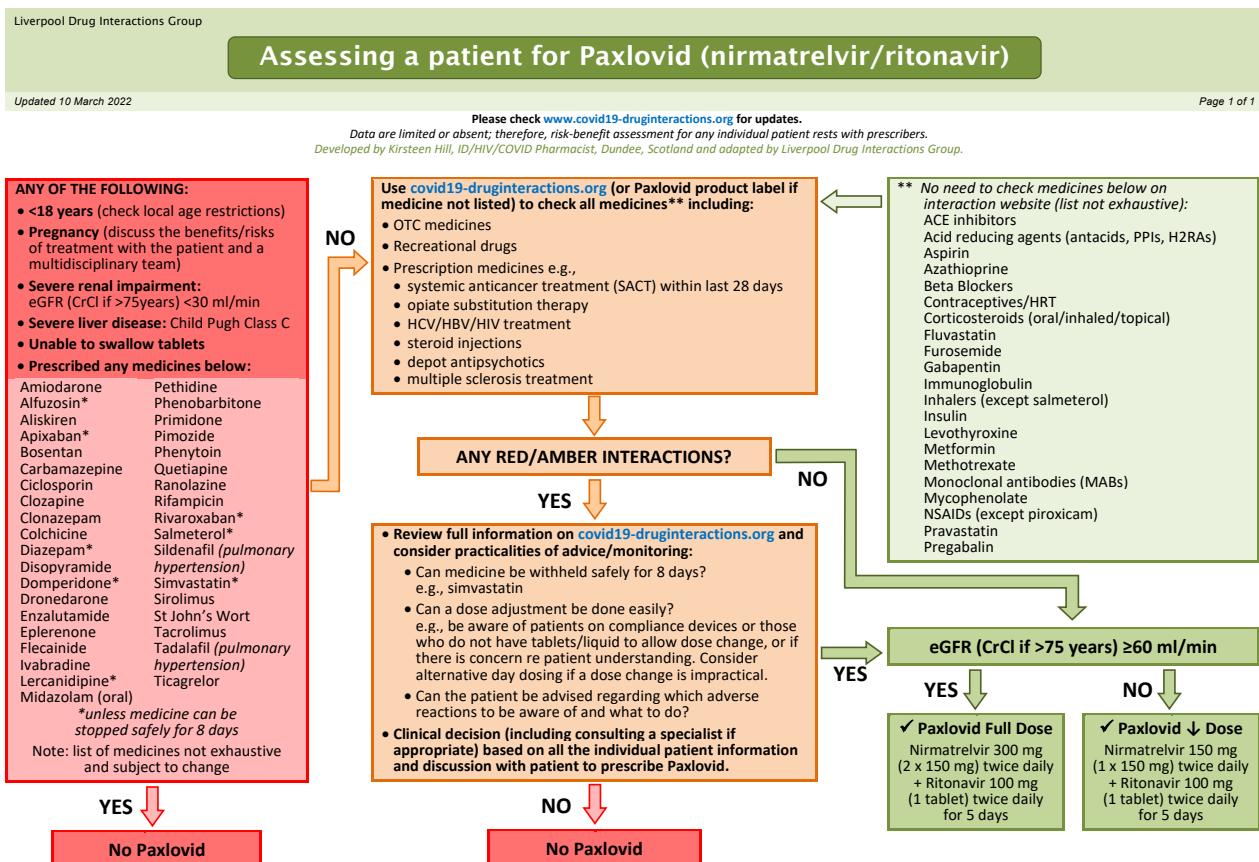
Rebound phenomenon

'Recurrence of COVID-19 symptoms or new positive viral test after negative testing within two to eight days of initial recovery'. This is unlikely to be uniquely associated with treatment.

OSCE Points

- Eligibility criteria:* probable or positive test for COVID, symptoms starting within 5-(7) days, difficulty breathing (O_2 support), immunocompromised/elderly

- Patient symptoms
- Pregnancy/breastfeeding
- Renal function (within 3-6/12 months): if $<30\text{ml/min}$, consider molnupiravir or refer
- Liver function
- Medication history and potential drug interactions
- Management plan e.g. withhold interacting medicine for 8 days



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Oral Antiviral Assessment Summary

Name

Address



PHARMACEUTICAL SOCIETY
of New Zealand Incorporated

Phone number (preferably mobile)

Age (over 18 years) NHI

Pregnant (or possibly pregnant) NO / YES = Refer

Confirmed/symptomatic COVID-19, < 5days AND NO supplemental O₂ YES/ NO = NOT eligible

IF ELIGIBLE FROM ABOVE CRITERIA – THEN USE PHARMAC ACCESS CRITERIA TOOL		
Eligible		Not eligible
ASSESS SYMPTOMS – MUST USE IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
• Patient has mild/moderate symptoms	• no significant clinical concern regarding severity of illness or possibility of a co-existent illness	• Patient referred (GP/Secondary Care)
ASSESS RENAL FUNCTION for nirmatrelvir/ritonavir - IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
• Renal Function eGFR > 60 mL/min	• Renal function eGFR <30 mL/min	
• Renal function eGFR ≥30 to <60 mL/min	• NO information	
ASSESS LIVER FUNCTION for nirmatrelvir/ritonavir - IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
No severe liver disease	• Severe liver disease	
REVIEW PATIENT MEDICATION HISTORY/IDENTIFY DRUG INTERACTIONS for nirmatrelvir/ritonavir MUST USE IN CONJUNCTION WITH ALL AVAILABLE CLINICAL RECORDS AND CLINICAL DECISION PATHWAY		
• GREEN - NO Interactions identified	• RED - Interaction cannot be managed	
• AMBER - Interaction can be managed with GP	• Not enough information	
SUPPLY DECISION		
• Nirmatrelvir/ritonavir supplied	• Molnupiravir supplied	• NO supply - referred
• GP Consultation notes (if required)		
PHARMACY DISPENSING SYSTEM DOCUMENTATION (NOT as an OTC product)		
• Label produced	• Actions documented (e.g. GP consultation, supply declined & reasons)	
CCCM DOCUMENTATION		
• Patient found or new patient created (NHI)	• Check timeline	• Send to GP
• Add GP Practice name and Practice ID (EDI)	• Clinical note added	• LOG OUT!
TELEHEALTH COUNSELLING		
• Patient understands how to take the medicine safely and appropriately	• Patient information leaflet supplied	
DELIVERY DETAILS CONFIRMED		
• Pickup (by non-isolating person)	• Delivery required	
Pharmacist	Date	

Measles (MeV)

Description

Measles is a highly contagious viral disease that can be life-threatening. It is transmitted via aerosolised respiratory secretions (inhalation, direct contact). The measles virus infects epithelial, lymphoid, and myeloid cells in lungs. It can then spread to lymph nodes, blood, and skin.



Did You Know?

In 2019, there was a measles outbreak in Samoa due to vaccine hesitancy - the nurse mixed up water with muscle relaxant diluent.



Signs & Symptoms

Measles begins as a non-infectious rash that starts at the head and spreads downwards. It is also associated with Koplik spots and a fever.



Remember the 3 C's

Measles is associated with Coryza (runny nose), Cough, Conjunctivitis.

Complications: CNS disease (encephalitis), immune suppression, ear infection, pneumonia

Non-Pharmacological Treatment

- No specific antiviral, supportive care
- Treat complications e.g. pneumonia (due to immune suppression)
- Vitamin A (low levels are risk factor for severe disease)

Prevention

- MMR (Priorix)

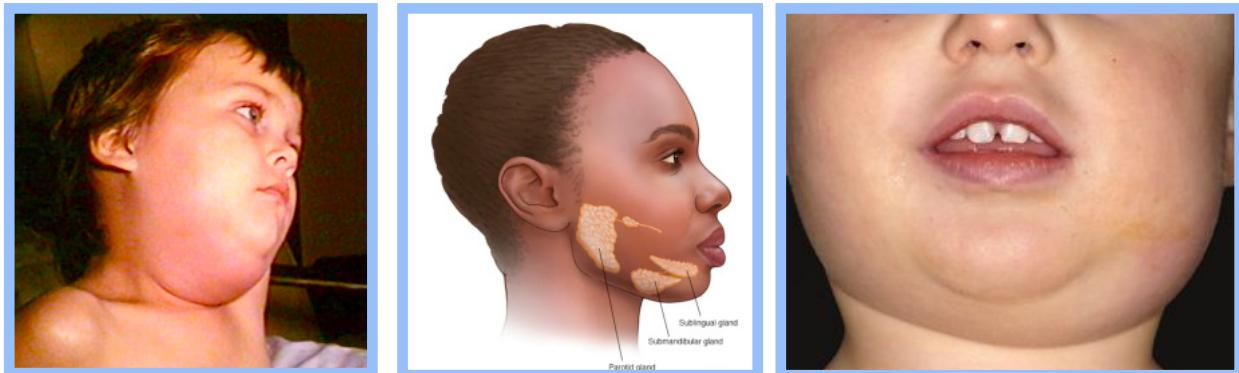
Vaccine	Vaccine Type	When
MMR (Priorix)	Live Attenuated Contraindicated if neomycin anaphylaxis, immunocompromised, pregnancy.	12 and 15 months. Give to contacts within 72 hours.

Mumps (MuV)

Description

Mumps is an acute viral illness that is moderate-highly contagious. It is transmitted via aerosolised respiratory secretions, and is a self-limiting infection.

The mumps virus infects **parotids** (salivary glands), epithelial lung cells and myeloid cells. The virus present in saliva before parotitis, and can spread to blood (systemic distribution).



Signs & Symptoms

Asymptomatic, swelling in the glands around the face (parotitis), **facial rash**, pain in the jaw, fever, chills, headache, malaise, myalgia, meningitis, pancreatitis, deafness, encephalitis, affects reproductive tract (ovaries, testicles, affects fertility), orchitis (+ epididymitis).

Non-Pharmacological Treatment

- No specific antiviral, self-resolving with support care
- Cold compress against swollen glands

Prevention

- MMR (Priorix)

Vaccine	Vaccine Type	When
MMR (Priorix)	Live Attenuated Contraindicated if neomycin anaphylaxis, immunocompromised, pregnancy.	12 and 15 months. Give to contacts within 72 hours.

Rubella (German Measles)

Description

A rare viral illness that causes a spotty rash. It is usually a mild illness but can be serious if a **pregnant woman** catches the disease, especially during the first 3 months of pregnancy as it can lead to birth defects. A mother can pass rubella onto the newborn baby. Rubella is spread through the air by droplets.



Signs & Symptoms

- Mild fever, malaise, swollen glands, mild red **rash**
- Miscarriage, stillbirth, birth defects. Congenital infection (cataracts, cardiac abnormalities, deafness, neurological impairment, behavioural disorders, diabetes), self-limiting postnatal infection (fever, aching, swollen lymph nodes, cough, sore throat)

Treatments

Symptom relief

Prevention

- MMR (Priorix)

Vaccine	Vaccine Type	When
MMR (Priorix)	Live Attenuated Contraindicated if neomycin anaphylaxis, immunocompromised, pregnancy.	12 and 15 months. Give to contacts within 72 hours.

LOWER RESPIRATORY TRACT CONDITIONS

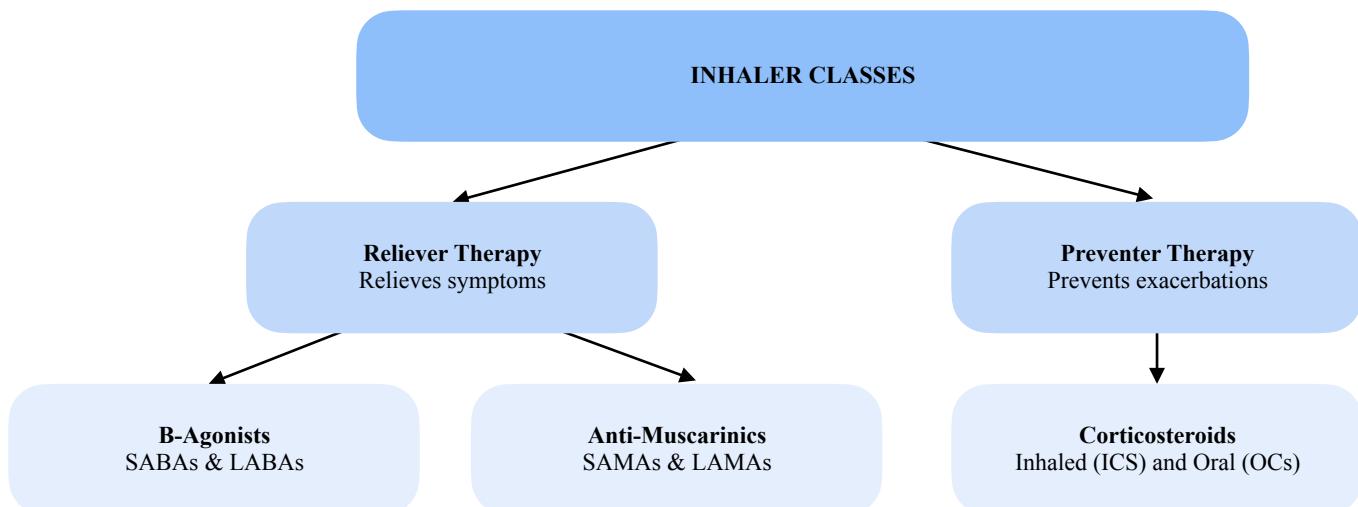
Description

Structures of the LRT include those within the thorax (chest) e.g. the lungs, the trachea and the bronchial tree (alveoli).

Introduction to Inhalers

Inhaler Classes

Asthma and COPD are two examples of Lower Respiratory Conditions we will cover — they are particularly of note because although treatment guidelines differ, the same inhalers are used. Please find below the treatment options here — respective guidelines can be found within the respective conditions. Please note all inhalers are prescription only items.



Other Options

1. mAbs (Omalizumab)
2. Mast cell stabilisers (Cromoglycate)
3. Methylxanthines (Theophylline)

Asthma & COPD Treatments					
	Category	Ingredients	MoA	Patient Counselling	Side Effects
RELIEVER THERAPY	β -Agonists	SHORT-ACTING B-AGONISTS (SABAS) <i>Salbutamol</i> (RespiGen, SalAir, Ventolin) <i>Terbutaline</i> (Bricanyl Turbuhaler)	Bronchial β_2 receptors agonists cause smooth muscle relaxation and bronchodilation	<ul style="list-style-type: none"> • Shake before use • Symptomatic relief • SABA used PRN 	Increased HR, tremors, palpitations, nervousness, sleep disturbances,
		LONG-ACTING B-AGONISTS (LABAS) <i>Salmeterol</i> (Severent) <i>Vitanterol, Indacaterol, Formoterol</i>			
	Anti-Muscarinics	SHORT-ACTING MUSCARINIC ANTAGONISTS (SAMAS) <i>Ipratropium Bromide</i> (Atrovent; Aerosol, Univent; Nebuliser)	Prevents smooth muscle contraction which causes bronchodilation and symptomatic improvement	Respimat: make sure not to cover the vent	Antimuscarinics effects (Spit, See, Shit) - blurred vision, dry mouth, GI disturbances, urinary retention
		LONG-ACTING MUSCARINIC ANTAGONISTS (LAMAS) <i>Tiotropium</i> (Spiriva - Handihaler, Respimat) <i>Glycopyrronium</i> (Seebri Breezehaler) <i>Umeclidinium</i> (Incruse Ellipta)			
PREVENTER THERAPY	Corticosteroids	INHALED CORTICOSTEROIDS (ICS) <i>Budesonide</i> (Pumicort Turbuhaler) <i>Fluticasone propionate</i> (Flixotide) <i>Beclomethasone dipropionate</i> (Qvar)	Has anti-inflammatory effects with reduces bronchial reactivity.	<ul style="list-style-type: none"> • Rinse mouth after use 	Oral candidiasis, growth delays, HPA axis suppression
		ORAL CORTICOSTEROIDS (CCS) <i>Prednisone</i>		<ul style="list-style-type: none"> • Short term use • Best taken in the morning 	Hunger, thirst, insomnia, oedema, dyspepsia, Cushing's syndrome

Combination Inhalers	
ICS + LAMA	ICS + LABA <i>Budesonide + Formoterol</i> (Symbicort Turbuhaler) <i>Fluticasone propionate + Salmeterol</i> (Seretide Accuhaler) <i>Fluticasone furoate + Vitanterol</i> (Breo Ellipta)
LAMA + LABA	LAMA + LABA <i>Glycopyrronium + Indacaterol</i> (Ultibro Breezehaler) <i>Tiotropium + Olodaterol</i> (Spiolto Respimat) <i>Umeclidinium + Vitanterol</i> (Anoro Ellipta)

Inhaler Counselling

1. [Salbutamol Inhaler - How to Use](#)
2. [Symbicort Inhaler - How to Use](#)
3. [Asthma Spacers - How to Use](#)
4. [Asthma Spacers - How to Clean](#): Do not dry with cloth as it can create static and cause the medicine to stick to the walls of the spacer.

Generally:

- Don't shake powder inhalers
- Rinse mouth after using steroid inhalers
- Powder inhalers = inhalation, Aerosol inhalers = puff
- Do not cover vents of powder inhalers

Funded Inhalers in New Zealand 2019

 Canterbury Clinical Network
Improving Health Care in Canterbury



Table 4: Inhaler devices recommended by age group

Inhaler device	< 2 years	2-4 years	5-7 years	8-11 years
pMDI, small volume spacer & mask	Yes	May transition to no mask		
pMDI & spacer No mask		Possible	Yes	Yes
pMDI (alone)*				Possible, but use with a spacer is preferable
Dry powder device			Possible	Yes
Breath-activated device			Possible	Yes

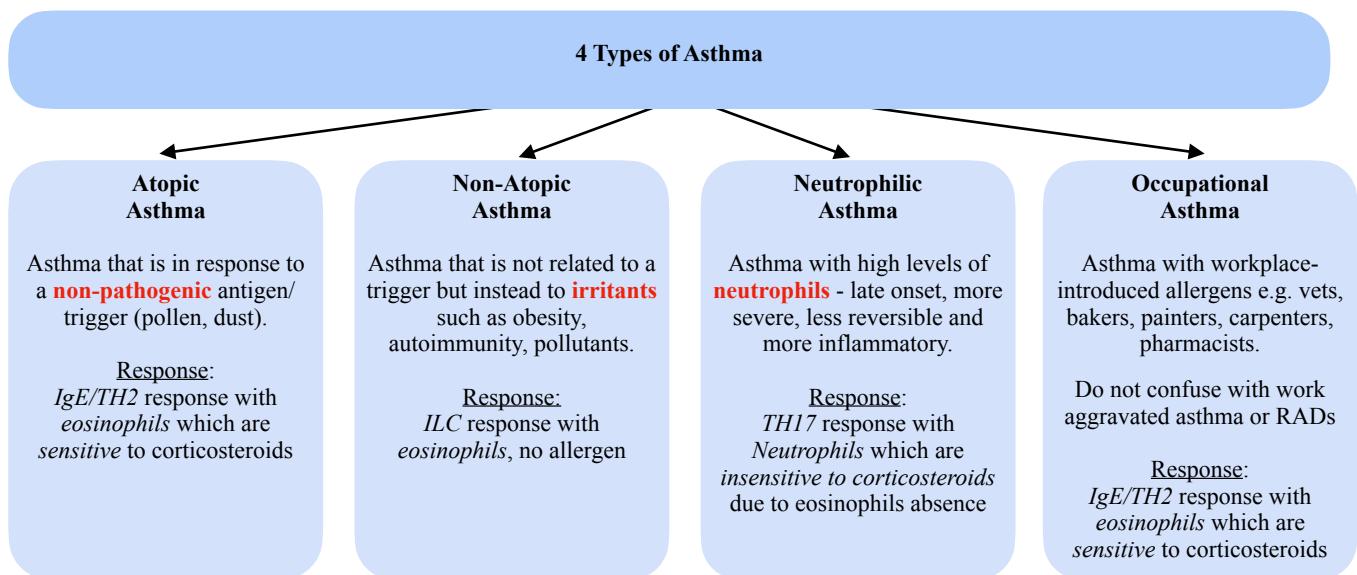
*A spacer should be used with the pMDI for the regular administration of ICS, and for the administration of SABA in the setting of an acute attack.

Obstructive/Restrictive Diseases & Infections

Asthma

Description

Asthma is a condition (an immune dysfunction specifically) in which a person's airways have an inappropriate inflammatory response to a *non-pathogenic* antigen - causing them to become episodically narrow, inflamed, swollen and have an excess production of mucus. This makes it difficult to breathe. Four types of asthma exist - however we will focus on Atopic Asthma.



Pathophysiology

Asthma a Type 1 and Type 4 Hypersensitivity reaction

Type 1 Hypersensitivity Reactions *IgE Mediated*

These kinds of reactions are allergic reactions provoked by re-exposure to an allergen. This reaction is quick and occurs within minutes.

Type 4 Hypersensitivity Reactions *TH1, TH2, CTL Mediated*

These kinds of reactions are delayed, cell mediated reactions.

We can thus break down the pathophysiology of asthma into 2 parts:

1 - The Sensitisation Phase *IgE Response (TH2 Cells involved)*

The sensitisation phase describes the period in which the person is first exposed/introduced to the allergen. This triggers IgE to coat mast cells - 'sensitising' them.

2 - The Inflammation Phase *Mast Cell Degranulation*

IgE-coated mast cells then go on to surveil the body for the allergen - when detected, mast cell degranulation occurs, causing the release of bronchoconstrictors and cytokines. The greater the amount of the allergen, the greater the inflammation.

And as we've seen, this causes the following responses:

5. Airway inflammation
6. Airway hyper-responsiveness (bronchoconstriction)
7. Airway oedema (swelling), and
8. Airway remodelling (due to recurrent asthma attacks)



Asthma & Reversibility

Please note that although asthma episodes are reversible - with recurrent attacks, we observe progressive and less reversible loss of lung function.

Signs & Symptoms

Symptoms are intermittent, worse at night, and provoked by triggers. There are three main hallmarks:

1. *Cough*: particularly at night, during and after physical activity and when giggling, laughing or crying
2. *Wheezing*: high-pitched raspy sound during breathing due to narrowed airways
3. *Chest Tightness and Breathlessness*: SOB, unable to complete a sentence

Risk Factors

1. *Medication* use in early childhood (macrolide antibiotics, paracetamol)
2. *Pollution* (irritant)
3. *Infection* (hygiene hypothesis)
4. *Diet*: early breastfeeding, vitamin D, soda intake
5. *Atopic March*: genetic and environmental predisposition to have an IgE mediated immune response

Diagnosis

Atopic Skin Testing

To test if someone has a particular allergy to an allergen: the allergen is applied as a drop to the skin and the skin is then broken with a lancet. A positive reaction should then develop within minutes

- False negatives are likely to occur if patient is on immunosuppressive drugs
- This test would **not** be done if patient has had an anaphylactic reaction to the allergen

Goal of Treatment

- Long term control using least amount of medication (infrequent use of SABA; <2 days per week)
- Improve ability to exercise and do hobbies
- Preventing chronic symptoms
- Maintain near or normal pulmonary function and activity levels that is satisfactory to caregivers/patient
- Prevent exacerbations and the need for hospitalisation.

Non-Pharmacological Treatment

1. Smoking cessation
2. Regular exercise
3. Correct inhaler technique
4. Always carry your inhalers with you
5. Allergen and trigger avoidance (although this may not always be practical)
 - Sickness — **flu vaccine** (funded for asthmatics) for prevention
 - Certain medications e.g. NSAIDs, non-selective β-blockers
 - Inhaled allergens e.g. cigarette smoke, dust mites, pollution, animal dander, mould, pollen
 - Emotional stress e.g. laughter
 - Temperature changes e.g. humidity
 - Food preservatives
 - Reflux
 - Strong perfumes
 - Exercise e.g. sexual activity

Pharmacological Treatment (Adult & Paediatric)

[Adult & Child Asthma Foundation Guidelines](#) [BPAC Asthma Management](#) [GINA Pocket Guidelines](#)

Inhalers used to treat asthma are generally either relievers and/or preventers. And as you would've seen earlier at the beginning of the *Lower Respiratory Tract Conditions* section - many options exist. Treatment guidelines can be found on the next page and depend on whether the patient is a child or adult.



Review! Review! Review

It is incredibly important that before you escalate therapy, you review inhaler technique! Poor technique is associated with disease progression, exacerbations and unnecessarily aggressive therapy. Sometimes it's possible that the patient is just simply not using their medications right.

A note on Asthma Immunotherapy (AIT)

Although asthma is conventionally treated with inhalers - they are not the sole option available. New therapies such as AIT are being developed as our current ones are not very successful. Three examples of it include:

1. Specific Allergen Therapy
2. Asthma prophylactic and therapeutic vaccines
3. Anti-IgE therapy (Omalizumab)

Adult & Adolescent Treatment Guidelines (12 years and above)

The first line treatment in 12+ years with asthma is Symbicort 200µg/6µg - a turbuhaler that is the combination of two medicines:

1. *Budesonide (LABA)* - reliever component for the symptomatic relief of attacks
2. *Formoterol (ICS)* - anti-inflammatory component for the prevention of exacerbations

This inhaler is recommended as guidelines suggest that all >12 years old with asthma should have **an inhaled corticosteroid** to prevent permanent lung damage. Symbicort can be used in two ways - either as SMART therapy (recommended) or as AIR therapy.

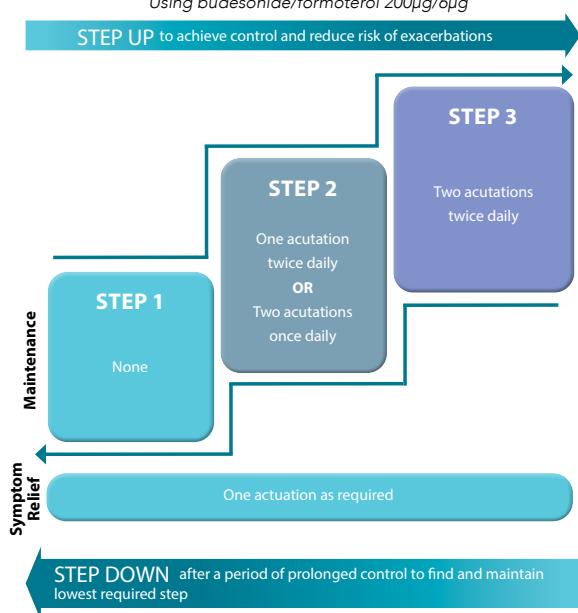
1. Single Inhaler Maintenance and Reliever Therapy (SMART)

- Person must take daily baseline maintenance doses, with additional inhalations for symptom relief being available for as required.
- Shown as Step 2 and Step 3 on the right of the diagram below.

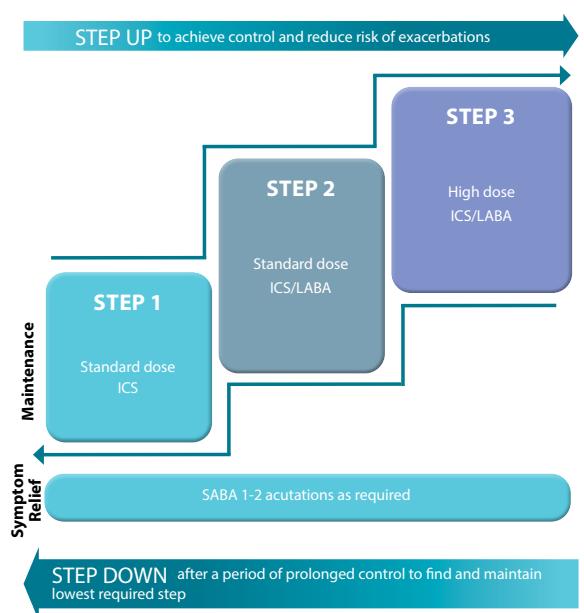
2. Anti-Inflammatory Reliever Therapy (AIR)

- This is used purely for symptomatic relief on an as required basis. Maintenance doses are not used.
- Shown as Step 1 on the right of the diagram below.

Anti-Inflammatory Reliever (AIR) Therapy Based Algorithm Using budesonide/formoterol 200µg/6µg



Traditional SABA Reliever Therapy Based Algorithm

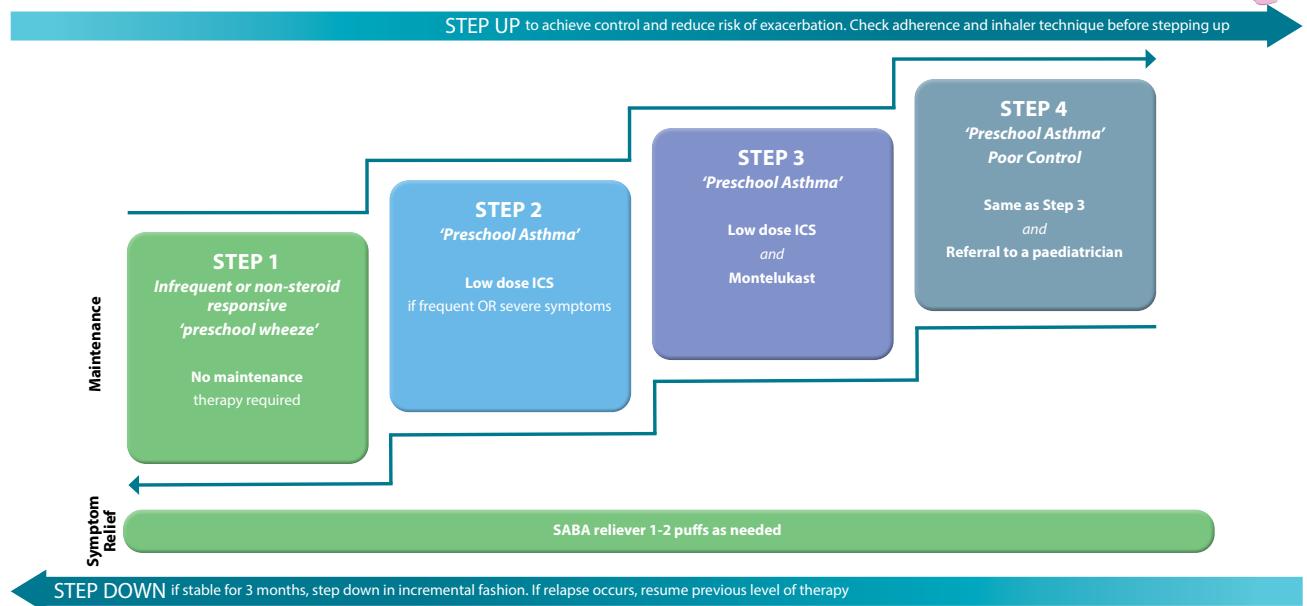


On the left, you will note that the traditional SABA reliever therapy guidelines are shown - these are the old guidelines prior to the introduction of Symbicort. In the past, reliever therapy and maintenance therapy were separate inhalers (usually one blue and one orange) - which caused many issues with adherence. Despite this no longer being the recommended method of approach in 12 year olds and above, you may still encounter asthmatic patients on multiple inhalers in practice.

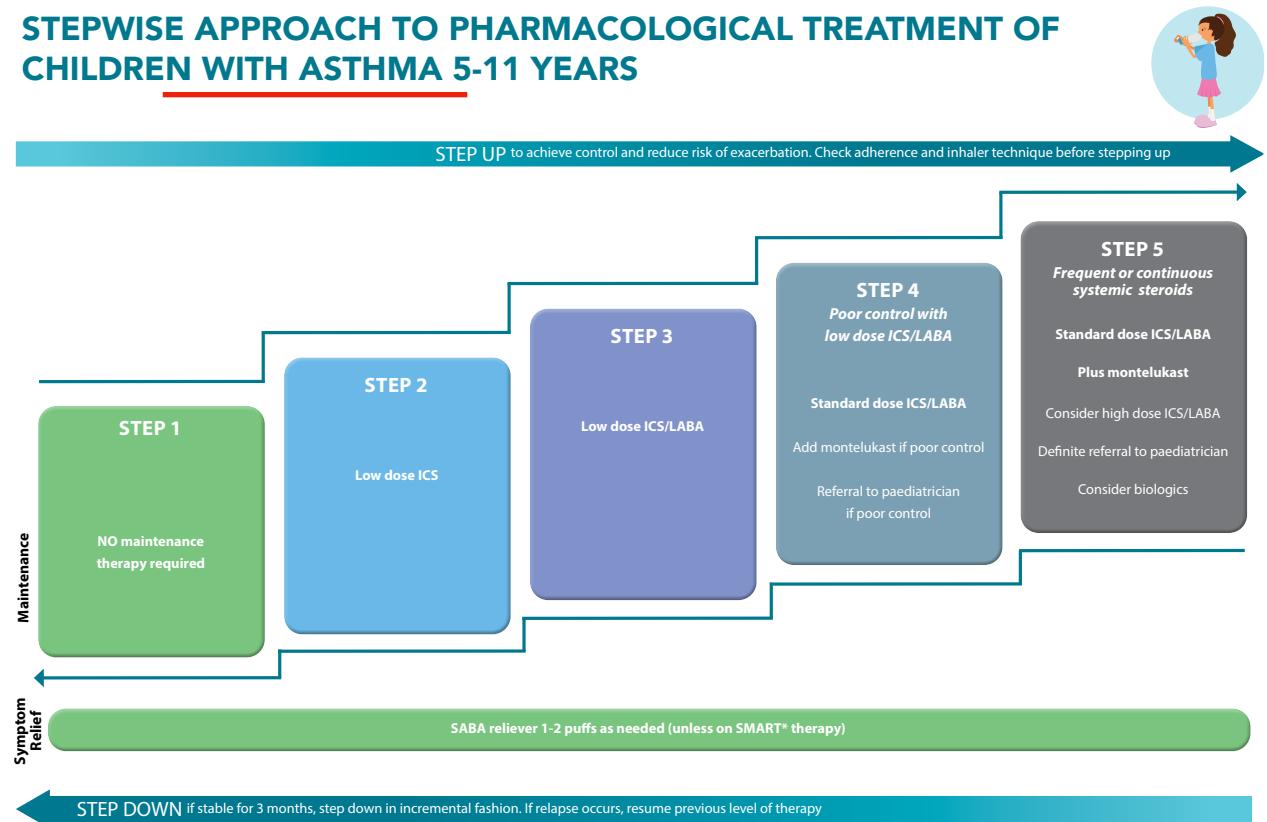
Children Treatment Guidelines (1 - 11 years)

As Symbicort has not been well studied in children, guidelines differ in this age group. Generally, symptom relief with a SABA is recommended initially - maintenance doses can be initiated (usually with an ICS/LABA) if control is inadequate.

STEPWISE APPROACH TO PHARMACOLOGICAL TREATMENT OF CHILDREN WITH WHEEZE 1-4 YEARS



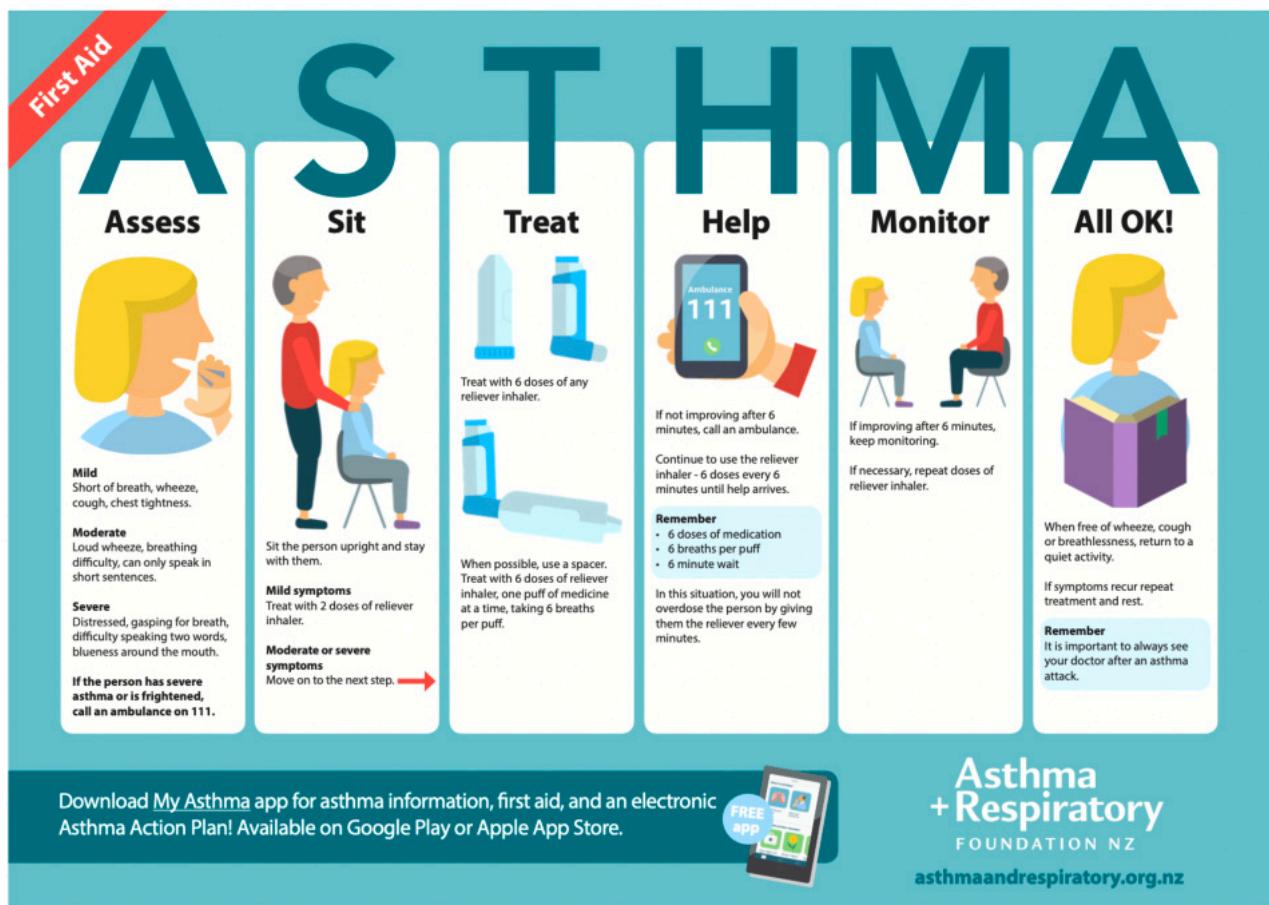
STEPWISE APPROACH TO PHARMACOLOGICAL TREATMENT OF CHILDREN WITH ASTHMA 5-11 YEARS



Asthma First Aid Plan

An asthma attack is a medical emergency characterised by the sudden and life-threatening worsening of the person's symptoms. We use a **salbutamol inhaler** to treat it and the first aid method for its administration is called '666' - see the steps below:

1. Determine if the patient has had medication for their asthma and if it was prescribed in the last 3-6 months (this allows you to give an emergency supply)
2. Grab a spacer (if possible) and initially load it with 2 doses of the reliever inhaler
3. You may then proceed to load 6 doses of the reliever - give them one puff at a time, with 6 breaths being taken per puff.
4. If after a 6 minute wait, there is no improvement - call an ambulance.
5. You can keep giving **6** doses of medications every **6** minutes (with **6** breaths per puff) - this will help you keep the patient breathing without overdosing them until help arrives.



Next Steps

After the attack settles down, your next steps are to:

- Advise them to see their doctor as soon as possible - this should always be done following an asthma attack in order to revise the asthma action plan)
- Contact their doctor to inform them of the situation - including the emergency supply
- Determine why did this person have an attack the first place e.g. incorrect inhaler technique?
- Ensure it gets addressed and monitor patient

Monitoring

Generally

- Asthma Action Plan & [Asthma Control Test](#) - see next page for examples
- FEV₁, FVC
- [Peak Expiratory Flow Rate \(PEFR\)](#)
 - Initially, take PEFR readings before using inhaler every morning and evening for 2 weeks — keep [track](#) using a diary. Manage with asthma wheel where appropriate.
 - *Cleaning:* wash every 6 months with mild detergent, agitate, and air dry

Signs & Symptoms of Poor Control

- Experiencing asthma symptoms more than **3 times per week**
- No symptom relief from usual dose of asthma medicine
- More frequent attacks: increasing use of prn inhaler
- Night waking due to coughing and wheezing
- Missing days from school or worked

Know your asthma symptoms

Your asthma is under control when

- you don't have asthma symptoms most days (wheeze, tight chest, a cough or feeling breathless)
- you have no cough or wheeze at night
- you can do all your usual activities and exercise freely
- most days you don't need a reliever

Your peak flow reading is above

Name:

Date of plan:

Doctor:

Doctor phone:

Know when and how to take your medicine

Preventer

[name]

actuation(s)

every morning

Reliever

[name]

actuation(s)

when you need it to relieve your asthma symptoms

Carry your reliever at all times

Other Medication

Feeling good

Getting worse

Severe

Emergency

Caution- your asthma is getting worse when

- you have symptoms most days (wheeze, tight chest, a cough or feeling breathless)
- you are waking at night with symptoms
- you are getting a cold

Your peak flow reading is below

Let's get prepared...

- Step up your preventer medicine:
- Take [] actuations four times each day
- Use your reliever as often as needed – through a spacer, if one can be used with your reliever inhaler

Other instructions:

Caution- your asthma is getting severe when

- Your symptoms are getting severe (wheeze, tight chest, a cough or feeling breathless)
- OR your reliever is only helping for 2-3 hours
- OR you are using more than 12 actuations a day
- OR you feel you need to see your doctor

Your peak flow reading is below

Let's take action...

- You need to see your doctor today
- Continue your medicine for "getting worse"
- Start prednisone if you have it:

Prednisone	mg	for	days
and then	mg	for	days

Other instructions:

Emergency

- Your symptoms are getting more severe quickly
- OR you are finding it hard to speak or breathe
- OR your reliever is not helping much
- OR you are using your reliever every 1-2 hours

Your peak flow reading is below

Let's keep calm...

- Dial 111 for ambulance
- Keep using your reliever as often as needed – through a spacer, if one can be used with your reliever inhaler
- Even if you seem to get better seek medical help right away
- If you haven't started taking your prednisone, start now

Other instructions:

Best peak flow: _____
Plan prepared by: _____
Next review date: _____
Signature: _____

Today's Date: _____

Patient's Name: _____

FOR PATIENTS:

Take the Asthma Control Test™ (ACT) for people 12 yrs and older.

Know your score. Share your results with your doctor.

Step 1 Write the number of each answer in the score box provided.

Step 2 Add up each score box for your total.

Step 3 Take the test to the doctor to talk about your score.

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?

All of the time	1	Most of the time	2	Some of the time	3	A little of the time	4	None of the time	5

SCORE

2. During the past 4 weeks, how often have you had shortness of breath?

More than once a day	1	Once a day	2	3 to 6 times a week	3	Once or twice a week	4	Not at all	5

SCORE

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	1	2 or 3 nights a week	2	Once a week	3	Once or twice	4	Not at all	5

TOTAL

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day	1	1 or 2 times per day	2	2 or 3 times per week	3	Once a week or less	4	Not at all	5

SCORE

5. How would you rate your asthma control during the past 4 weeks?

Not controlled at all	1	Poorly controlled	2	Somewhat controlled	3	Well controlled	4	Completely controlled	5

TOTAL



The American Lung Association supports the Asthma Control Test and does not endorse products.



If your score is 19 or less, your asthma may not be controlled as well as it could be. Talk to your doctor.

FOR PHYSICIANS:

The ACT is:

- Clinically validated by spirometry and specialist assessment¹
- Supported by the American Lung Association
- A self-administered, brief, 5-question assessment that can help you assess your patients' asthma during the past 4 weeks

Reference: 1. Nathan RA et al. J Allergy Clin Immunol. 2004;113:595.



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Childhood Asthma Control Test for children 4 to 11 years old. Know the score.

This test will provide a score that may help your doctor determine if your child's asthma treatment plan is working or if it might be time for a change.

How to take the Childhood Asthma Control Test

Step 1 Let your child respond to the first four questions (1 to 4). If your child needs help reading or understanding the question, you may help, but let your child select the response. Complete the remaining three questions (5 to 7) on your own and without letting your child's response influence your answers. There are no right or wrong answers.

Step 2 Write the number of each answer in the score box provided.

Step 3 Add up each score box for the total.

Step 4 Take the test to the doctor to talk about your child's total score.

Have your child complete these questions.

1. How is your asthma today?



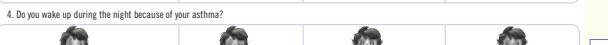
2. How much of a problem is your asthma when you run, exercise or play sports?



It's a big problem. I can't do what I want to do. It's a problem and I don't like it.

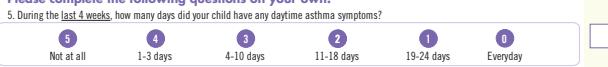
It's a little problem but it's okay.

It's not a problem.

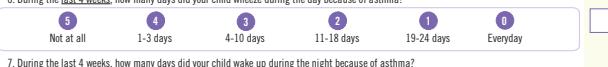


Please complete the following questions on your own.

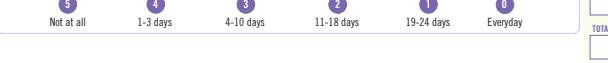
5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?



6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?



7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?



Asthma-COPD Overlap Syndrome (ACOS)

Description

Asthma-COPD Overlap Syndrome (ACOS) is a condition in which a person shares symptoms of both asthma and COPD.

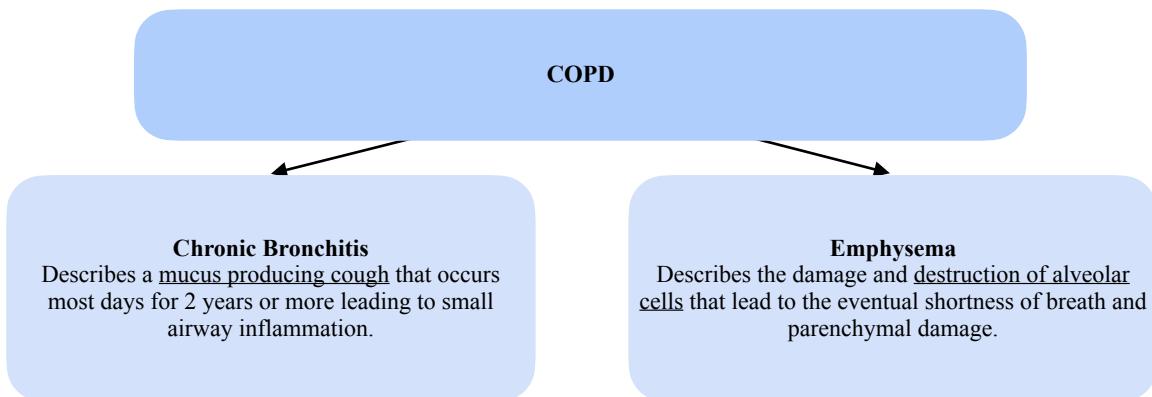
COMPARISON		
ASTHMA	ACOS	COPD
Inflammatory Disease	Mixture of both	Inflammatory Disease
Often begins in childhood		Begins in middle age or later on in life (> 35 y)
Response to non pathogenic antigen (atopy) e.g. pollen		Response to polluting substance e.g. smoking
Reversible damage (if promptly treated) - patients can become better over time with treatment, and even symptom free.		Non reversible damage - symptoms get worse over time even with treatment.
Lung function is normal between episodes		Lung function is consistently poor.
Episodic attacks of wheezing and tightness in your chest.		Symptoms are usually more constant and can include a cough that brings up phlegm
Made worse by exercise		Triggered by exercise

Chronic Obstructive Pulmonary Disease (COPD)

Description

Chronic Obstructive Pulmonary Disease (COPD) is a chronic and progressive disease characterised by the persistent obstruction and inflammation of the airway that occurs due to the long-term exposure to airway irritants e.g. cigarette smoke.

It is in fact, an umbrella term that describes two long term lung conditions that usually occur concurrently: chronic bronchitis & emphysema.



Signs & Symptoms

The presenting complaint is usually a chronic cough and recurrent chest infections. So much so, that patients tend to present with multiple prescriptions for antibiotics over a period of time before a diagnosis of COPD is made.

1. *Generally:* persistent airflow/airflow obstruction, inflammation, chest tightness, coughing particularly at night or early morning, SOB, breathlessness on exertion, wheezing, dyspnoea, sputum production.
2. *Acute exacerbations:* reduction in activities and more pronounced breathlessness (defined as 'hard work, painful, frightening, continuous fight' and worsened by anxiety).

Complications: Gas exchange abnormalities, pulmonary hypertension, accelerated ageing, osteoporosis, depression & anxiety, and other cardiovascular diseases.

Risk Factors

Although it is possible for non-smokers to develop COPD, most cases are **smoking-related**. It is a complex disease with an interplay between genetics and environment:

1. *Genetics:* Immune function, metabolism of toxins, lung development, oxidative stress responses
2. *Environment:* Smoking & ambient particulate matter, pollution, occupation, social determinants of health, these also contribute to frequent exacerbations which is a poor prognostic factor.

Diagnosis

1. Risk factor exposure
2. Symptoms (with a focus on cough, sputum, and dyspnea)
3. Imaging
4. Spirometry & Pulmonary Function Testing

Staging

- A. *Disease* is staged/classified using the **GOLD 1-4** standard (**after bronchodilator**)
- B. *Treatment Choice* is based using **GOLD A-D** (symptoms & exacerbations)
- C. *Mortality Risk* is estimated with **DOSE** (Dyspnoea, Obstruction, Smoking, & Exacerbation scale)

GOLD 1-4 CLASSIFICATION (Post-Bronchodilator Response) Estimates Disease Staging		
Gold Type	Severity	FEV ₁
1	Mild	FEV ₁ ≥ 80% of predicted
2	Moderate	50% ≤ FEV ₁ < 80% of predicted
3	Severe	30% ≤ FEV ₁ < 50% of predicted
4	Severe	FEV ₁ < 30% of predicted

Note: FEV₁ is a measure of the rate at which air can be expelled from the lungs in 1 second, while FVC is a measure of the vital capacity. Given COPD is an obstructive disease, FVC remains unchanged. Spirometry Testing showing FEV₁:FVC <0.7 post-bronchodilator indicates COPD.

GOLD A-D CLASSIFICATION (Level of Symptoms and Exacerbation Risk) Estimates Treatment Choice				
Gold Type	Characteristic	Exacerbations per year	mMRC	CAT
A	Less symptoms: low exacerbation risk	≤ 1 not leading to hospitalisation	0-1	<10
B	More symptoms: low exacerbation risk		≥ 2	≥ 10
C	Less symptoms: high exacerbation risk	≥ 2 or 1, requiring hospitalisation	0-1	<10
D	More symptoms: high exacerbation risk		≥ 2	≥ 10
Note: use either <u>mMRC</u> or <u>CAT</u>				

DOSE INDEX SCORING SYSTEM (Dyspnoea, Obstruction, Smoking & Exacerbation Scale) Estimates Mortality Risk				
Components	Dose Index Points			
	0	1	2	3
mMRC Scale	0-1	2	3	4
FEV ₁ % of predicted	≥50	30-49	<30	-
Smoking Status	Non-Smoker	Smoker	-	-
Exacerbations in Previous Year	0-1	2-3	>3	-

Goal of Treatment

- To provide symptoms control (main goal | breathlessness)
- To reduce risk of exacerbations
- To increase patient's capacities to attend rehabilitative therapies and exercise (physiotherapy)

Non-Pharmacological Treatment

- Smoking Cessation
- Individual breathlessness plans e.g. hand-held fan therapy, diaphragmatic breathing, breathing exercises
- Integrated interprofessional care
 - *Physiotherapy* (strength training, rehab programmes, specific gym programmes)
 - *Nutrition*: Malnutrition and obesity contribute to morbidity and mortality in COPD. Consider referral to a dietitian, or high-calorie nutritional supplements, or weight loss advice.
 - *Exercise*: Promote 20-30 minutes per day of "huff and puff" exercise, or exercise which causes the patient to feel breathless. Muscle strengthening activities at least twice a week.
 - *Sputum Management*
 - *Pulmonary Rehabilitation*
 - *Housing*: smoke-free, warm, dry home environment is likely to improve COPD control

Pharmacological Treatment

[NZ COPD Guidelines](#), [BPAC COPD Prescribing Guidelines](#), [BPAC COPD Antibiotics Guidelines](#)

COPD is a treatable but non curable condition - this is because the level of lung tissue destruction is not entirely reversible by that point. Treatment for COPD mainly exists to aid patients attend physiotherapy sessions.

As mentioned, the treatment choice for COPD relies on the GOLD A-D. See below the treatment guidelines summarised. Additionally, a **back-pocket antibiotic script (5-10 day course)** is common with COPD in the case of an infection which exacerbates the condition.

Therapeutic Controversy (ICS): While ICSs can reduce exacerbations in high blood **eosinophils** (>100 cells/ mL i.e. $\geq 0.3 \times 10^9/\text{L}$), they **increase the risk of pneumonia** in patients that are:

- Current Smokers > 55 years
- BMI **<25**
- Have had prior exacerbations of pneumonia
- Evidence of **severe** airflow obstruction

COPD PRESCRIBING GUIDELINES				
Gold A <i>Less Symptoms Low Exacerbation Risk</i>	BPAC Gold A Guidelines 1. Short-acting bronchodilator: Initially SAMA OR SABA OR SABA/SAMA as prn , OR 2. Long-acting bronchodilator: LAMA (first line) OR LABA (second line)			
Gold B <i>More Symptoms Low Exacerbation Risk</i>	BPAC Gold B Guidelines 1. LAMA OR LABA initially (if mild-moderate COPD & persistent breathlessness, or if using a short-acting bronchodilator more than four times per day) 2. If severe breathlessness: consider a combination LABA/LAMA			
Gold C <i>Less Symptoms High Exacerbation Risk</i>	BPAC Gold C Guidelines 1. Initially: LAMA			
Gold D <i>More Symptoms High Exacerbation Risk</i>	BPAC Gold D Guidelines 1. Initially: LAMA 2. If severe breathlessness: consider LABA/LAMA 3. ICS may be first choice for some patients i.e. blood eosinophil counts $\geq 0.3 \times 10^9/L$			
Asthma-COPD Overlap	1. Initially: ICS/LABA • LABA monotherapy in patients with asthma is associated with a small but significantly increased mortality risk. 2. If ACOS suspected: ADD LAMA			
COPD INHALER & DOSES <i>Reminder: Do not give SAMAs and LAMAs together</i>				
Short Acting				
SABA <i>Salbutamol (Salair, Ventolin, Respigen)</i> • 1-2 puffs prn up to qid <i>Terbutaline (Bricanyl)</i> • 1-2 inhalations prn up to qid	SAMA <i>Ipratropium (Atrovent)</i> • 2 puffs prn up to qid	SABA + SAMA <i>Salbutamol + Ipratropium</i> • 2 puffs prn up to qid		
Long Acting				
LABA <i>Salmeterol (Serevent)</i> • Two puffs, bd <i>Salmeterol (Servant Accuhaler)</i> • One inhalation, bd <i>Indacaterol (Breezhaler device with Onbrez capsules)</i> • One inhalation of 150 mg or 300 mg, od <i>Formeterol (Foradil capsules via Aerolizer device)</i> • 1 inhalation of 12 micrograms od or bd <i>Formeterol (Oxis 6 Turbuhaler)</i> • Two inhalations of 6 micrograms, twice daily	LAMA <i>Glycopyrronium (Breezhaler device & Seebri capsules)</i> • Once inhalation, once daily <i>Umeclidinium (Incruse Ellipta)</i> • One inhalation, once daily <i>Tiotropium (Spiriva Respimat)</i> • Two puffs, once daily <i>Tiotropium (Handihaler device & Spiriva capsules)</i> • One inhalation, once daily	LABA/LAMA — SA required <i>Indacaterol + Glycopyrronium (Breezhaler device with Ultibro capsule)</i> • One inhalation, once daily <i>Olodaterol + Tiotropium (Spiolto Respimat)</i> • Two puffs, once daily. MDI delivered as a mist (non-propellant) <i>Vilanterol + Umeclidinium (Anoro Ellipta)</i> • One inhalation, once daily		
ICS Formulations				
ICS + LABA <i>Fluticasone + Vilanterol (Breo Ellipta)</i> • One inhalation, once daily <i>Budesonide + Formoterol (Symbicort)</i> • Two inhalations of 200+6 twice daily or one inhalation of 400+12 twice daily. <i>Budesonide + Formoterol (DuoResp Spiromax)</i> • Two inhalations of 200 + 6 micrograms, twice daily OR One inhalation of 400 + 12 micrograms, twice daily <i>Budesonide + Formoterol (Vannair)</i> • Two puffs of 200 + 6 micrograms, twice daily <i>Fluticasone + Salmeterol (Seretide Accuhaler)</i> • 1 inhalation of 250 + 50 micrograms bd				

Monitoring

- Set activity targets and address / review target attainment!
- Dyspnoea and related symptoms should improve within **6 weeks**
- Record exacerbations over **6-12 months**
- Review inhaler technique
- Smoking Cessation
- Minimise hospitalisations or infections
- Take the [COPD Self-Assessment Test](#) (CAT)
- [Peak Expiratory Flow Rate \(PEFR\)](#)

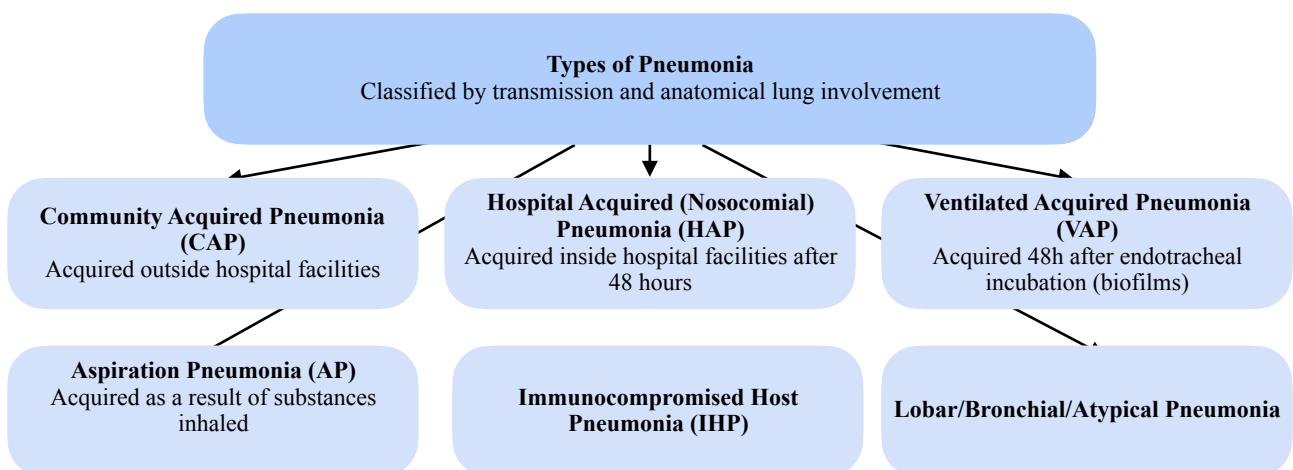
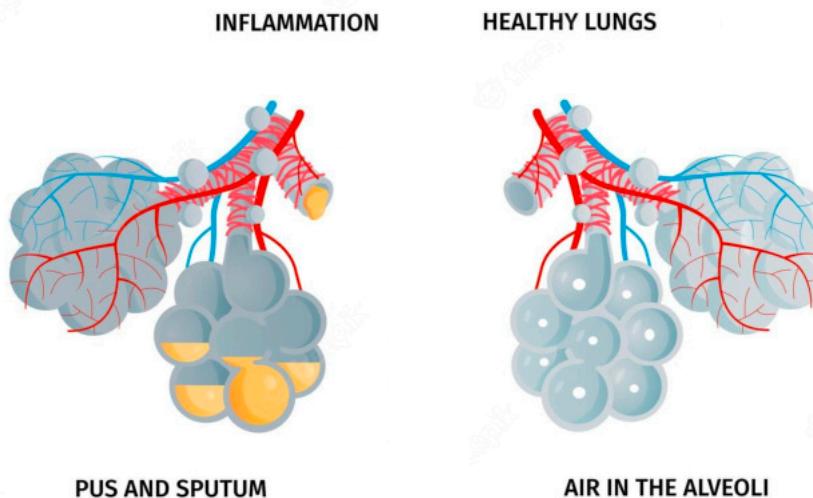
ASSESSMENT OF EXACERBATION SEVERITY			
<i>Adapted from National NZ Ambulance Guidelines - note that not all patients will have all of these features</i>			
Characteristic	Mild - Moderate	Severe	Life-Threatening/Imminent Respiratory Arrest
SoB	More short of breath than usual	Very short of breath	Extremely
Speaking	Able to speak in sentences	Only a few words per breath	Unable to speak
Wheezing	Usually have some	-	May not have a wheeze
Balance	-	Tripod positioning	-
SpO₂	SpO ₂ near usual level	SpO ₂ well below their usual level	SpO ₂ rapidly falling
Consciousness	Normal level of consciousness	May be agitated	Severe agitation and/or falling level of consciousness

Pneumonia

BPAC Community Acquired Pneumonia Management

Description

Pneumonia is an infection of the lungs caused by accumulation of bacteria, viral, and rarely fungi resulting in inflammation of the air sacs in one or both lungs, which fill with pus and may solidify.



Signs & Symptoms

- High fever $>38^{\circ}\text{C}$, chills, malaise, headache, tachypnoea
- Painful, **productive** cough which is worse at night (may have sputum stained red)
- SOB, GI symptoms

Red Flags: Fever >38° C, SOB with cough, increased respiratory rate, O₂ saturation <92%, chest pain unrelated to coughing, haemoptysis, cough persisting more than 21 days.

Complications: Bacteremia, meningitis

Risk Factors

Community Acquired Pneumonia (CAP)

- Children: attending daycare, smoking in the house, premature, immunocompromised
- Elderly: smoking, immunocompromised, cochlear implants

Diagnosis

1. Chest X-Ray
2. Pulse Oximetry
3. Full Blood Count: WCC, CRP, U&E
4. LRT Culture
5. Arterial Blood Gases (ABG)
6. Chest CT

Management

CURB-65 Score is a score that estimates the 30-day mortality risk in those affected by pneumonia. Please note that CURB65 has only been studied in those >18 years

CURB-65 SCORE Estimates 30 Day Mortality Risk		
	Clinical Feature	Points
C	Confusion	1
U	Urea >7 mmol/L	1
R	RR ≥30	1
B	SBP ≤90 or DBP ≤60 mmHg	1
65	Age >65	1

Non-Pharmacological Treatment

1. Hand hygiene
2. Supportive Care: **Fluids**, Oxygen, Paracetamol
3. Keep people moving

Pharmacological Treatment

[BPAC Pneumonia Adult Antibiotic Guidelines](#), [BPAC Pneumonia Child Antibiotic Guidelines](#)

1. *Antibiotics* (see [Wellington Antibiotic Spectrums](#), The Pink Book: [CAP](#), [HAP](#))
2. *Prevention for some types of infection:*
 - Pneumococcal vaccine (Synflorix PVC10)
 - Haemophilus influenzae b (HiB) vaccine (Infanrix-hexa, Hiberix)

Monitoring — BPAC CAP

Improvement is expected within 48 - 72 hours

- FBC: WBC, CRP
- Symptoms (purulent cough), fever, O₂ sat
- CURB: Mental status, Urea (may not be readily available in community setting), RR, BP
- Chest X-ray (no abnormalities)
- Up to date immunisation

Community Acquired Pneumonia (CAP)					
Typical Bacteria		Atypical Bacteria		Viral	Fungal
Streptococcus pneumoniae (G+ve)	<ul style="list-style-type: none"> • Macrolides • Penicillin • Amoxicillin • Augmentin • Tazocin • Doxycycline • Cephalosporins 	Legionella Pneumophilia (G-ve) <i>Consider if patient works with soil or garden</i>	<ul style="list-style-type: none"> • Macrolides (Azithromycin, clarithromycin, erythromycin) • Doxycycline • Quinolones (Ciprofloxacin, moxifloxacin) 	Respiratory Syncytial Virus	Pneumocystis jirovecii (PCP) —causes pneumocystis pneumonia (PCP) often in immunocompromised
Haemophilus Influenzae (G-ve)	<ul style="list-style-type: none"> • Amoxicillin • Augmentin • Cephalosporins • Tazocin 	Mycoplasma Pneumoniae <i>Often presents with a rash</i>	<ul style="list-style-type: none"> • Macrolides • Quinolones • Rifampicin • Doxycycline 	Influenza A or B	
Staphylococcus Aureus (G+ve)	<ul style="list-style-type: none"> • Cephazolin • Cephalexin • Augmentin • Tazocin • Doxycycline 	Chlamydophila pneumoniae	<ul style="list-style-type: none"> • Macrolides • Doxycycline • Quinolones 	COVID-19	
Hospital Acquired Pneumonia (HAP)					
Gram -ve Bacteria		Ventilator Associated Pneumonia (VAP): Biofilm on the endotracheal tube		Aspiration Pneumonia: Food, saliva, liquids, vomit is breathed into the lungs instead of stomach	
Pseudomonas aeruginosa (<i>Opportunistic</i>)	<ul style="list-style-type: none"> • Amoxicillin + Clavulanic Acid 	Pseudomonas aeruginosa (<i>Opportunistic</i>)	<ul style="list-style-type: none"> • Amoxicillin + Clavulanic Acid 	<ul style="list-style-type: none"> • Contact Accident & Emergency 	
Escherichia coli		Escherichia coli			
Klebsiella pneumoniae		Klebsiella pneumoniae			
Acinetobacter species		Staphylococcus Aureus (G+ve)			



CHAPTER 8

THE CARDIOVASCULAR SYSTEM



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Chapter 8

The Cardiovascular System

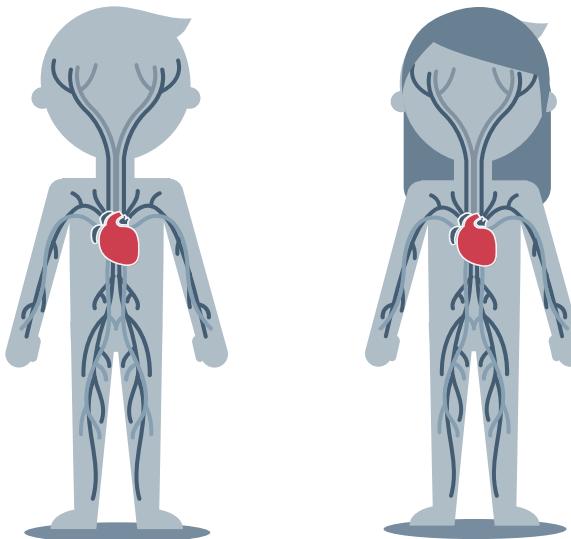
General Overview of the Heart

Chapter Resources

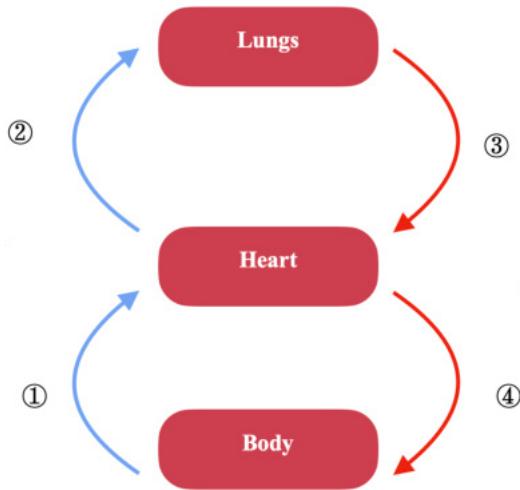
Useful chapter resources include the [Heart Foundation](#) and the [CVD Risk Calculator](#).

Introduction to the Cardiovascular System

The Cardiovascular System is one of the most complex body systems we will investigate in this book - before we dwell in to the conditions that afflict this system, it is important to have understanding of its anatomical composition and the laboratory investigations undertaken to measure its performance. You will find that there are many links to the Renal System Chapter given these two systems are closely associated.



The purpose of the cardiovascular system can be simply narrowed down to the carriage of oxygen and nutrients via blood vessels to all parts of the body. The heart functions primarily to maintain adequate cardiac output and mean arterial via many compensatory mechanisms (e.g. ↑ HR, ↑ Contractility, ↑ H₂O/Na⁺).



Heart Chambers

The heart consists of 4 chambers divided into atriums and ventricles that exist on each side of the heart. Two valves exist in order to allow blood flow through these:

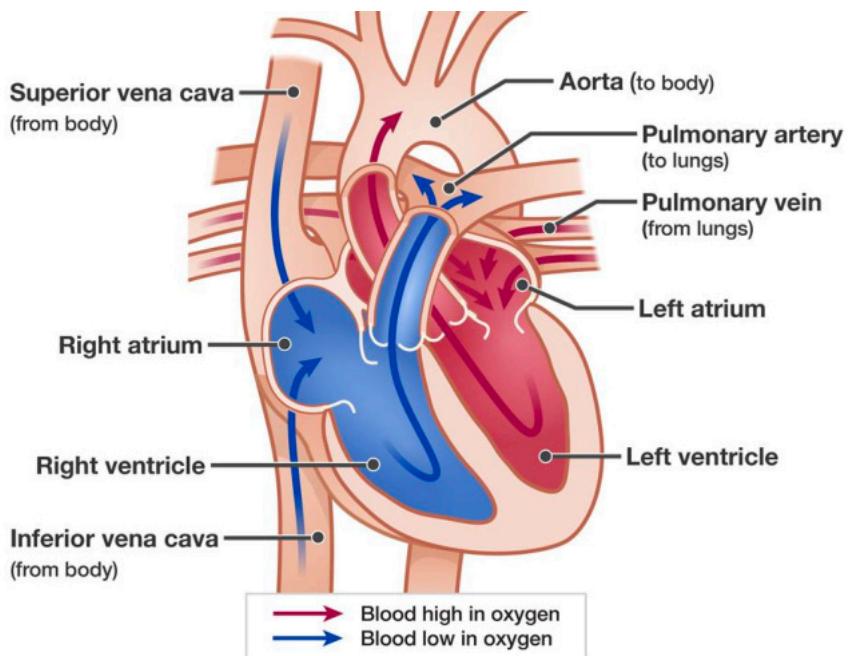
1. *Atrio-Ventricular (AV) valves* allow blood flow through the chambers (bicuspid and tricuspid)
 2. *Semi-Lunar (SL) valves* allow blood flow to and from the AV system (pulmonary and aortic)

Note: The heartbeat sound ("lub dub") is produced by the closing of the AV and SL valves, respectively.

The Cardiac Cycle

The cardiac cycle can be divided into 2 phases:

1. *Diastole* occurs when the heart muscle relaxes prior to contraction. The AV valves open to allow the ventricles to fill with blood and the SL values are closed.
 2. *Systole* occurs when the ventricles of the heart contracts, causing the ejection of blood into the aorta and pulmonary trunk. The SL valves open to allow this and the AV valves close to prevent backflow of blood into the ventricles.



Vessels Involved

Blood is pumped through three types of vessels:

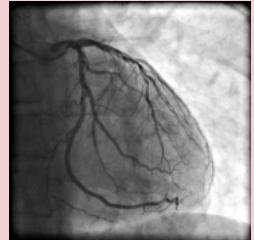
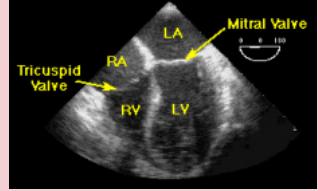
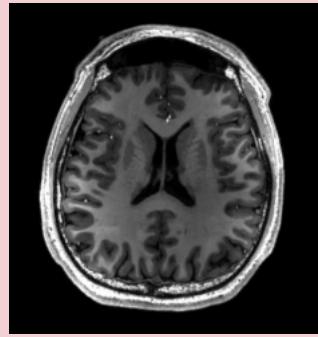
- *Arteries/Arterioles* carry oxygenated blood from your heart (except for pulmonary artery) to your body's tissues. Blood flows under high pressure. White platelet rich clots can form.
- *Veins/Venules* carry deoxygenated blood back to your heart (except for pulmonary vein). They contain valves and blood flows under low pressure. Red fibrin-rich clots can form.
- *Capillaries* are small blood vessels where your body exchanges oxygen-rich and oxygen-poor blood i.e. where venules and arterioles meet.

Investigations & Tests

Laboratory Investigations

Lab Investigation	Description	Measured by	Equations
Heart Rate (HR) 75 bpm (60 - 100 bpm)	<ul style="list-style-type: none"> The number of heart beats per minute, with each beat pumping blood through the atria and then ventricles. 	<ul style="list-style-type: none"> Physical Examination Portable Monitors ECG 	<ul style="list-style-type: none"> $CO = HR \times SV$
Blood Pressure (BP) 120/80mmHg (120-140 / 80-90mmHg)	<ul style="list-style-type: none"> The hydrostatic pressure exerted by the circulating blood on the (arterial) vessel wall. 	<ul style="list-style-type: none"> BP monitor (sphygmomanometer) +/- stethoscope 	<ul style="list-style-type: none"> $BP = SBP / DBP$
Mean Arterial Pressure (MAP) 90mmHg (65 - 110mmHg)	<ul style="list-style-type: none"> The average arterial blood pressure / the perfusion pressure reaching a body organ. 	<ul style="list-style-type: none"> Equations 	<ul style="list-style-type: none"> $MAP = CO \times TPR$ $MAP = DBP + (PP/3)$ $MAP = \frac{2}{3}DBP + \frac{1}{3}SBP$
Cardiac Output (CO) 5.5 L/min (4-5 L/min)	<ul style="list-style-type: none"> The volume of blood pumped through the ventricles of the heart <u>per minute</u> to supply the organs. Depends on BSA 	<ul style="list-style-type: none"> Doppler echocardiography 	<ul style="list-style-type: none"> $CO = HR \times SV$
Stroke Volume (SV) 75 ml/beat (60 - 120 ml/beat)	<ul style="list-style-type: none"> The volume of blood ejected from the ventricles <u>per heart beat</u> (ml/beats). Scaled by BSA area 	<ul style="list-style-type: none"> Echocardiography 	<ul style="list-style-type: none"> $SV = EDV - ESV$
Ejection Fraction (EF) 60% (Can be elevated or appear 'normal' in HF)	<ul style="list-style-type: none"> The fraction of blood pumped from the ventricles with each heart beat. (Not all the blood is pumped out of the ventricle with each beat, some volume of blood will remain). 	<ul style="list-style-type: none"> Echocardiogram or angiography 	<ul style="list-style-type: none"> $EF = SV/EDV$
Central Venous Pressure (CVP) 2 - 6 mmHg <i>Indicator of Preload</i> CVP = Lungs = Right Ventricular Preload	<ul style="list-style-type: none"> Preload measures the VOLUME in the ventricles at the end of diastole (EDV). CVP estimates preload by measuring the hydrostatic pressure on the right side of the heart (blood supply to the lungs). This approximates the right <u>atrial pressure</u>, which estimates the right <u>ventricular preload</u>. 	<ul style="list-style-type: none"> CV Catheters Jugular Venous Pressure 	<ul style="list-style-type: none"> $SV = EDV - ESV$
Afterload Pressure <i>Indicator of Total Peripheral Resistance (TPC)</i> Left Ventricular Pressure = TPR = Body Right Ventricular Pressure = Lungs	<ul style="list-style-type: none"> The PRESSURE that the heart must work against to eject blood out of the semi-lunar valves to push blood to the lungs and to the body when the ventricles contract during systole. 	N/A	N/A

Diagnostic Tests of the Heart

Test	Description	Photo
Blood Test	When your muscle has been damaged, as in a heart attack, your body releases substances in your blood. Blood tests can measure the substances and show if, and how much of, your heart muscle has been damaged. Blood tests are also done to measure the level of other substances in your blood, such as blood fats (e.g. cholesterol and triglycerides), vitamins and minerals.	-
Coronary Angiogram	A coronary angiogram, sometimes called ‘cardiac catheterisation’, may be done after a heart attack or angina. A catheter (a small tube) is put into an artery in your groin, arm or wrist. The catheter is moved up inside the artery until it reaches your heart. A special dye is injected into your coronary arteries and an X-ray is taken. The X-ray shows your doctor where and how much your coronary arteries are clogged or blocked. It also shows how well your heart is pumping. Coronary angiograms help your doctor decide the best treatment for you.	
Computed Tomography Angiogram (CTA)	This is a specialised type of computed tomography (CT) scan that may be used to help identify if plaque build up has narrowed coronary arteries, thus help to diagnose coronary artery disease. It is a non-invasive test for people who may be experiencing unusual cardiac symptoms.	
Electrocardiogram (ECG)	An ECG reads your heart’s electrical impulses. It shows how well your heart is beating. It can diagnose a heart attack or abnormal heart rhythms (called ‘arrhythmias’). Exercise stress test: A stress test, sometimes called a ‘treadmill’ or ‘exercise’ test, is a type of ECG that is done while you are exercising. It helps your doctor to find out how well your heart works when you are physically active	-
Echocardiogram (Ultrasound)	It gives a picture of your heart using ultrasound, a type of X-ray. It uses a probe either on your chest or down your oesophagus (throat). It helps your doctor check if there are any problems with your heart’s valves and chambers, and see how strongly your heart pumps blood.	
MRI	An MRI uses very strong magnets and radio waves to create detailed images of your heart on a computer. It can take still or moving pictures of your heart. Sometimes a special dye is used to make parts of the heart and coronary arteries easier to see. This test shows your doctor the structure of your heart and how well it is working, so they can decide the best treatment for you.	

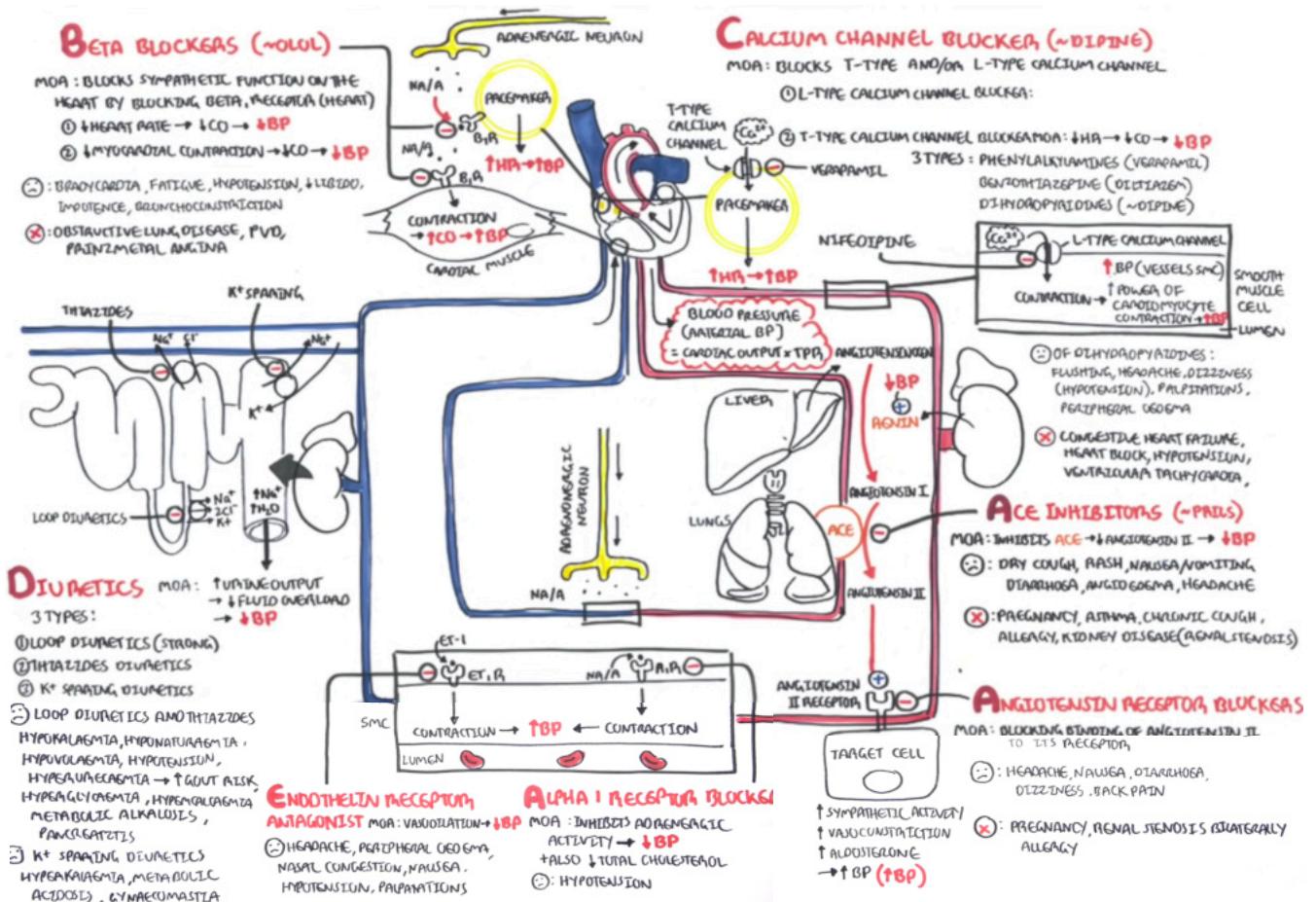
Overview of Pharmacological Interventions

When medical conditions afflict this system, the primary purpose of drug treatment is to:

1. Regulate heart rate (HR)
2. Improve heart contractility to modify stroke volume (SV)
3. Reduce venous pressure to modify central venous pressure (CVP)

- Vasodilate to modify total peripheral resistance (TPR) or mean arterial pressure (MAP), therefore reduce heart load.
- Improve organ perfusion

Please find below a summary of drugs that are used in this chapter.



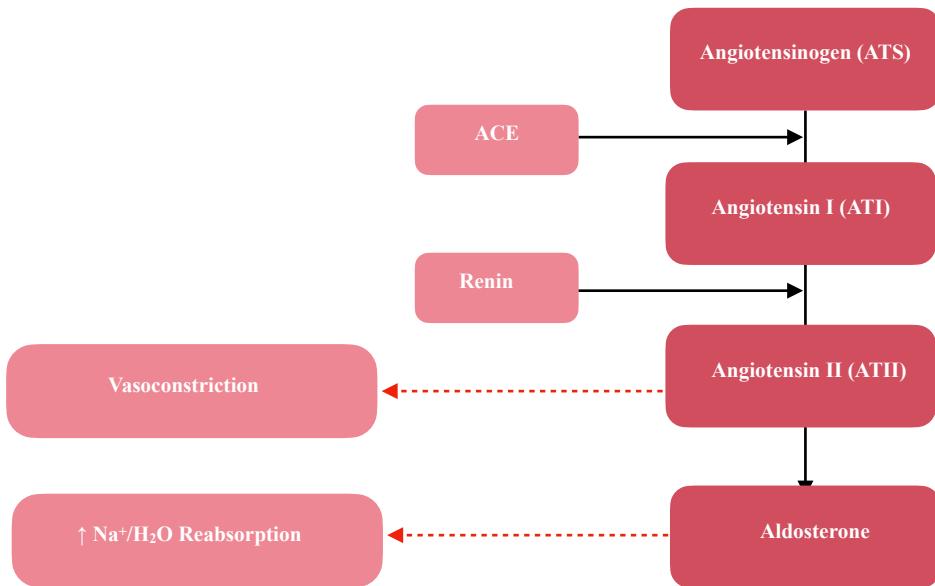
As well as a recommendation as to when they should be initiated.

Table 3: The pharmacological management of cardiovascular risk based on the 2018 CVD consensus statement

Risk category	Recommended management		
	New thresholds (based on NZ Primary Prevention equations)	Old thresholds (based on Framingham equations)	
Low risk	< 5%	< 10%	<p>Cardiovascular medicines are not generally recommended as this is believed to be the point below at which the harms of treatment are likely to exceed the benefits of treatment.</p> <p>It is estimated that approximately three-quarters of the population will have a five-year cardiovascular risk < 5% using the new equations.</p>
Intermediate risk	5-15%	10-20%	The benefits and risks of blood-pressure and lipid-lowering medicines should be discussed and initiation of treatment considered, particularly for those with a risk at the higher end of this spectrum.
High risk	≥ 15%	≥ 20%	Blood pressure and lipid-lowering medicines are recommended. Aspirin for primary prevention of CVD should be considered for patients who are aged under 70 years. In general, patients with a high CVD risk should be managed in the same way as patients with established CVD.

Preview: Renin-Angiotensin Aldosterone System (RAAS)

The RAAS system describes responses that occur in the body that afflict the renal-cardiovascular system. It is central to the many mechanisms of drugs used in the Cardiovascular Chapter. Please see *Chapter 10 - the Renal System* for more information on it.



NON-CARDIOVASCULAR DISEASES

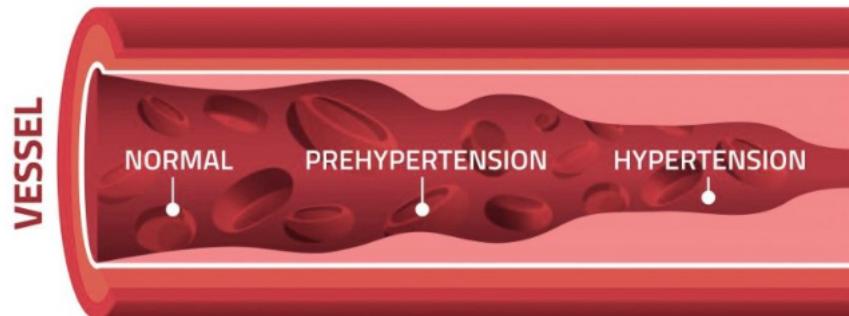
Introduction

Hypertension and hyperlipidaemia (not atherosclerosis), although themselves not considered cardiovascular diseases, are strong independent risk factors for one. Good management of patients presenting at this stage can prevent progression of their state and any other complications.

Hypertension (HTN)

Description

Hypertension is a silent, insidious, chronic and progressive disease that essentially means high blood pressure. It is the result of the excessive blood force exerted on arterial walls where the pressure eventually leads to tissue hypertrophy (e.g. left ventricular hypertrophy). While it itself is not a cardiovascular disease, it is a risk factor for it and many other complications including stroke, myocardial infarction, heart failure, atrial fibrillation, kidney disease, cognitive decline.



Signs & Symptoms

HTN is an asymptomatic condition, however patients may experience a headache. Please visit *Chapter 16 - The Neurologic System* for more information on Hypertension Headaches



Hypertension & Adherence

As HTN is usually an asymptomatic, many patients struggle to adhere to blood-pressure lowering medications because they can't really 'feel their blood pressure' - proper education on the risks and complications associated with HTN can help with this.

Complications: stroke, MI, HF, Afib, kidney disease, cognitive decline.

Risk Factors

1. Primary HTN (unknown cause/idiopathic) | 90%

- *Environmental:* Diet high in salt/fat/cholesterol, overweight, inactivity, stress, age
- *Genetics:* Familial History of HTN / CVD

2. Secondary HTN (underlying cause) | 10%

- *Medical Conditions:* CKD, Cushing Syndrome, Obstructive sleep apnoea, Thyroid Disease
- *Medicine-Induced:* Glucocorticoids, NSAIDs, OCs, some SSNRIs, methylphenidate, cyclosporine

Diagnosis

1. *Normal:* BP > 120/80 mmHg
2. *Mild:* $\geq 140/90$
3. *Moderate:* $\geq 160/100$
4. *Severe:* $\geq 180/\geq 110$



White Coat Hypertension

White-coat hypertension is the event in which the patient measures a higher blood pressure than normal in the presence of a healthcare professional. Be careful of misdiagnosis in otherwise normotensive patients.

Treatment for HTN can be drug or lifestyle-centred depending on the **5 Year CV Risk**.

Table 1: Thresholds for blood-pressure lowering interventions in patients aged under 75 years based on five-year cardiovascular risk⁴

New thresholds (based on NZ Primary Prevention equations)	Old thresholds (based on Framingham equations)	Recommendation
< 5%	< 10%	Lifestyle modifications are recommended for all patients with a blood pressure $\geq 130/80$ mmHg. Blood pressure-lowering medicines are not recommended.
5 – 15%	10 – 20%	Discuss the benefits and harms of initiating blood pressure-lowering medicines for patients with a blood pressure persistently $\geq 140/90$ mmHg
$\geq 15\%$	$\geq 20\%$	Blood pressure-lowering medicines are strongly recommended for patients with a blood pressure persistently $\geq 130/80$ mmHg
$\geq 160/100$ mmHg with any level of cardiovascular risk		Blood pressure-lowering medicines are generally recommended

Non-Pharmacological Treatment

1. Dietary sodium restriction, low-fat diet, vegetables and fruit
2. Weight reduction in overweight or obese individuals
3. Regular physical activity (30 minutes of moderate activity most days a week)
4. Moderation of alcohol consumption (no more than 2 standard drinks per day for men and 1 for women)
5. Smoking cessation

Pharmacological Treatment

BPAC Managing Blood Pressure, BPAC - Which Anti-Hypertensives?

5 classes of anti-hypertensives exist

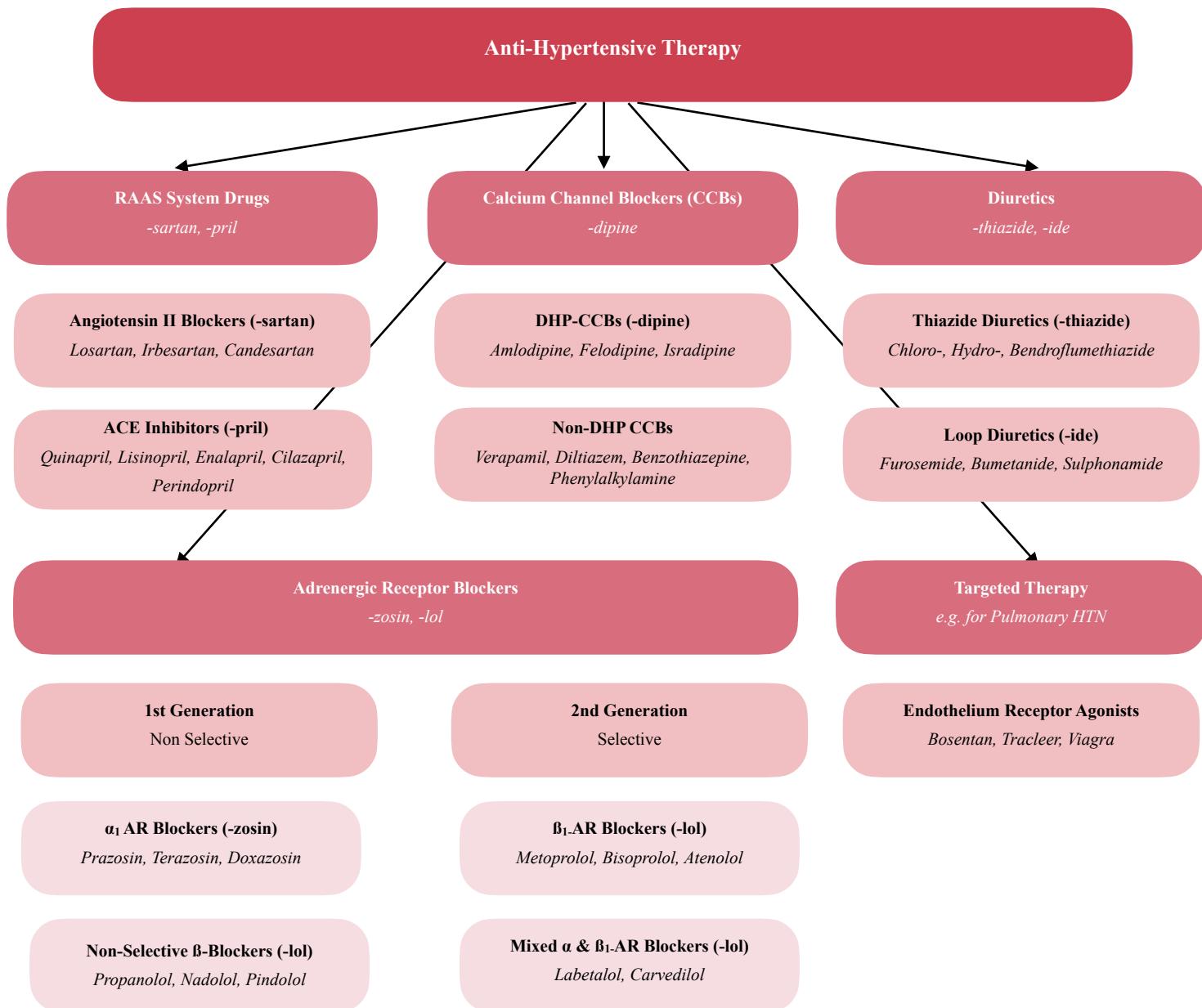
1. ACE Inhibitors/ARB
2. Calcium Channel Blockers (CCB)
3. Thiazide diuretics
4. B-blockers
5. Endothelium Receptor Agonists



Blood Pressure Target

BP <140/90 mmHg for most people

BP <130/80 mmHg if CVD, HF, CKD, T1/T2DM



	Drug	Mechanism of Action	Side Effects
RAAS System	[PRESCRIPTION] ACE Inhibitors (-pril) Enalapril, Cilazapril (Zapril), Quinapril, Lisinopril, Perindopril (Coversyl),	Vasodilation + Reduced Blood Volume due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H ₂ O/Na ⁺ uptake) Note: These are renoprotective and are prodrugs (enalapril → enalaprilat exceptions are lisinopril and captopril) Do not use ACEI/ARB in pregnancy. Labetalol, nifedipine, hydralazine are instead recommended.	Dry cough (due to bradykinin buildup, which usually gets broken down by ACE), hyperkalaemia, dizziness, postural hypotension, GI disturbances (N/V/D, rashes, angioedema, headache)
	[PRESCRIPTION] ARB Blockers (-sartan) Candesartan (Candesartan), Losartan, Irbesartan	Vasodilation + Reduced Blood Volume due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H ₂ O/Na ⁺ uptake) Note: Losartan is not a prodrug as both losartan and its metabolite are biologically active	Headache, nausea, diarrhoea, dizziness, hypotension, hyperkalaemia, back pain
Adrenergic Receptor Antagonists (ARA)	[PRESCRIPTION] α_1 Blockers (-zosin) Prazosin, Terazosin, Doxazosin <i>Mixed (α and β) Blockers (-lol)</i> Labetalol, Carvedilol	Vasodilation due to blocking of α_1 and/or β receptors in blood vessels. Note: Adrenergic receptor antagonists block the binding of adrenaline and noradrenaline, causing vasodilation — they have no activity at the receptor (antagonist).	Dizziness, Postural Hypotension , Dizziness, Dry mouth, GI disturbances, Oedema
	[PRESCRIPTION] β -Blockers (-olol) <i>1st Gen (Non-Selective)</i> Propranolol, nadolol, pindolol (avoid in asthmatics) <i>2nd Gen (β_1-Cardioselective)</i> Metoprolol succinate (Betaloc), bisoprolol, atenolol, esmolol	Decrease Heart Rate. β_1 receptors are found in the heart - their activation increases heart rate, contractility, electrical activity and cardiac output. β_2 agonists in asthma serve to cause bronchodilation. β blockers overall are thus not to be used in asthmatics whereas β_1 receptors (second generation) are okay as they are cardioselective. Note: Preferred anti-HTN in arrhythmia. Always use long acting β -blockers.	Bradycardia, Bronchoconstriction in non-selective or high dosage, fatigue, hypotension, decrease in libido, bronchoconstriction
Calcium Channel Blockers (CCBs)	[PRESCRIPTION] DHP-CCBs (-dipine) Amlodipine, felodipine, isradipine, nifedipine, nimodipine	Vasodilation via blocking the action of calcium on calcium channels which prevents muscle contraction in the heart and arteries and allows their relaxation. This decreases the afterload pressure.	Headache, dizziness, palpitations, flushing, constipation, peripheral oedema, bradycardia, grapefruit intolerances.
	[PRESCRIPTION] Non-DHP CCBs (-mil, zem) Phenylalkylamine: Verapamil (interaction with statins) Benzothiazepine: Diltiazem	Vasodilation + Heart Activity Relaxation In addition to the DHP mechanisms, non-DHPs additionally slow down the electrical activity of the heart Note: Bradycardia risk if combined with B-blockers . Note: Verapamil is a CYP3A4 inhibitor (statin interaction)	DHP: more vascular-selective (more potent vasodilators) Non-DHP: more myocardial selective, thus tend to reduce HR (marked negative inotropic effects)
Diuretics	[PRESCRIPTION] Thiazide Diuretics [-thiazide] Chlorothiazide, hydrochlorothiazide, bendroflumethiazide	Reduce Blood Volume. Thiazide diuretics increase the rate of urine formation via Na ⁺ -Cl ⁻ symporter blockage — they resultantly encourage natriuresis; excretion of Na ⁺ and water which reduces blood pressure and causes arteriole vasodilation	
	[PRESCRIPTION] K ⁺ Sparing Diuretics/ Aldosterone-receptor antagonist (ARA) Spironolactone	Decreased Blood Pressure due to decreased H ₂ O/Na ⁺ uptake. This drug is less relevant to HTN and more in HF (kidneys think there isn't enough fluid and uptake it more)	Hypokalaemia or hyperkalaemia, hyponatraemia, hypovolaemia, hypotension, hyperuricaemia (gout), hyperglycaemia (careful in diabetes), hypercalcaemia, hypochloeraemia, hypomagnesemia, metabolic ketoacidosis, pancreatitis
	[PRESCRIPTION] Loop Diuretics [-ide] Furosemide, Bumetanide	Loop diuretics inhibits NKCC2 (Na/K/2Cl) luminal co-transporter. They are not stand-alone anti-hypertensives but can be used in combination for HTN treatment. They have a more ceiling/profound effect which is useful for oedema treatment of water retention i.e. in heart failure	
Other	[PRESCRIPTION] Endothelium Receptor Antagonists Bosentan (Tracleer, Viagra)	N/A	N/A

Treatment Considerations

Monotherapy is usually preferred however most people will need combination therapy to achieve their target blood pressure. Please note that a patient's co-morbidities will influence what therapy is appropriate for them.

CHOICE OF ANTIHYPERTENSIVE IN PATIENTS WITH CO-MORBIDITIES		
Condition	Potentially Beneficial	Avoid
Diabetics	ACEI/ARB for renoprotection CCBs	Thiazide and β-blockers are associated with a higher risk of developing diabetes β-blockers can mask symptoms of hypoglycaemia.
CKD	ACEI/ARB for renoprotection	N/A
Angina, IHD	β-blockers, CCBs, ACEI for early cardioprotection	N/A
Afib	CCBs, β-blockers for rate control	N/A
Post MI	β-blockers, ACEI for early cardioprotection	N/A
Post stroke	ACEI/ARB for renoprotection	Thiazide in older people or those with poor fluid intake which could contribute to hypotension
HF	Thiazide Diuretic: In HF, CO is compromised so HR is elevated. RAAS activation causes water and sodium retention. Low dose β-blocker ACEI/ARB to prevent LVH	Avoid CCBs (especially non-DHP CCBs): In HF, the heart is also compensating by contracting harder, therefore avoid CCBs as this will weaken the strength of contractions. Avoid Alpha and β-blockers if heart failure is uncontrolled or there is aortic stenosis.
Symptomatic BPH	Alpha - blockers,	Alpha blockers can lead to postural hypotension in older people
Asthma	N/A	Avoid β-blockers
Gout	N/A	Thiazides can precipitate gout (however this is unlikely if they are well controlled with allopurinol)

Patient Counselling Notes

1. Abruptly stopping anti-hypertensive treatment can cause rebound hypertension!
2. Do not switch positions too quickly due to risk of postural hypotension

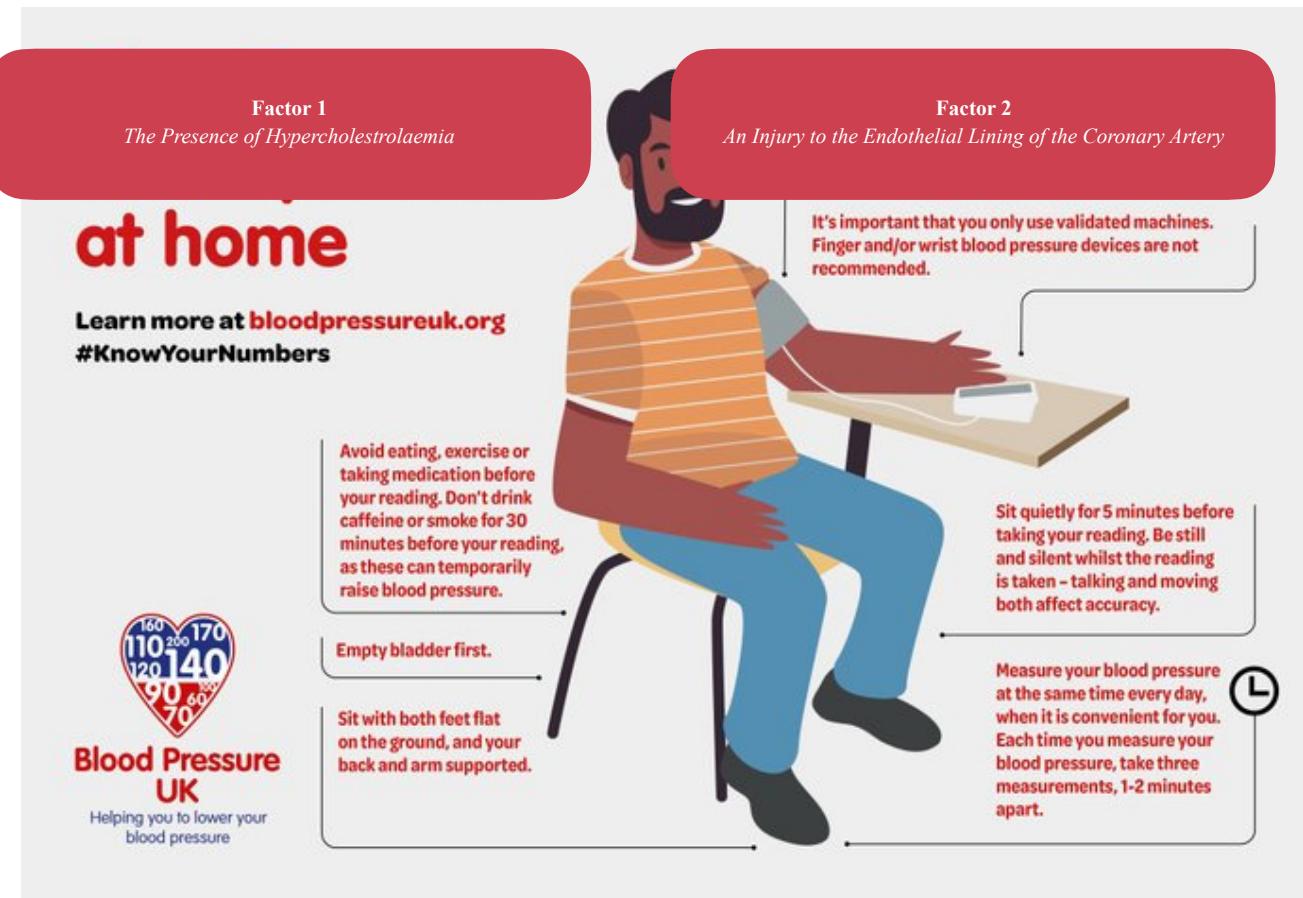
Primary Prevention

Aspirin should only be considered in:

1. People aged **<70 years, and**
2. Estimated 5 year CVD risk of **≥15%**

Monitoring

- *Initially:* measure BP twice daily for a week (adjust according to risk), then once monthly when stable
- *At 1 - 2 weeks:* Check renal function & electrolytes
- *At 1 month:* Follow up on self-monitoring to assess treatment, side effects, and adherence. Take clinical measurements to see if target goals have been achieved.
- *At 3 - 6 month intervals:* if actively modifying health behaviours, patients should be followed-up at those intervals
- *Annual Reviews:* once target is reached



Hyperlipidaemia (HLD) & Atherosclerosis

Description

Hyperlipidaemia is a disorder of elevated lipid levels in the blood such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and triglycerides (TGs). Hyperlipidaemia, much like HTN, although not a cardiovascular disease itself, dangerously contribute to a patient's overall CV risk due to the risk of developing atherosclerosis.

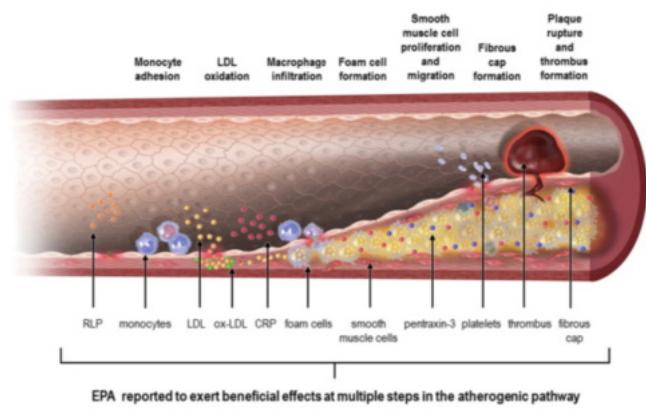
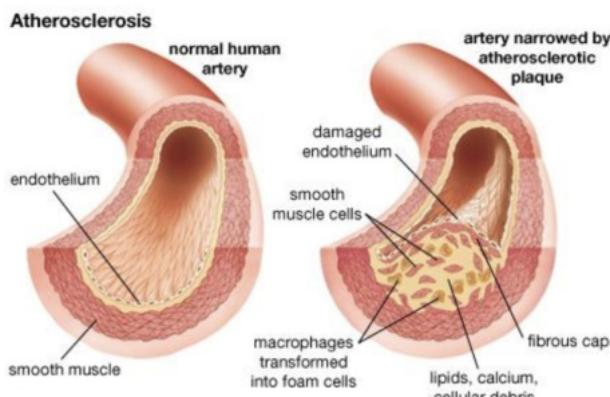
A note on Atherosclerosis

Atherosclerosis is a disease of the arteries that is characterised by the deposition of fatty material build up in walls of coronary arteries - causing the vessels to narrow. The formation of an atherosclerotic plaque requires only two things:

The injury allows for fats, cholesterol, proteins, calcium and immune cells to get trapped and build up.

Injuries to coronary arteries can be caused by many different things - common irritants include smoking, hyperglycaemia, HTN.

The presence of atherosclerotic plaques and the subsequent narrowing of the arteries they are found leads to Coronary Heart Disease (CHD), a condition in which there is an imbalance between the myocardial oxygen demand and supply. This can progress to the rupturing of the plaque, which is associated with even deadlier circumstances due to the formation of a thrombus.



Pathophysiology

Cholesterol from our diet is absorbed in the intestine and carried via lipoproteins such as chylomicrons, which in turn can either deposit fats in adipose tissue for storage or deposit it elsewhere to be used for energy. However, with the presence of risk factors such as a fatty diet, this process can become pathological.

Signs & Symptoms

This is an asymptomatic disorder, and can only be determined by a blood test. Thus much like hypertension, issues with patient adherence to lifestyle changes and/or medications are often encountered as this disorder cannot be felt.

Skin manifestations

Xanthomas can sometimes occur - which are fatty deposits that leak out of blood vessels.

Risk Factors

1. Primary Dyslipidaemia | Inherited

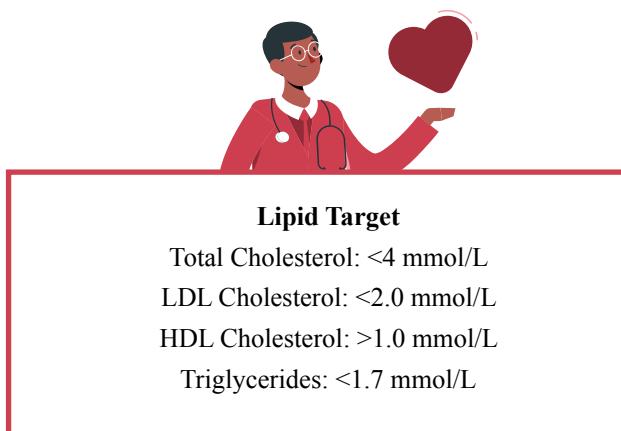
- *Familial Hypercholesterolaemia*: genetic disorder where the body is unable to remove LDL
- *Family History* of HTN, HLD, CVD
- *Ethnicity/Race*: Māori and Pacifica have higher cholesterol levels

2. Secondary Dyslipidaemia | Acquired

- *Environmental*: High salt/fat/cholesterol diet, overweight, inactivity, age, smoking, alcohol abuse
- *Gender*: younger men (smoking likelihood), older women (live longer)
- *Medical Conditions*: CKD, Diabetes, Hypothyroidism, PCOS, Liver Disease, Metabolic Syndrome, Pregnancy (Gestational Hypertension, Pre-Eclampsia)
- *Medicines*: Anti-HTNs (β -blockers, Diuretics), Corticosteroids, OCs, Ciclosporin

Diagnosis

Normal lipid ranges as stated below are exceeded in this disorder. However it is important to keep in mind that lipid profiles differ between populations.



Non-Pharmacological Treatment (Adjunctive Role Only)

Lifestyle modifications will decrease the risk but will **not** achieve the required lipid profiles on its own.

1. *Diet*: Mediterranean diet comprises of a lower intake of trans and saturated fats
2. *Exercise*: 30 minutes of moderate intensity exercise at least 5 times a week

Table 1: Five-year CVD risk levels for lipid-lowering interventions in patients aged under 75 years^{1,4,7}

New CVD risk level (based on NZ Primary Prevention equations)	Old CVD risk level (based on Framingham equations)	Recommendation
< 5%	< 10%	Lifestyle interventions are recommended for all people. Lipid-lowering medicines are not recommended.
5–15%	10–20%	The benefit of lipid lowering treatment is likely to outweigh adverse effects in most people. Discuss clearly the benefits and harms of initiating lipid-lowering medicines for patients and encourage dietary changes. If lipid-lowering medicines are started, a target reduction in LDL-C of ≥ 40% is recommended.
≥ 15%	≥ 20%	Lipid-lowering medicines are strongly recommended for patients in addition to dietary changes. An LDL-C treatment target of < 1.8mmol/L is recommended.
TC:HDL-C ratio ≥ 8 with any level of cardiovascular risk		Lipid-lowering medicines are recommended
• Familial hypercholesterolaemia • Hypertriglyceridaemia		Individualised management is required, lipid-lowering medicines are usually recommended regardless of estimated CVD risk

Pharmacological Treatment

BPAC Lipid Lowering Therapy (Statins)

Lipid-lowering medicines are recommended for patients with existing CVD or a $\geq 15\%$ five-year risk



Note

Lipid Lowering Therapy is **NOT** suitable in pregnancy and/or breastfeeding.

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] Statins (First line) Atorvastatin (Lorstat), Simvastatin, Rosuvastatin, Pravastatin	<ul style="list-style-type: none"> Excellent for LDL ($\downarrow 25\% - 62\%$) Moderately \downarrow TAGs Slightly \uparrow HDL <p>Statins inhibit HMG-CoA reductase, thus preventing the synthesis of cholesterol in the liver.</p>	<ul style="list-style-type: none"> <i>Simvastatin, Pravastatin and any other short half-life statins need to be taken at night as cholesterol synthesis peak overnight.</i> <i>Atorvastatin does not require a particular time given its long half life.</i> Interactions with Azoles, Macrolides, SSRIs, CCBs, Warfarin, Amiodarone. If a macrolide antibiotic must be initiated, pause the statin. 	Mostly emerge in the first 3 months Inhibition of the cholesterol synthesis pathways affects other products. Statins are generally well tolerated (most side effects will subside within 3 months) <ul style="list-style-type: none"> Elevated Liver Enzymes Myopathy Rhabdomyolysis <p>Statins & Hyperglycaemia <i>Note:</i> statins increase the risk of hyperglycaemia and insulin resistance, however they should still be used even in those at risk or those that develop T2DM (CV risk $>$ statin induced T2DM) <ul style="list-style-type: none"> Pravastatin: lowest risk Atorvastatin: moderate risk Rosuvastatin: highest risk </p>
[PRESCRIPTION] Fibrates Bezafibrate	<ul style="list-style-type: none"> Excellent for TAGs ($\downarrow 20\% - 50\%$) Moderately \uparrow HDL (9-30%) <p>Not recommended as stand-alone tx Fibrates reduce triglyceride rich lipoproteins and increase HDL levels — by reducing apoproteins B, C3, and E (on TAGs), and increasing apoproteins A1, A2 (on HDL) by activating PPAR-α.</p>	<ul style="list-style-type: none"> Increased risk of myopathy/rhabdomyolysis with concurrent statin use & renal insufficiency 	Fibrates are generally well tolerated. <ul style="list-style-type: none"> Dyspepsia, abdominal pain, diarrhoea, flatulence, rash, muscle pain, fatigue
[PRESCRIPTION] Bile Acid Binding Agents Cholestyramine, Colestipol	<ul style="list-style-type: none"> Excellent for LDL <p>Bile acid binding agents form a complex with bile (cholesterol-based detergents that emulsify and solubilise fats to allow for their digestion), causing it to be excreted in the faeces. The loss of bile will trigger a ‘compensatory’ response which converts more hepatic cholesterol stores to bile, therefore overall decreasing cholesterol levels.</p>	<ul style="list-style-type: none"> If taking other medicines, space out doses so that their absorption is not affected. 	<ul style="list-style-type: none"> This drug is not absorbed into the systemic circulation, thus side effects are limited to the GI tract. e.g. Constipation, bloating, flatulence.
[PRESCRIPTION] Cholesterol Absorption Inhibitors Ezetimibe	<ul style="list-style-type: none"> Excellent for LDL — Use synergistically with statins, rarely used alone. <p>These interact with cholesterol transporters in the intestinal brush border membrane to prevent cholesterol reabsorption from the GIT. This is recommended as monotherapy for familial hypercholesterolaemia.</p>	<ul style="list-style-type: none"> These should be prescribed with another lipid lowering agent (statins, fibres or nicotinic acid derivative) and are rarely given by themselves. 	<ul style="list-style-type: none"> Muscle pain, GI symptoms
[PRESCRIPTION] Nicotinic Acid Derivatives	<p>Good for all lipids - No longer used due to side effects</p> <p>These are no longer recommended either in monotherapy or in conjunction.</p>	N/A	<ul style="list-style-type: none"> Flushing of the head, neck and upper torso.

Monitoring (Statins)

- Reduction of LDL within 2 weeks of initiation, with a maximum response by 4 weeks.
- Monitor non-fasting lipid levels every 3-6 months until stable, then annually thereafter.
- Monitor liver function, monitor risk of pregnancy
- Not necessary to check creatine kinase (CK) unless symptoms of muscle pain, tenderness, and weakness.
 - *Muscle pain without rise in CK:* Decrease dose or discontinue statin. Re-challenge later.
 - *Myopathy with 3-10x CK rise:* Decrease dose or discontinue statin. Monitor symptoms & CK weekly
 - *Rhabdomyolysis: $\geq 10x$ CK rise:* Discontinue immediately. No re-challenge.
 - Note: Creatine kinase (CK) is an enzyme that's found in your skeletal muscle, heart muscle and brain. When any of these tissues are damaged, they leak creatine kinase into your bloodstream.

CLOT-RELATED CARDIOVASCULAR CONDITIONS

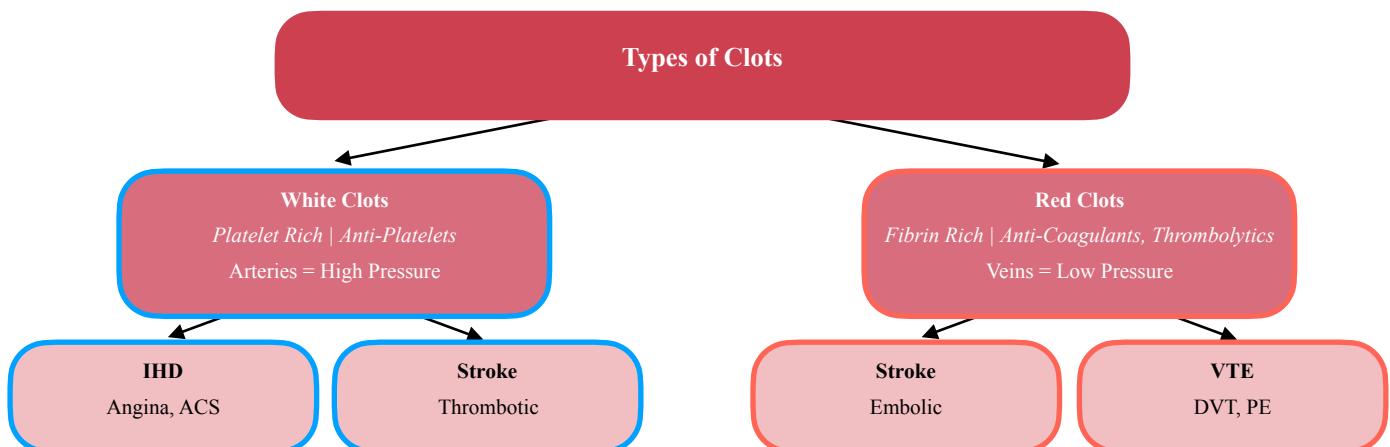
Introduction

The formation of blood clots plays a prominent role in cardiovascular disease as they inhibit the circulation and have deadly outcomes. This section will outline the physiological process undertaken by the clotting cascade that leads to the eventual formation of a clot (a fibrin mesh) as well as the type of clots.

Understanding Clots

Types of Clots

Clots can either be white or red in nature. Red clots are fibrin rich clots that form in veins and are often the result of blood stagnation. White clots, on the other hand, are usually due to lipid plaques and form in arteries. So how do clots form in the first place?

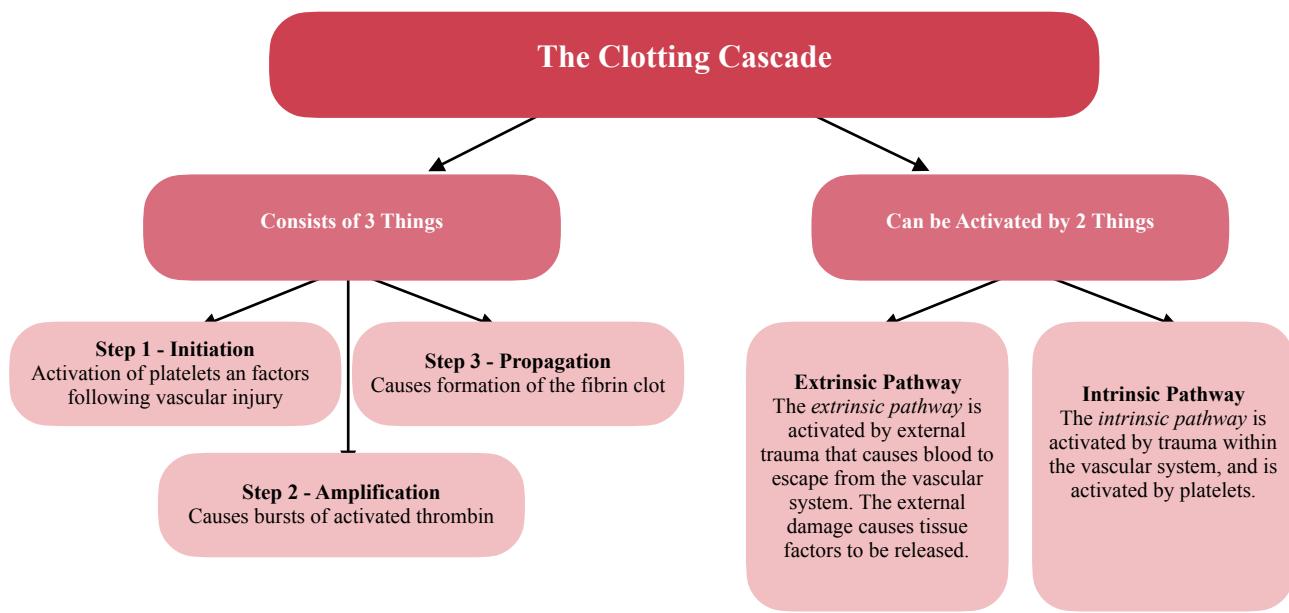


Note

- Clot that begins in deep veins = DVT
- Clot that dislodges from the vein and travels to the pulmonary artery = PE
- Clot that begins in the coronary artery = Angina
- Clot that begins in coronary artery and ruptures = ACS
- Clot that begins in an artery supplying the brain and/or dislodges = Stroke (thrombotic / embolic)

The Clotting Cascade

The clotting cascade is a chemical process that uses pro-coagulant proteins, also known as blood coagulation factors, that interact with each other to change the state of the blood from a liquid to a solid at the site of an injury. This can play a protective role (e.g. ensuring you don't bleed out from a paper cut) or a pathological role (stroke, venous thromboembolisms).



1. Initiation (Activation of platelets + factors X and IX): following a vascular injury

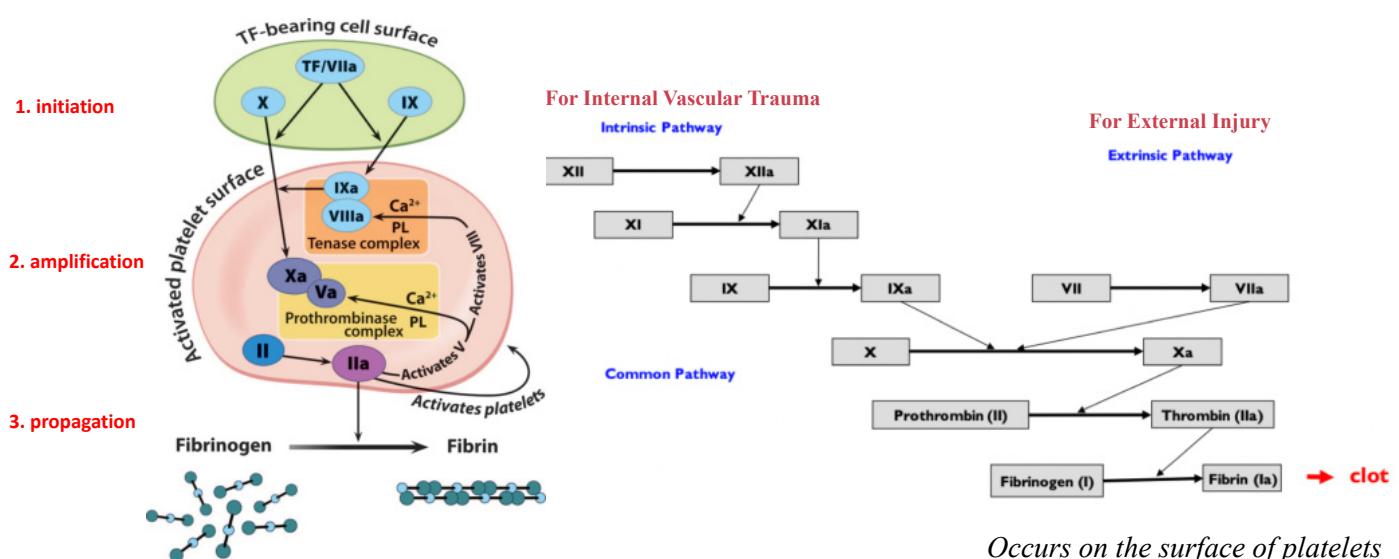
Upon injury, platelets adhere to the vessel. Platelet aggregation provides a site for clotting. However, this alone is not enough to secure the damage in the vessel wall. The vessel itself releases a compound called a tissue factor (TF) which activates factors **X** (10) and **IX** (9).

2. Amplification (of factors Xa/Va causing a burst of activated thrombin)

This is like the activation of a motor. X, IX, Xa, and Va just start the process. Factor X specifically goes on to activate **Xa** and Va, which cause bursts of **thrombin (2a)** to clot the area. **Note that factor Xa bridges the intrinsic and extrinsic pathway.**

3. Propagation (formation of the fibrin clot)

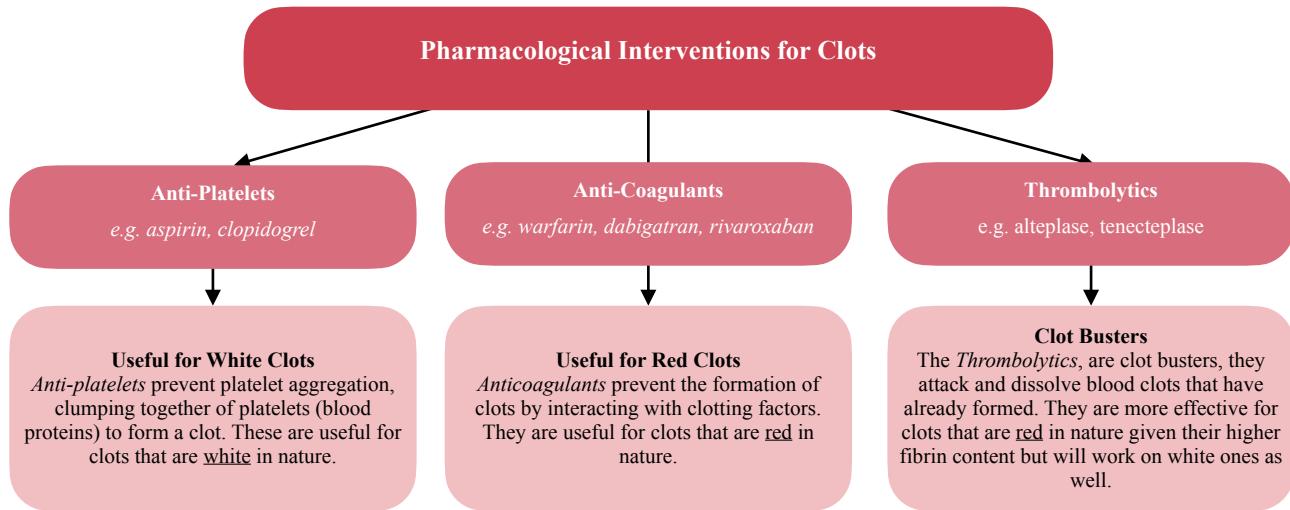
The activation of the factors causes the production of thrombin which causes fibrinogen to convert to fibrin to form a mesh to stabilise the clot.



Summary of Pharmacological Interventions for Clots

Anti-Platelets, Anti-Coagulants & Thrombolytics

There are 3 classes of drugs available to treat and/or prevent clots - please find an overall summary below:



CHOICE OF ANTI-PLATELET, ANTI-COAGULANT & THROMBOLYTIC THERAPY							
	Stroke			ACS		VTE	
	Short Term	Long Term	Stroke Prevention for AFib	Short Term	Long Term	Short Term	Long Term
Antiplatelets	If non-cardioembolic or TIA (24h post alteplase)	-	-	Aspirin or clopidogrel	Aspirin PLUS clopidogrel or ticagrelor (6-12 months)	-	✓
Anticoagulants	If cardioembolic or TIA	✓	-	Heparins	-	✓	-
Thrombolytic	(More effective in red clots)	-	-	✓	-	If haemodynamically unstable PE	-

ANTI-PLATELETS				
Drug	Mechanism of Action		Side Effects	
[PRESCRIPTION] <i>NSAID</i> Aspirin	Aspirin inhibits COX1 which decreases TxA2 which decreases platelet activation and aggregation. For anti-platelet effects, the dose is quite low compared to the dose required for an analgesic effect.		Interaction with warfarin (bleeding). Peptic Ulcers (give with omeprazole to prevent this in long term use)	
THROMBOLYTICS				
Drug	Mechanism of Action		Side Effects	
[PRESCRIPTION] <i>Anti-Platelet</i> Clopidogrel	<p>A P2Y12 antagonist, is metabolised to an active derivative that irreversibly inhibits ADP binding to the P2Y12 receptor on platelets. This prevents subsequent activation of the glycoprotein (GPIIb/IIa) receptor complex necessary for fibrinogen-platelet binding, reducing platelet activation and aggregation for the life of the platelet, preventing thrombus formation</p> <p><i>Note:</i> The recommendation generally with anti-platelets is to use two for a period of 6-12 months (usually Aspirin +/- Clopidogrel (Dual Anti-Platelets Therapy) after which only aspirin should be used.</p>		Dyspepsia, abdominal pain, diarrhoea, bleeding disorders	
[PRESCRIPTION] <i>Fibrinolytic/Thrombolytic</i> Alteplase (Actilyse)	<p>Short Term Acute Treatment More effective for fibrin-rich red clots</p> <p>Alteplase is a fibrinolytic (rT-PA - clot buster). Fibrinolytic drugs binds to fibrin in the thrombus, then converts entrapped plasminogen to plasmin. Plasmin degrades fibrin which causes thrombolysis. It is formulated as an injection for immediate effect.</p>		Bleeding, reperfusion arrhythmias and recurrent ischaemia and angina after MI. Strict eligibility criteria exists to prevent this drug from being given in haemorrhagic strokes.	
ANTI-COAGULANTS				
Class	Drug	Mechanism of Action	Monitoring	Antidote
Vitamin K Antagonist	Warfarin Coumadin, Maveran	<p>Target: Vitamin K Epoxide Reductase</p> <p>Effect: Reduced Thrombin (IIa)</p> <p>Inhibits Vitamin K epoxide reductase and thus reduces the production of Vitamin K, a co-factor necessary in the formation of clotting factors ↓ (2, 7, 9, 10) in the liver.</p> <p><i>Note:</i> S Warfarin Enantiomer is 3-5 times more potent than R Warfarin.</p>	<p>INR Normal = 1 Target = 2-3</p> <ul style="list-style-type: none"> Measures time taken for blood to clot. ↑INR = ↑ Time Although the half life of warfarin is short (~24 hours), the course of INR change is determined by clotting factor turnover, not warfarin plasma concentrations. Since half life of factor 2a (thrombin) is 60h, the effect of clotting takes 10 days to reach steady state (stable INR) Measure every 2 - 3 days upon initiation Measure every 2-4-6 weeks once stable See next page for corrective actions based on INR results 	<p>Vitamin K</p> <p><i>Low INR: Clotting → Stroke, DVT, PE</i></p> <ul style="list-style-type: none"> Painful and constant swelling or redness in feet/lower legs/arms, blurred vision, numbness of face/hands/feet, dizziness, difficulty breathing, chest pain, weakness, sudden confusion <p><i>High INR: Bleeding, bruising</i></p> <ul style="list-style-type: none"> Pale, tired, weak, SOB, prolonged bleeding from gums/cuts/nose, blood in stools (black, tarry), blood urine, usually heavy periods, coughing up blood or vomit (coffee grounds)
	Unfractionated Heparin (UFH) <i>Given IV or SC</i> Heparin Sodium	<p>Target: Antithrombin (ATIII)</p> <p>Effect: Activate AT and inhibit IIa and Xa</p> <p>ATIII is a natural endogenous anti-coagulant. UFHs and LMWHs enhances its binding to activated clotting factors (IIa and Xa) i.e. removes it from the clotting process</p>	<p>aPTT Normal = 24 - 40 sec Target = 1.5 - 2.5 x the control value</p> <ul style="list-style-type: none"> Monitoring Required Measures the time taken to clot in a test tube 	Protamine sulphate

Heparins	Low Molecular Weight Heparin (LMWH) Given SC Enoxaparin, fondaparinux	The primary difference between the two heparins is their relative inhibition of the two factors. UFH: Xa = IIa (Thrombin) LMWH: Xa >> IIa (Thrombin)	Anti-Xa assay Target = 0.5 - 1 IU/ml • Not Routinely Required • Not Widely Available • Not required as more predictable than UFH in terms of bioavailability and elimination.	Protamine sulphate (partial reversion)
NOACs	Dabigatran	Target: Thrombin (IIa) Effect: Reduce IIa Dabigatran etexilate is a prodrug which is converted to dabigatran that competitively and reversibly inhibit free and clot bound thrombin (IIa)	Anti-IIa Assay • Not Routinely Required	Idarucizumab
	Rivaroxaban	Target: Factor Xa Effect: Reduce Xa Competitive and reversible inhibition of free and clot bound Xa	Anti-Xa assay Target = 0.5 - 1 IU/ml • Not Routinely Required	Andexanet alpha

COMPARISON OF ANTI-COAGULANTS

	Warfarin	UFH	LMWH	Dabigatran	Rivaroxaban
Monitoring	Required (INR)	Required (aPTT)	Not Required (anti Xa)	Not Required (anti IIa and anti Xa)	
Onset of Action	Much slower onset of action (but makes it forgiving)		Immediate		Faster Onset of Action But makes it less forgiving than Warfarin. Does not require heparinisation (bridging period)
Maintenance Dose	Unknown Maintenance Dose - Guided by INR		Average Maintenance Dose Known		Average Maintenance Dose Known
Bioavailability	Really Good Oral Bioavailability	SC or IV	SC	Low Oral Bioavailability	Good Oral Bioavailability
Reversible Effect	Antidote Available (Vitamin K)	LMWH more predictable than UFH in terms of bioavailability and elimination. Protamine Sulphate.		Effect cannot be readily reversed Expensive Antidote	

MOCK CPAMS Warfarin Nomogram

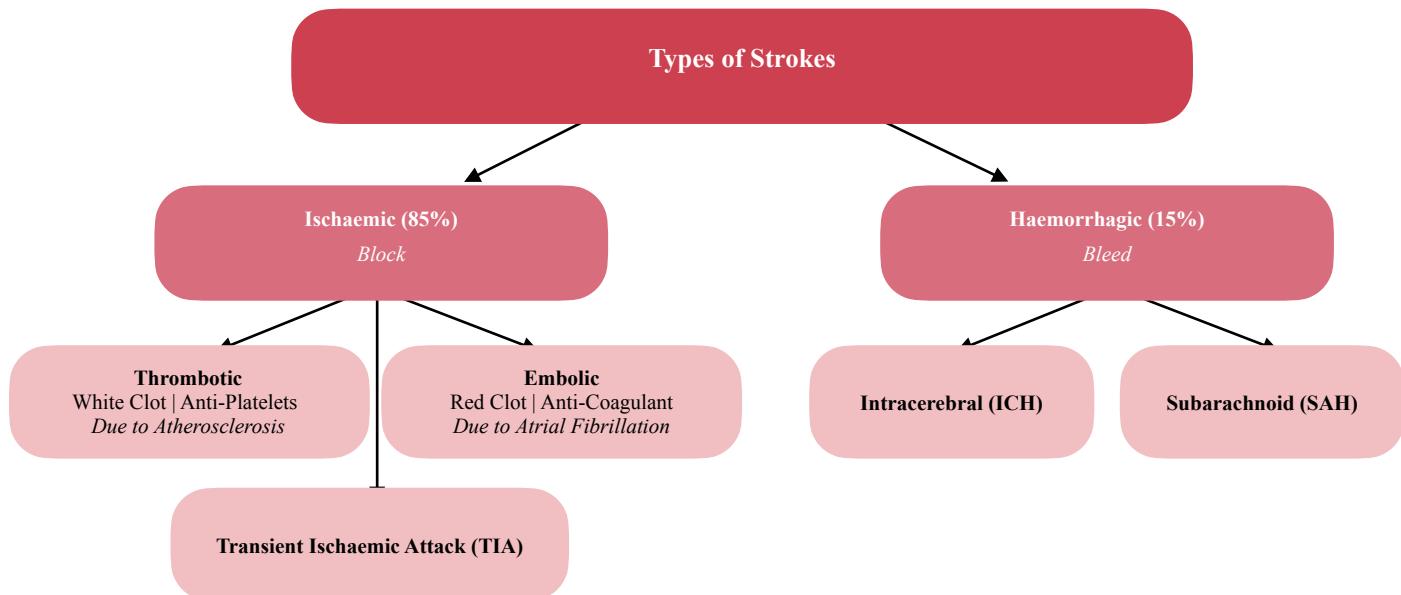
Target INR 2 - 3	Action
< 1.5	<ul style="list-style-type: none"> INR Online software will send a review message to the prescriber. Consult with the prescriber about next steps. <ul style="list-style-type: none"> Give one extra dose. Increase weekly dose by 10 – 20%. Increase monitoring frequency. Tell patient it has been sent for prescriber review.
1.5 – 1.9	<ul style="list-style-type: none"> Increase weekly dose by 5 – 10%. Increase monitoring frequency.
2 – 3	No change
3.1 – 3.5	<ul style="list-style-type: none"> Decrease weekly dose by 5 – 10%. Increase monitoring frequency.
3.6 – 3.9	<ul style="list-style-type: none"> Hold one dose. Decrease weekly dose by 10 – 20%. Increase monitoring frequency.
4 – 4.5	<ul style="list-style-type: none"> INR Online software will send a review message to the prescriber. Consult with the prescriber about next steps. <ul style="list-style-type: none"> Hold one dose. Decrease weekly dose by 10 – 20%. Increase monitoring frequency. Tell patient it has been sent for prescriber review.
4.6 – 4.9	<ul style="list-style-type: none"> INR Online software will send a review message to the prescriber. Consult with the prescriber about next steps. <ul style="list-style-type: none"> Hold one dose. Decrease weekly dose by 10 – 20%. Repeat INR the following day. Tell patient it has been sent for prescriber review.
5 – 9	<ul style="list-style-type: none"> Stop warfarin INR Online software will send a review message to the prescriber. Speak to the prescriber about next steps. <ul style="list-style-type: none"> Test INR daily until it has returned to the therapeutic range Restart warfarin with a reduced dose when INR < 5 Give vitamin K 1.0 – 2.5 mg, orally if INR fails to reduce, or if there is high risk of serious bleeding Tell patient it has been sent for prescriber review.
> 9	<ul style="list-style-type: none"> Urgent evaluation. Contact prescriber.

Arterial & Venous Clot-Related Conditions

Stroke

Description

A stroke is an abrupt onset of a focal neurological deficit secondary to a vascular event, lasting more than 24 hours. In simple layman terms, a stroke is the damage that occurs to the brain from the interruption of its blood supply, leading to neuron damage and death —which causes the symptoms we observe. There are 2 types:



1. [Block/Occlusive]: Ischaemic Stroke (85% prevalence | 25% mortality)

An ischaemic stroke occurs when a blood clot blocks an artery (or rarely a vein) in the brain. The clot usually forms in a small blood vessel inside the brain that has become narrowed through high blood pressure (HTN), high cholesterol (atherosclerosis), diabetes, or smoking. There are three types of Ischaemic Strokes:

1. Thrombotic Strokes
2. Embolic Strokes
3. Transient Ischaemic Attacks

Treatment revolves around replenishing blood supply.

Ischaemic Stroke	Description	Treatment
Thrombotic Stroke (Arteries)	Blood clot (thrombus) forms in an artery that supplies the brain and therefore blocks the flow of blood in the brain. Atherosclerotic plaques rupturing are the culprit, resulting in a platelet-rich white clot	• Anti-platelets
Embolic Stroke (Veins)	A clot or fatty plaque forms somewhere else (e.g. neck —carotid arteries, heart —AF) which breaks off (embolism) and travels to the brain to block an artery. The resulting blood clot is a fibrin-rich red clot .	• Anti-coagulants

Transient Stroke (Transient Ischaemic Attack, TIA)	<p>Presents in the same way a stroke would but symptoms resolve within 24 hours (usually 5-30 minutes). They may be a warning for a full stroke, therefore they are considered a medical emergency [FAST]. 1 in 12 will have a stroke in a week. Treatment is centred about stroke prevention.</p>	<ul style="list-style-type: none"> • Anti-coagulants • Anti-platelets • Lipid treatment • Blood pressure treatment
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1. [Bleed]: Hemorrhagic Strokes (15% prevalence | 50% mortality)

Haemorrhagic strokes occur due to a break in the blood vessel resulting in a brain aneurysm (bleeding which compresses the brain). Treatment involves control of bleeding, seizures, blood pressure, intracranial pressure.

Haemorrhagic Stroke	Description	Treatment
Intracerebral (ICH)	<p>Arteries or veins rupture due to abnormal trauma or intracranial pressure. Be careful of bleeds caused by anti-coagulants.</p>	<ul style="list-style-type: none"> • Routine surgical evaluation is not recommended.
Subarachnoid (SAH)	<p>Usually a swollen blood vessel bursts (aneurysm) and leads to bleeding into the space surrounding the brain.</p>	<ul style="list-style-type: none"> • N/A

Signs & Symptoms

A stroke is always a medical emergency. **Think FAST**.

- **Face drooping:** sudden dropping, weakness and/or numbness of face/arm/leg on one side
- **Arm weakness:** sudden weakness of the arm or leg, dizziness, loss of balance, movement control failure
- **Speech difficulty:** sudden difficulty speaking (dysarthria) or understanding (aphasia)
- **Take action:** call 111
- **Other:** Blurred vision in one or both eyes, headaches (more in hemorrhagic strokes)

Complications

The longer the time taken to remove the blockage, the longer the brain is deprived of oxygen, therefore the more damage. Within **4.5 hours**, we have irreversible cell death (neuron loss equivalent to 3.6 years of ageing). This is particularly important as the complications of stroke can be devastating:

- **Mortality:** Permanent loss of function (stroke on the left side of the brain affects the right side of the body)
- **Long term effects:** impaired vision or speech, severe weakness (hemiparesis) or paralysis (hemiplegia) of limbs, swallowing difficulties (dysphagia), memory loss, depression.

Risk Factors

1. Non-Modifiable:
 - *Age* (usually >65y), family history, personal history (stroke, TIA), female (?hormonal), Māori/Pacific
2. Modifiable:
 - *Medical Conditions:* HTN, hyperlipidaemia, AF, IHD, HF, diabetes
 - *Other:* Medicines, stress, physical inactivity, alcohol, obesity, smoking, migraines

Diagnosis

1. Clinical assessment
2. Blood glucose (hyperglycaemia is a symptom of severe stroke in the absence of T2DM)

3. Platelets and Coagulation Screen (PT/INR/aPTT)
4. **Head CT** to rule out haemorrhage
5. **Head MRI** to show area and extent of ischaemia
6. ECG (especially of risk of AF)



Head CT & MRI

It is often difficult to remember all the different brain imaging techniques that exist and what they each do - an easy way to remember is to know CT and MRI tells us simply where and what kind of stroke.

Goal of Treatment

Every patient should receive timely, person-centred, evidence-based and culturally responsive stroke rehabilitation that will help patient achieve optimal recovery. We want:

- Prevention of stroke (HTN, AF)
- Prompt recognition and treatment (the larger the clot, the greater the damage)
- Brain recovery and rehabilitation
- Secondary prevention of stroke (HTN, AF)
- Have specialised stroke unit cares.

Prevention

If caused by Afib: rate/rhythm control

Non-Pharmacological Treatment

Lifestyle

- Nutritional advice (diet with fruit, vegetables, grains, low fat dairy, fish, low salt, poultry)
- Reduce foods with high glycemic index if at risk of diabetes, reduce salt if BP is elevated.
- Regular physical activity, weight loss.
- Smoking cessation
- Alcohol consumption moderation

Rehabilitation

- Physiotherapy
- Speech Therapy
- Occupational Therapy (adapting the home to their current condition)

Pharmacological Treatment for Ischaemic Stroke

[NZF - Stroke Management & Treatment Guidelines](#)

[NZF - TIA, Ischaemia, Haemorrhagic Stroke Management & Treatment Guidelines](#)

Treatment we will cover will focus on solely on ischaemic strokes. It is important to note while all three types of ischaemic strokes share the same short-term management, they differ in the long-term.

Indication	Treatment Goal	Short Term Treatment (4.5 h - 24h)	Long Term Treatment (3m - 6m)
Ischaemic Stroke	<ul style="list-style-type: none"> • Revascularisation • Control BP • Clot Management • Prevention 	Revascularisation <ol style="list-style-type: none"> 1. Fibrinolytic/Thrombolytic (alteplase) 2. If not qualified for alteplase & exclude haemorrhagic: dual antiplatelet therapy for 3 weeks (within 24h of stroke) 3. Surgery (Thrombectomy) BP control <ol style="list-style-type: none"> 4. IV DHP-CCB if BP > 220/120mmHg Clot Management <ol style="list-style-type: none"> 5. Anti-platelets (Allow 24h post alteplase) 	<i>Non-cardioembolic (embolus not from the heart):</i> <ol style="list-style-type: none"> 1. Anti-platelets: consider dual therapy, then reduce to single agent thereafter 2. Moderate/high intensity statin 3. BP control: ACEI, ARB, thiazide, CCB <i>Cardioembolic (embolus from the heart): e.g. AFib</i> <ol style="list-style-type: none"> 1. Anticoagulants
Transient Ischaemic Attack	<ul style="list-style-type: none"> • Prevent ischaemic stroke 		<i>TIA: (brief blockage, no permanent damage)</i> <ol style="list-style-type: none"> 1. Anti-platelets: 3 weeks dual therapy (aspirin + clopidogrel), then aspirin only thereafter 2. Anticoagulants 3. Statin (regardless of HLD) 4. BP control: ACEI, ARB, thiazide, CCB

Eligibility for Thrombolysis (Alteplase Therapy)

Alteplase is a fibrinolytic/thrombolytic used in reperfusion therapy following occlusive events - it is however more effective for **red clots**. As ischaemic strokes can be caused by either white (thrombotic) or red clots (embolic) - it is therefore possible that alteplase therapy will be less successful in thrombotic strokes. This is because red clots are richer in fibrin than white clots. It is important to note that while alteplase can be given for ischaemia strokes, they cannot be given in hemorrhagic strokes as this will cause bleeding. Therefore patients need to meet a strict inclusion criteria in order to receive alteplase therapy.

Inclusion criteria:

- Age 18 – 85 years
- Clinical diagnosis of ischaemic stroke causing measurable neurological deficits
- Clearly defined onset of symptoms within **4.5 hours** of treatment initiation
- Patient able to undergo CT before alteplase administration

Exclusion criteria (some examples):

- Coma, minor or non-disabling symptoms
- History of stroke in previous 12 weeks
- Myocardial infarction within past 30 days
- Conditions involving risk of bleeding (e.g. recent trauma, ulcerative wounds, hemorrhagic stroke)
- Thrombocytopenia (platelet deficiency that causes risk of bleeding)

Limitations of Thrombolysis

Strict inclusion criteria, short-time window (within 4.5 hours of stroke onset) and embolic strokes means only 15% of patients end up qualifying (being thrombolysed)

	Drug	Mechanism of Action	Side Effects
Revascularisation <i>(Both should be arranged at the same time)</i>	[PRESCRIPTION] Fibrinolytic/ Thrombolytic Alteplase (Actilyse)	Short Term Acute Treatment Alteplase is a fibrinolytic (rT-PA - clot buster). Fibrinolytic drugs binds to fibrin in the thrombus, then converts entrapped plasminogen to plasmin. Plasmin degrades fibrin which causes thrombolysis. It is formulated as an injection for immediate effect. More effective for fibrin-rich red clots	Bleeding, reperfusion arrhythmias and recurrent ischaemia and angina after MI. Strict eligibility criteria exists to prevent this drug from being given in haemorrhagic strokes.
	[REFERAL] Surgery Thrombectomy	Mechanically re-perfuse the brain or to repair a damaged vessel.	
Anti-Coagulants	[PRESCRIPTION] Anti-Coagulant Warfarin (Marevan, Coumadin)	Used for long term treatment of stroke if cardioembolic. Coumarin anticoagulants inhibit vitamin K epoxide reductase used for producing clotting factors. Need to monitor INR and adjust warfarin dosage (CPAMS service). It takes 10 days to reach a stable INR (steady state) Interactions: amiodarone, fluconazole, quinolones, macrolides, azoles, phenytoin, rifampicin	Haemorrhage, N/V/D, jaundice, hepatic dysfunction Vitamin K can also be used as an antidote to warfarin overdose
	[PRESCRIPTION] NOAC Anti-Coagulant Dabigatran (Pradaxa)	Used for long term treatment of stroke if cardioembolic. Dabigatran, given orally as the product dabigatran etexilate, is a direct thrombin inhibitor. It prevents thrombin-induced platelet aggregation and thrombus development. Regular dosing without the need for monitoring unlike warfarin	N/V/D, dyspepsia, abdominal pain, anaemia
	[PRESCRIPTION] NOAC Anti-Coagulant Rivaroxaban (Xarelto)	Used for long term treatment of stroke if cardioembolic. Rivaroxaban is a direct inhibitor of activated factor X (Xa) that interrupts the coagulation cascade and inhibits both thrombin formation and thrombus development.	N/V/D, dyspepsia, abdominal pain, anaemia
Anti-Platelets	[PRESCRIPTION] NSAID Aspirin	Acute Tx 24h post alteplase + long term in non-cardioembolic. Aspirin inhibits COX1 which decreases TXA2 which decreases platelet activation and aggregation. For anti-platelet effects, the dose is quite low compared to the dose required for an analgesic effect.	Interaction with warfarin (bleeding). Peptic Ulcers (give with omeprazole to prevent this in long term use)
	[PRESCRIPTION] Anti-Platelet Clopidogrel	Acute Tx 24h post alteplase + long term in non-cardioembolic. A P2Y12 antagonist, is metabolised to an active derivative that irreversible inhibits ADP binding to the P2Y12 receptor on platelets. This prevents subsequent activation of the glycoprotein (GPIIb/IIa) receptor complex necessary for fibrinogen-platelet binding, reducing platelet activation and aggregation for the life of the platelet, preventing thrombus formation	Dyspepsia, abdominal pain, diarrhoea, bleeding disorders
Cholesterol Lowering Therapy	[PRESCRIPTION] Statins (-statin) Atorvastatin (Lorstat)	Long-Term Cholesterol Lowering Therapy Liver HMG - CoA reductase inhibitors which results in decreased cholesterol production. They decrease risk of CVD events (stroke, CHD, deaths, etc...)	GI disturbances, myalgia (muscle pain), elevated LEs, myopathy, rhabdomyolysis
Blood Pressure Control <i>Avoid β-blockers unless indicated</i>	[PRESCRIPTION] ARB Blockers (-sartan) Candesartan Cilexetil (Candestar)	Use if BP>140/90mmHg Vasodilation + Reduced Blood Volume due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H2O/Na+ uptake)	Headache, nausea, diarrhoea, dizziness, back pain
	[PRESCRIPTION] ACE Inhibitors (-pril) Cilazapril (Zapril)	Use if BP>140/90mmHg Vasodilation + Reduced Blood Volume due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H2O/Na+ uptake)	Dry cough (due to bradykinin buildup), hyperkalaemia, dizziness, postural hypotension, GI disturbances (N/V/D, rashes, angioedema, headache).

for a co-existing condition.	[PRESCRIPTION] <i>IV DHP CCB</i> <i>(if BP>220/120mmHg)</i> Amlodipine, felodipine, nifedipine	Use if BP>220/120 mmHg. Vasodilation via blocking the action of calcium on calcium channels which prevents muscle contraction in the heart and arteries and allows their relaxation. This decreases the after load pressure.	Note: be careful of bradycardia risk if combined with BBs. Sinoatrial block, AV block, palpitations, dizziness, hypotension, malaise, asthenia, headaches, hot flushes, GI disturbances, oedema (notably of ankles).
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Monitor

- Blood glucose for first 72 hours following ischaemic stroke regardless of diabetic status

Ischaemic Heart Disease (IHD)

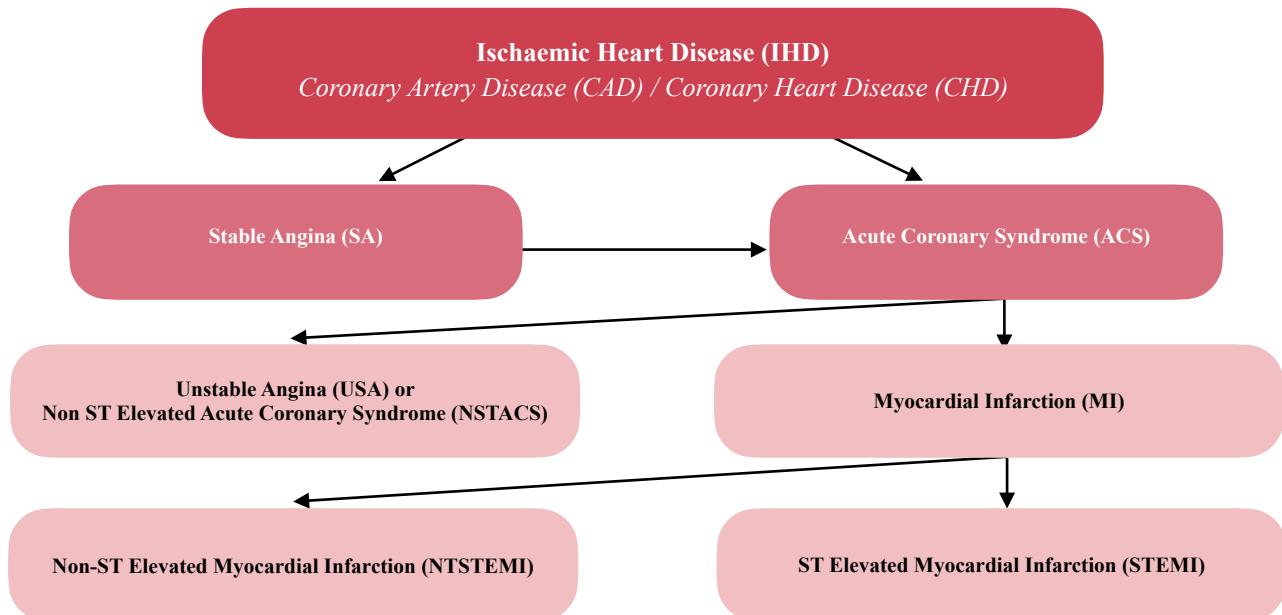
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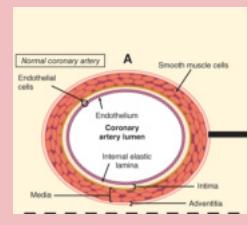
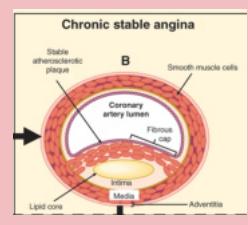
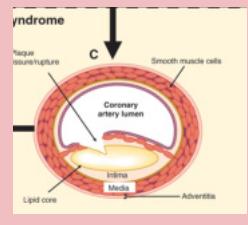
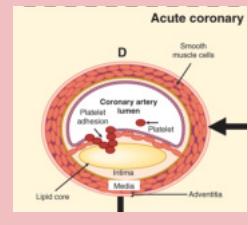
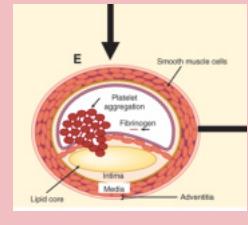
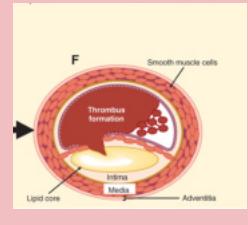
Ischaemic Heart Disease (IHD), also known as Coronary Heart Disease (CAD) or Coronary Artery Disease (CHD), is defined as the decreased supply of oxygenated blood to the heart muscle, resulting in an imbalance between myocardial oxygen supply and oxygen demand.

Pathophysiology

IHD is caused by the stenosis (narrowing) in one or more of the major coronary arteries, which are arteries that specialise in the supply of blood to the heart. As we've seen, atherosclerotic plaques are usually to blame.

The blockage and ensuing cardiac ischaemia caused by IHD can occur at different extents. Therefore, IHD is categorised into two types: Stable Angina (SA) and Acute Coronary Syndrome (ACS). The urgency of the condition (SA vs ACS), and the severity of ACS (NSTEMI vs STEMI) can be further classified.



Normal		
Panel A		<p>Panel A depicts the cross-section of a normal coronary artery.</p>
Chronic Stable Angina		
Panel B		<p>Panel B depicts the cross-section of a coronary artery with a stable atherosclerotic plaque. Note that the lipid core of the plaque is relatively small in size and the fibrous cap is made up of several layers of smooth muscle cells. As the arteries grow narrower due to the plaque, the person can experience pain or discomfort. This is called angina. Angina is particularly likely to occur during exercise as this is when a discrepancy between myocardial oxygen demand and supply is often created.</p>
Acute Coronary Syndrome (ACS)		
Panel C		<p>When the plaque that causes the blockage of blood flow becomes unstable - it ruptures, aggregation occurs and this is known as Acute Coronary Syndrome.</p> <p>Panel C depicts an unstable atherosclerotic plaque with a larger lipid core, and a thin fibrous cap composed of a single layer of smooth muscle cells with a fissure or rupture.</p>
Panel D		<p>Panel D depicts platelet adhesion in response to the fissured plaque - their purpose is to block the plug, which although is a natural response to injury, it becomes pathological here.</p>
Panel E		<p>Panel E depicts that platelet activation may ensue, leading to platelet aggregation as fibrinogen binds platelets to one another to form a mesh-like occlusion in the coronary lumen - obstructing it even more.</p>
Panel F		<p>Panel F - At this stage, patients may experience symptoms of acute coronary syndrome. If endogenous anticoagulant proteins fail to halt this process, platelet aggregation continues and fibrinogen is converted to fibrin, resulting in an occlusive thrombus.</p> <p>When the blockage causes a complete stop of blood flow to a part of the heart due to thrombus formation, we call that a heart attack (myocardial infarction). This can progress to heart failure.</p>

	Chronic Stable Angina (SA) 50% Prevalence	Acute Coronary Syndrome (ACS) USA, NSTEMI, STEM 50% Prevalence
Patho physiology Summary	<p>Ischaemia The reduced blood flow to the heart (ischaemia) caused by the thick obstructive atherosclerotic lesions in the coronary arteries creates a momentary chest pain or discomfort that is known as angina.</p> <p>Vasospasm (at the site of atherosclerotic lesions) may further constrict blood flow, contribute to angina, and precipitate ACS.</p>	<p>Thrombus Formation The rupture of the thin atherosclerotic plaque and subsequent thrombus (clot) formation causes a sudden blockage of blood to the heart.</p> <p><i>Unstable Angina (USA):</i> Chest pain that often indicates the beginning of a heart attack.</p> <p><i>Myocardial Infarction (MI):</i> The eventual aggregation of platelets and the formation of the thrombus as a response to the plaque rupture causes a complete stop of blood flow to a part of the heart. This can eventually progress to heart failure. MI can be subdivided into two different categories:</p> <ul style="list-style-type: none"> • Non-ST Elevated Myocardial Infarction (NSTEMI) • ST-Elevated Myocardial Infarction (STEMI) — more ischaemia extent than NSTEMI
Signs & Symptoms	<ul style="list-style-type: none"> • It usually occurs during exercise as this is most likely to create the imbalance between myocardial oxygen supply and demand. • Generally no acute distress • Pain that lasts a few minutes (sensation of pressure, heaviness, tightness, or squeezing in the anterior chest area), often provoked by exertion (emotional stress, walking, exercise) and relieved by sublingual GTN or rest. May radiate to the neck, jaw, shoulder, back or arm • Dyspnoea, nausea, vomiting or diaphoresis 	<ul style="list-style-type: none"> • Severe substernal angina that lasts at least 20 minutes, often occurring at rest. May radiate to the shoulder, down the left arm and to the back of the jaw • Dyspnoea, N/V, diaphoresis, arrhythmia's, tachycardia, bradycardia, heart block
Short Term Goal	<ul style="list-style-type: none"> • Alleviate acute symptoms (e.g. chest pain) and prevent recurrent symptoms. • Prevention progression of the disease (e.g. ACS) • Reduce IHD complications (e.g. fibrous cap bursting) • Avoid or minimise adverse treatment effects 	<ul style="list-style-type: none"> • Early restoration of blood flow to the artery or prevention of complete occlusion • Prevention of death and other MI complications • Prevention of coronary artery re-occlusion • Relief of ischaemic chest discomfort and • Resolution of ST-segment and T-wave changes on the ECG
Long Term Goal		<ul style="list-style-type: none"> • Control CV risk factors • Prevention of additional CV events, indulging re-infarction, stroke, HF • Improvement in quality of life.
Diagnosis	<ul style="list-style-type: none"> • Physical clinical picture and History • ECG & Stress Testing (ECG with treadmill) • Coronary Angiogram 	<ul style="list-style-type: none"> • ECG: ST-Segment Elevation (STEMI), ST-segment depression or T-Wave Inversion (NSTEMI) • Increase in plasma cardiac enzymes (e.g. troponin) • Thrombus visualised during angiography

Complications: arrhythmia, HF

Risk Factors

1. **Modifiable:** Cigarette smoking, physical inactivity, low daily fruit and vegetable consumption, alcohol overconsumption, dyslipidaemia, T2DM, HTN, obesity ($BMI > 30$)
2. **Non-Modifiable:** Age (≥ 45 for men, ≥ 55 for women), men and post-menopausal women, family history of premature CVD (< 55 for male relatives, < 65 for female relatives)

Non-Pharmacological Treatment

1. Nutritional advice
2. Regular physical activity, weight loss
3. Moderation of alcohol consumption
4. Smoking cessation

Pharmacological Treatment

[BPAC ACS Treatment Guidelines](#), [NZF - Management of NSTEMI](#), [NZF - Management of STEMI](#)

Note: Time is muscle. The more time you delay the treatment, the more cardiac muscle is going to die.

Indication	Treatment Goal	Short Term Treatment	Long Term Treatment
Chronic Stable Angina	<ul style="list-style-type: none"> • Increase myocardial O₂ supply (by dilating the cardiac vasculature) • Decreasing O₂ demand (by decreasing heart rate, myocardial contractility, afterload) — CCB, BB 	Anti-Anginal Therapy <ol style="list-style-type: none"> 1. Nitrate +/- 2. β_1-blocker 3. (Non-DHP) CCB* 	<ol style="list-style-type: none"> 1. Anti-platelets 2. ACEI/ARB 3. β_1-blocker 4. Statins
ACS	<ul style="list-style-type: none"> • Re-vascularisation to establish blood flow • Thrombus removal 	Initial Management <ol style="list-style-type: none"> 1. Nitrate 2. Morphine (IV)/Fentanyl 3. Antiemetic: metoclopramide 4. Oxygen 5. Statin (if STEMI) Revascularisation <p><i>Mechanical:</i></p> <ul style="list-style-type: none"> • PCI (angiography + angioplasty) • CABG (emergency) <p><i>Chemical:</i></p> <ul style="list-style-type: none"> • Fibrinolytics • Anti-platelet: Aspirin or clopidogrel • Anti-coagulants (heparins) 	Secondary Prevention <ol style="list-style-type: none"> 1. Anti-Platelets <ul style="list-style-type: none"> • Dual antiplatelet therapy (6 - 12 months): Aspirin PLUS clopidogrel or ticagrelor • Single antiplatelet therapy: aspirin thereafter 2. β-blocker (unless HF) 3. ACEI/ARB 4. Statin 5. Angina symptoms: Nitrate, CCB



Note

BBs are first line and CCBs are second suitable line. However in the event of combination, use **non-rate limiting (DHP) CCB** to avoid cumulative risk of **bradycardia**.

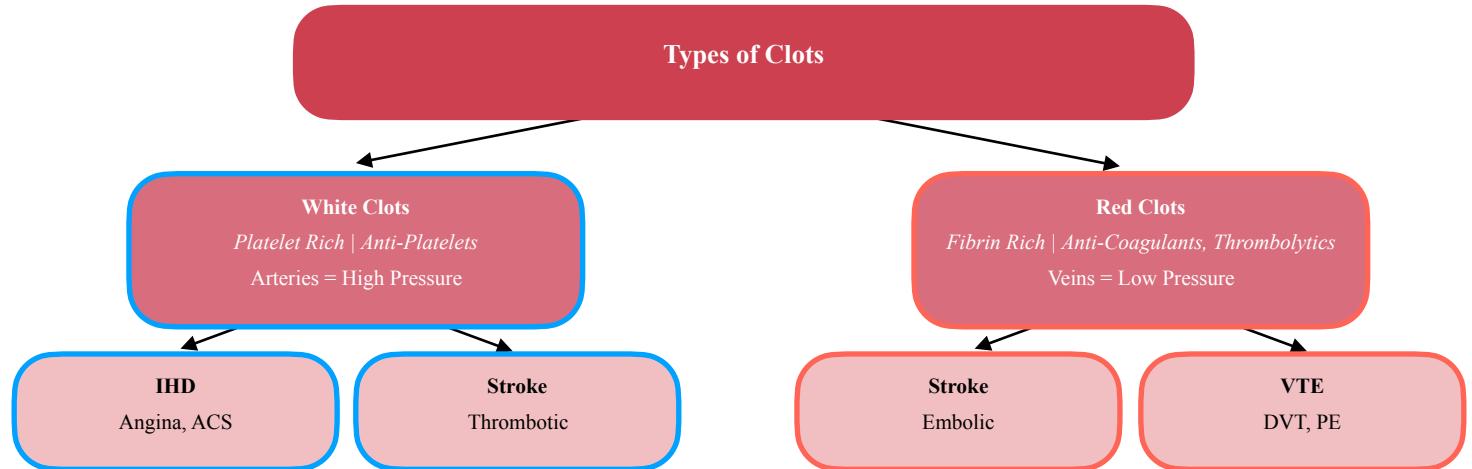
Indication	Drug	Mechanism of Action	Side Effects
Break down thrombus	[PRESCRIPTION] <i>Fibrinolytics/ Thrombolytics</i> Alteplase, Tenecteplase (Metalyse)	Revascularisation in severe IHD Fibrinolytic drugs activate plasminogen to form plasmin. Plasmin degrades fibrin which causes thrombolysis. Formulated as an injection for immediate effect for short term treatment	Bleeding, reperfusion arrhythmias and recurrent ischaemia and angina after MI
Symptom Relief	[PRESCRIPTION] <i>GTN</i> Nitroglycerin (Nitrolingual), Isosorbide mononitrate (ISMN)	Dilate blood vessels and reduce cardiac load (ACS & SA) <i>Normally formulated as a spray. The dose can be taken under the tongue.</i> Nitrates provide a source of nitric oxide (NO) which increases intracellular cGMP resulting in relaxation of smooth muscles and vasodilation. Peripheral vasodilation reduces venous return and lowers left ventricular diastolic volume and pressure (preload), therefore reducing myocardial oxygen demand. They also decrease arterial resistance, reducing after-load and dilate coronary vessels, improving collateral flow to ischaemic regions.	Postural hypotension, tachycardia, throbbing headache, dizziness
	[PRESCRIPTION] <i>Non-DHP CCBs</i> Benzothiazepine (diltiazem)	Dilate blood vessels and reduce cardiac load (ACS & SA) In addition to the DHP mechanisms, Non DHPs additionally slow down the electrical activity of the heart the conduction of heart. Be careful of bradycardia risk if combined with BBs.	Flushing, headache, dizziness, palpitations, flushing, constipation peripheral oedema, bradycardia, grapefruit intolerances.
	[PRESCRIPTION] <i>β Blockers</i> Metoprolol (β_1), Bisoprolol	Dilate blood vessels and reduce cardiac load (ACS & SA) Angina Prevention & Therapy Decrease Contractility, Heart Rate and O ₂ Demand Slow Ventricular Remodelling + Anti-Arrhythmic Always use long acting β-blockers. β-blockers can mask hypoglycaemic symptoms (carvedilol has the least effect)	Bradycardia, Bronchoconstriction in unselective or high dosage, fatigue, hypotension, decrease in libido, bronchoconstriction
	[PRESCRIPTION] <i>ACE Inhibitors (-pril)</i> Cilazapril (Zapril)	Dilate blood vessels and reduce cardiac load (ACS & SA) Angina Prevention + In ACS to prevent LVH due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H ₂ O/Na ⁺ uptake)	Dry cough (due to bradykinin buildup), hyperkalaemia, dizziness, postural hypotension, GI disturbances (N/V/D, rashes, angioedema, headache.
	[PRESCRIPTION] <i>ARB Blockers (-sartan)</i> Candesartan Cilexetil (Candestar)	Angina Prevention due to blocking of angiotensin production (which causes vasoconstriction) and aldosterone (which increases H ₂ O/Na ⁺ uptake)	Headache, nausea, diarrhoea, dizziness, back pain
Stabilise Atherosclerotic Plaques	[PRESCRIPTION] <i>Statins (-statin)</i> Atorvastatin (Lorstat)	Stabilise atherosclerotic plates Angina Prevention Liver HMG - CoA reductase inhibitors which results in decreased cholesterol production. They decrease risk of CVD events (stroke, CHD, deaths)	GI disturbances, myalgia (muscle pain), elevated LEs, myopathy, rhabdomyolysis
Prevent Platelet Aggregation (Anti-Platelets)	[PRESCRIPTION] <i>NSAID</i> Aspirin	Angina Prevention Reduces prostaglandin production by inhibiting COX enzymes. For anti-platelet effects, the dose is quite low compared to the dose required for an analgesic effect.	Interaction with warfarin (bleeding). Peptic Ulcers (give with omeprazole to prevent this in long term use)
	[PRESCRIPTION] <i>Anti-Platelet</i> Clopidogrel	Angina Prevention A P2Y12 antagonist, is metabolised to an active derivative that irreversible inhibits ADP binding to the P2Y12 receptor on platelets. This prevents subsequent activation of the glycoprotein (GPIIb/IIa) receptor complex necessary for fibrinogen-platelet binding, reducing platelet activation and aggregation for the life of the platelet, preventing thrombus formation	Dyspepsia, abdominal pain, diarrhoea, bleeding disorders
Prevention Thrombus Propagation (Anti-Coagulants — Heparins)	[PRESCRIPTION] <i>Unfractionated Heparin</i> Heparin sodium	Angina Prevention UFH increases the inhibitory action of anti-thrombin (AT) on factors Xa and IIa (and to some extent XIIa, XIa, IXa)	Bleeding, heparin-induced thrombocytopenia
	[PRESCRIPTION] <i>LMWH Anti-Coagulant</i> Enoxaparin (Clexane)	Angina Prevention LMWH are anticoagulants that bind to antithrombin II, enhancing the inhibition of factor Xa and to a much lesser extent thrombin (factor IIa). This reduces the amount of fibrin formed, preventing new thrombi or extension of existing thrombus	Bleeding, heparin-induced thrombocytopenia
Pain Relief	[PRESCRIPTION] <i>Opioids</i> Morphine (M-Eslon, Sevredol)		

Venous Thromboembolism (VTE)

Description

Venous thromboembolism describes the formation of a clot in a vein due to blood stagnation or vessel/valve damage. These clots are fibrin rich (red clot). VTE can be further subdivided into two categories:

1. *Deep Vein Thrombosis (DVT)*: A thrombus blocking a deep vein (commonly in the leg, pelvis, abdomen)
2. *Pulmonary Embolism (PE)*: A thrombus that dislodges (embolus) from its original site and travels to through the bloodstream to block a pulmonary artery or one of its branches.



Signs & Symptoms

DVT: Unilateral leg swelling, oedema, pain, warmth, erythema, change of colour in the leg (blue, purple, red)

PE: Cough, chest pain/tightness, SOB, orthopnoea, haemoptysis, palpitations, dizziness, syncope. May be preceded by signs & symptoms of DVT.

Risk Factors (VTE)

1. *Age* (risk doubles with each decade after 50)
2. *History of VTE*
3. *Venous Stasis*: HF, MI, ischaemic stroke, acute infection, major surgery, obesity, varicose veins
4. *Vascular Injury*: Major surgery, trauma
5. *Hypercoagulopathy*: Cancer, factor V Leiden, abnormal clotting factors concentration, pregnancy
6. *Drugs*: Estrogen (COC, HRT), tranexamic acid

Complications: Chronic venous insufficiency (e.g. oedema, cellulitis, venous ulceration)

Diagnosis

Deep Vein Thrombosis (DVT)

- Positive Homans Sign through Physical Examination (calf pain at dorsiflexion of foot)
- Elevated D-dimer (product of fibrin degradation)
- Duplex Ultrasound

Pulmonary Embolism (PE)

- Elevated D-dimer (product of fibrin degradation)
- Ventilation Perfusion Scan (V/Q) or CT scan

Goal of Treatment

- Prevention/prophylaxis and detect VTE early
- Prevention further clots/emboli
- Re-vascularise/re-perfuse
- Prevent recurrent events and prevent/reduce venous complications
- Avoid adverse side effects of treatment (mostly bleeding)

Pharmacological Treatment

Appropriate prophylaxis may be required in some situations.

Indication	Treatment	Antidotes & Adjustments
Immediate Treatment	Haemodynamically unstable PE patients only <i>(massive PE, extremely hypotensive SBP < 90mmHg)</i> <ol style="list-style-type: none"> 1. Fibrinolytics/Thrombolytics: Alteplase 2. Often require resuscitation: IVF, O₂, vasopressors (often hypotensive), Intubation/Ventilation 	N/A
Short-Term Treatment (~5 days)	Anti-coagulants <ol style="list-style-type: none"> 1. Unfractionated Heparin (UFH): Heparin sodium 2. Low Molecular Weight Heparin (LMWH): Enoxaparin 	<i>Adjustment</i> <ul style="list-style-type: none"> • UFH adjusted as per aPTT • LMWH adjusted as per anti-Xa <i>Heparin Antidotes:</i> <ul style="list-style-type: none"> • Protamine sulphate
Long-Term Treatment (3m, 6m, Indefinite)	Anti-coagulants <ol style="list-style-type: none"> 1. Warfarin 2. Dabigatran 3. Rivaroxaban Antiplatelets?	<i>Adjustment</i> <ul style="list-style-type: none"> • Warfarin adjusted as per INR • Dabigatran (IIa) & Rivaroxaban (anti-Xa) but don't need to be monitored <i>Antidotes:</i> <ol style="list-style-type: none"> a) Vitamin K (Warfarin) b) Idarucizumab (Dabigatran) c) Andexanet alfa (Rivaroxaban)

Indication	Drug	Mechanism of Action	Side Effects
Break down thrombus	[PRESCRIPTION] <i>Fibrinolytics/ Thrombolytics</i> Alteplase, Tenecteplase (Metalyse), Reteplase	Revascularisation in severe IHD Fibrinolytic drugs breaks down fibrin stabilised clots by enhancing activation of plasminogen to plasmin (natural way of dissolving clots). Formulated as an injection for immediate effect for short term treatment.	Bleeding, reperfusion arrhythmias and recurrent ischaemia and angina after MI
Prevent Platelet Aggregation	[PRESCRIPTION] <i>NSAID</i> Aspirin	Angina Prevention Aspirin inhibits COX1 which decreases TxA2 which decreases platelet activation and aggregation. For anti-platelet effects, the dose is quite low compared to the dose required for an analgesic effect.	Interaction with warfarin (bleeding). Peptic Ulcers (give with omeprazole to prevent this in long term use)
	[PRESCRIPTION] <i>Anti-Platelet</i> Clopidogrel	Angina Prevention A P2Y12 antagonist which irreversibly inhibits ADP binding to the P2Y12 receptor on platelets. This prevents subsequent activation of the glycoprotein (GPIIb/IIa) receptor complex necessary for fibrinogen-platelet binding, reducing platelet activation and aggregation for the life of the platelet, preventing thrombus formation	Dyspepsia, abdominal pain, diarrhoea, bleeding disorders
Prevention Thrombus Formation & Propagation (Anti-Coagulants)	[PRESCRIPTION] <i>Anti-Coagulant</i> Warfarin (Marevan, Coumarin)	Angina Prevention Coumarin anticoagulants inhibit vitamin K epoxide reductase used for producing clotting factors. Need to monitor INR and adjust warfarin dosage (CPAMS service). It takes 10 days to reach a stable INR (steady state) Interactions: amiodarone, fluconazole, quinolones, macrolides, azoles, phenytoin, rifampicin	Haemorrhage, N/V/D, jaundice, hepatic dysfunction Vitamin K can also be used as an antidote to warfarin overdose
	[PRESCRIPTION] <i>NOAC Anti-Coagulant</i> Dabigatran (Pradaxa)	Angina Prevention Dabigatran, given orally as the product dabigatran etexilate, is a direct thrombin (2a) inhibitor. It prevents thrombin-induced platelet aggregation and thrombus development. Regular dosing without the need for monitoring unlike warfarin, competitive and reversible	N/V/D, dyspepsia, abdominal pain, anaemia
	[PRESCRIPTION] <i>NOAC Anti-Coagulant</i> Rivaroxaban (Xarelto)	Angina Prevention Rivaroxaban is a direct inhibitor of activated factor X (Xa) that interrupts the coagulation cascade and inhibits both thrombin formation and thrombus development.	N/V/D, dyspepsia, abdominal pain, anaemia
	[PRESCRIPTION] <i>Unfractionated Heparin</i> Heparin sodium	Angina Prevention UFH increases the inhibitory action of anti-thrombin (AT) on factors Xa and IIa (and to some extent XIIa, XIa, IXa)	Bleeding, heparin-induced thrombocytopenia
	[PRESCRIPTION] <i>LMWH Anti-Coagulant</i> Enoxaparin (Clexane)	Angina Prevention LMWH are anticoagulants that bind to antithrombin II, enhancing the inhibition of factor Xa and to a much lesser extent thrombin (factor IIa). This reduces the amount of fibrin formed, preventing new thrombi or extension of existing thrombus	Bleeding, heparin-induced thrombocytopenia

Heart Failure (HF)

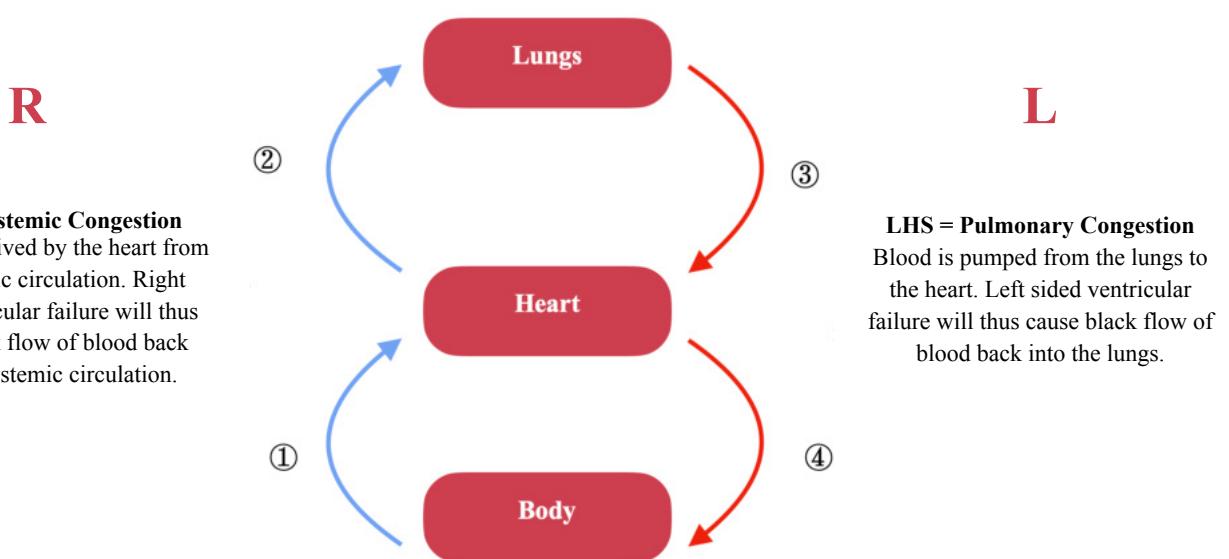
NZF Chronic Heart Failure

Description

Heart failure (HF) is a clinical syndrome caused by structural or functional abnormalities of the heart that impair the ability of ventricles to fill and eject blood, resulting in *reduced cardiac output and stroke volume*. The heart is therefore unable to pump enough blood to meet the metabolic demands of the body.

Three types of heart failure exist - left sided, right sided and congestive. It is important to note that while Left Ventricular Failure (LVF) is more common, both ventricles eventually fail.

Types of Heart Failure	
Left-Sided Heart Failure	<p><i>Systolic Heart Failure — Heart Failure with reduced Ejection Fraction (HFrEF)</i></p> <ul style="list-style-type: none">• EF < 40% and affects $\frac{1}{3}$ of HF patients• The ventricle(s) are stretched and weakened, therefore can't pump blood properly <p><i>Diastolic Heart Failure — Heart Failure with preserved Ejection Fraction (HFpEF) — better prognosis</i></p> <ul style="list-style-type: none">• EF > 50% (CO is still reduced) and affects $\frac{1}{3}$ of HF patients• CO = HR x SV and EF = SV/EDV• EDV is reduced (\downarrow ventricular filling/reduced preload) which gives the illusion of a preserved EF• The ventricle(s) are thick and stiff, therefore can't fill with blood properly between beats
Right -Sided Heart Failure	Often develops from left-sided heart failure
Congestive Heart Failure (Acute Decompensated Heart Failure)	This type of heart failure is very severe. Congestion refers to the leakage of fluids into the lungs, liver, and peripheries (oedema) due to the back flow of blood <ul style="list-style-type: none">• Lung symptoms are more common with left ventricular failure due to the back flow of blood coming from the lungs.• Systemic symptoms are more common with right ventricular failure which leads to the accumulation of fluid in the peripheries.



Pathophysiology

Heart Compensatory Mechanisms

The first result of impaired cardiac function is a decrease in cardiac output ($\downarrow CO$). This leads to the activation of the following compensatory mechanisms by the heart in which the body believes will fix the problem (e.g. activation of the RAAS system to maintain CO via Na^+/H_2O retention). However, these mechanisms paradoxically worsen HF (cardiac damage, pathological remodelling, symptoms).

Example: HF presents with low blood volume in the vessels. Therefore, the RAAS is activated to maintain cardiac output and blood pressure via Na^+/H_2O retention and vasoconstriction. However, this causes fluid retention and increases afterload pressure as the heart has to contract harder to pump blood out.

$CO = HR \times SV$	System	Compensatory Mechanism	Consequences	Drugs
Heart Rate (Pump) <i>SNS Controlled</i> Stimulation of β -AR	SNS	Tachycardia $\uparrow HR \& \uparrow CO$	$\uparrow O_2$ demand + \uparrow Ischaemia \downarrow Diastolic filling time \uparrow Ventricular Arrhythmias β_1 -AR downregulation	β_1 -Blockers
	RAAS & AGTII	Ventricular Hypertrophy & Remodelling $\uparrow CO$	$\uparrow O_2$ demand \uparrow Structural Changes leading to myocyte death \downarrow Filling AND Contraction Force \uparrow Ventricular Arrhythmias	ACEI/ARB Spironolactone
Stroke Volume <i>A function of Preload, Afterload & Contractility</i>	RAAS	Increased Preload Volume Na/H_2O Retention when $\downarrow CO$ leads to \uparrow venous return and $\uparrow SV$	The ventricles fail to fill up and eject, resulting in back flow (\uparrow Oedema & Congestion)	Sacubitril Diuretics (Loop, Spironolactone) ACEI/ARB
	SNS	Increase contractility $\uparrow CO$	$\uparrow O_2$ demand + \uparrow Ischaemia \downarrow Diastolic filling time \uparrow Ventricular Arrhythmias β_1 -AR downregulation	β_1 -blocker Digoxin
	RAAS & SNS	Vasoconstriction (via release of vasopressin) Maintains BP and perfusion when $\downarrow CO$	\uparrow Afterload pressure	ACEI/ARB Sacubitril

Signs & Symptoms

1. Congestion that develops behind failing ventricles due to **backflow** of blood
 - *Lung Congestion:* cough, dyspnoea, orthopnoea and tachypnoea
 - *Systemic Congestion:* peripheral oedema (weight gain), fatigue, JVD elevation
2. Decreased Organ Perfusion
 - \downarrow Renal Output, \uparrow Mental Confusion, \uparrow Cold Extremities
3. Tachycardia
 - Compensatory mechanism of the heart

Risk Factors

Primary HF: IHD (atherosclerotic plaques & MI), chronic HTN

- *Heart problems:* AF, valve defects (RHD), IHD
- *Metabolic syndrome:* HTN, Obesity, T2DM
- *Drugs:* alcohol, amphetamines/anabolic steroids, chemotherapy
- *Medicines:*
 - Negative inotropes: Flecainide, β -blockers, non-DHP CCBs
 - Cytotoxics: Doxorubicin, epirubicin, cyclophosphamide, trastuzumab
 - Na^+ & H_2O retention: NSAIDs (COX-2 inhibitors), glitazones, glucocorticoids, estrogen

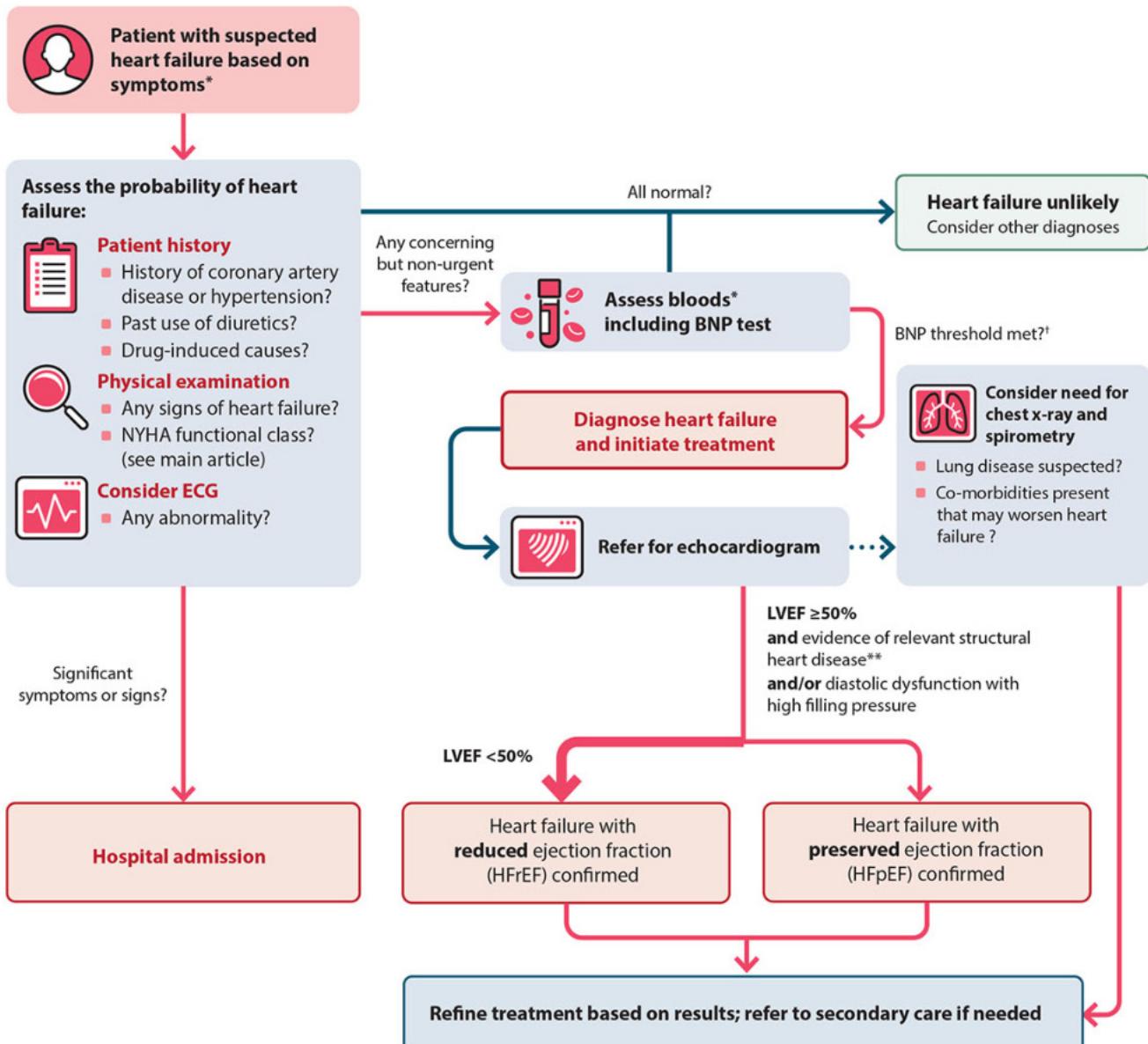
Differential Diagnosis

Heart attacks (MI) are when there is a loss of blood supply to the heart, while heart failure is when the heart is unable to pump blood around the body efficiently.

Diagnosis

New York Heart Association (NYHA) Classification	
Class I	<ul style="list-style-type: none">• No limitations• Ordinary physical activity does not cause undue fatigue, dyspnoea, or palpitations (asymptomatic LV dysfunction)
Class II	<ul style="list-style-type: none">• Slight limitation of physical activity• Ordinary physical activity results in fatigue, palpitation, dyspnoea, or angina pectoris (mild CHF)
Class III	<ul style="list-style-type: none">• Marked limitation of physical activity• Less than ordinary physical activity leads to symptoms (moderate CHF)
Class IV	<ul style="list-style-type: none">• Unable to carry on any physical activity without discomfort• Symptoms of CHF present at rest (severe CHF)

Diagnostic Test	Diagnostic Value
Elevated BNP >100 pg/mL	BNP is a hormone that the ventricles release when the heart cannot pump the way it should.
Elevated NT-BNP > 300 pg/mL	Non-active pro-hormone is released from the same molecule that produces BNP. Both are released in response to changes in pressure inside the heart.
ECG (Heart Rhythm)	Myocardial ischaemia, AF, bradycardia, Left Ventricular Hypertrophy (LVH)
Serum Creatinine (SCr)	SCr is increased due to renal hypoperfusion in which the kidneys are not filtering SCr out. CKD can cause hypervolaemia (fluid overload) as the body thinks it is dehydrated.
Haemoglobin Concentrations	HF can cause anaemia
Chest X-ray (CXR)	Cardiomegaly, pulmonary congestion
Echocardiogram	LV size, valvular function, and EF%



Common blood tests for heart failure:

- BNP/NT-proBNP[†]
- Complete blood count
- Electrolytes and renal function
- Liver function
- Thyroid function
- HbA_{1c} and lipids as part of a CVD risk evaluation

Other blood tests as appropriate:

- Thyroid function
- CRP if infection is suspected
- Serum troponin if acute onset of symptoms or an acute coronary syndrome is possible
- Iron studies (including iron levels, ferritin, transferrin saturation)[†]

Goal of Treatment

- Investigate and manage the cause (IHD, BP, DM)
- Prevent onset of symptoms in stable/compensated HF
- Improve signs and symptoms of the disease
- Slow its progression and prevent/reduce risk of hospitalisation and mortality
- Improve exercise tolerance
- Reduce the incidence of acute exacerbations

Non-Pharmacological Treatment

1. Sodium (< 2g/d) and fluid restriction (< 2L/d)
2. Smoking and alcohol cessation
3. Physical activity
4. Immunisation

Pharmacological Treatment

[BPAC \(Be Quick\) Heart Failure Treatment Guidelines](#)

In HF, drug therapy is aimed at controlling compensatory mechanisms. The following is recommended:

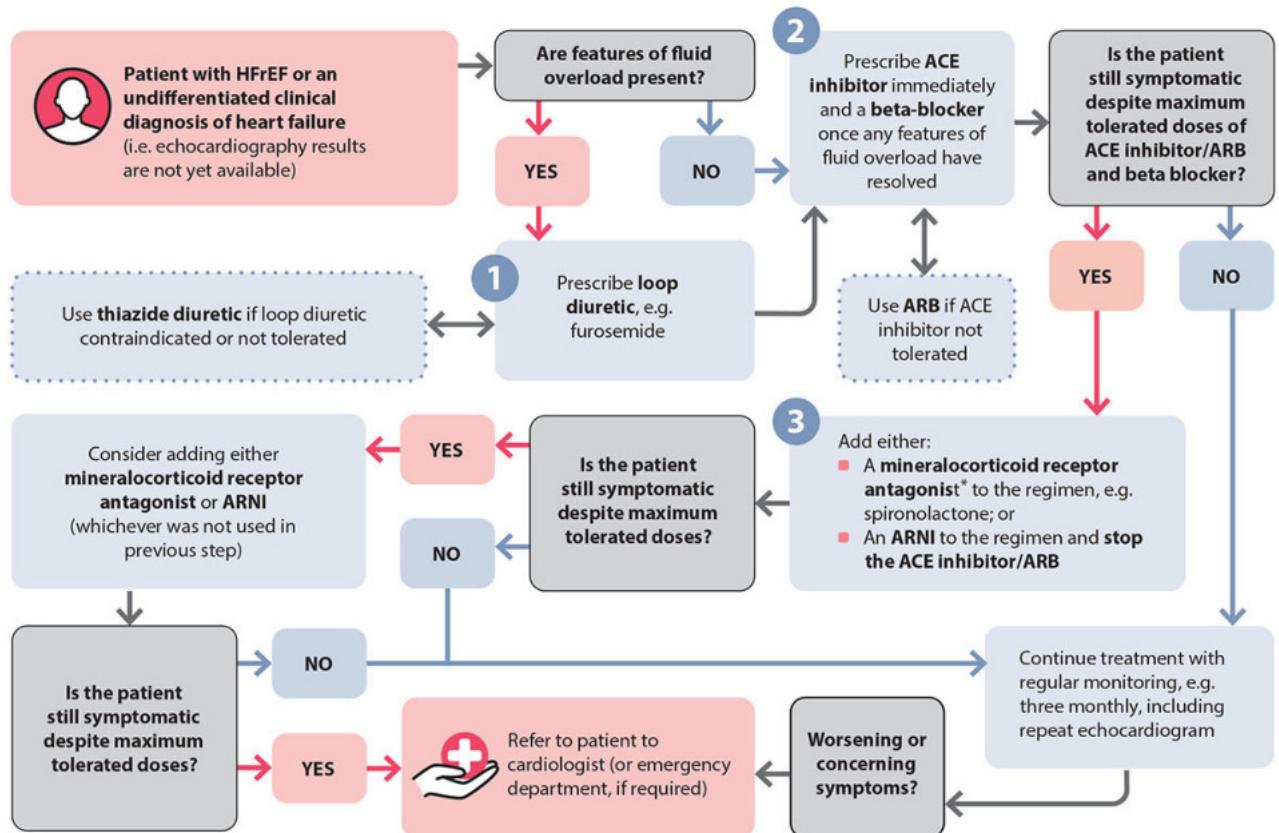
1. *First Line*: Diuretic (loop diuretic is recommended in HF, thiazides are second line if not tolerated)
2. ACEI/ARB (reduce symptoms and prevent ventricular hypertrophy)
3. β -blocker (improve ventricular function)
4. Spironolactone (if the patient remains symptomatic)
5. Digoxin / anticoagulants (as appropriate)

Notes:

- **Avoid** NSAIDs (nephrotoxic)
- **Avoid** non-DHP CCBs in HFrEF due to negative inotropic effect which will impair ventricular function.
- Entresto: Sacubitril inhibits angiotensin II breakdown and is therefore used in combination with valsartan

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Loop Diuretics</i> Furosemide	<p>1) ↓ Oedema & Congestion 2) ↓ Ventricular Hypertrophy/Remodelling</p> <p>Loop diuretics inhibit the activity of the Na-K-2Cl co-transporter predominantly from the ascending limb of the loop of Henle in the renal tubule, promoting excretion of water resulting in increased urinary volume.</p>	<ul style="list-style-type: none"> Due to the decline in diuretic effect with worsening renal function (amount of drug reaching the renal tubule is reduced), large doses of loop diuretics are used in CKD 	GI disturbances, electrolyte disturbances
[PRESCRIPTION] <i>K+ Sparing Diuretics/ Aldosterone Receptor Antagonists (ARA)</i> Spironolactone (<i>Spiractin</i>)	<p>1) ↓ Oedema & Congestion 2) ↓ Ventricular Hypertrophy/Remodelling</p> <p>Spironolactone competitively binds receptors at the aldosterone-dependent Na⁺/K⁺ exchange channels in the distal convoluted renal tubule. This action leads to increased excretion (diuretic and anti-hypertensive effects), but increased K⁺ retention.</p>		
[PRESCRIPTION] <i>ACEIs & ARBs</i> Cilazapril, Captopril, Enalapril... Candesartan, Losartan, Valsartan	<p>1) ↓ Ventricular Hypertrophy/Remodelling 2) Vasodilation (increase renal blood flow) 3) ↓ Oedema & Congestion (↓ RAAS activation)</p> <p>They both cause vasodilation which decrease blood pressure, systemic vascular resistance and increase renal blood flow.</p>	<ul style="list-style-type: none"> Due to low renal perfusion in HF, aggressive use of ACEIs/ARBs can paradoxically cause AKI — start at low doses and titrate upwards. 	Dizziness/Postural Hypotension, Hyperkalaemia, Dry Cough
[PRESCRIPTION] <i>β-Blockers (or DHP-CCB)</i> Metoprolol, Bisoprolol (β ₁) Carvedilol (αβ) Amlodipine, felodipine	<p>1) ↓ Tachycardia 2) Anti-arrhythmic effects 3) ↓ Ventricular Hypertrophy/Remodelling</p> <p>Inhibits the SNS to decrease contractility, HR, O₂ demand</p>	<ul style="list-style-type: none"> Always use long-acting β-blockers — start at low doses and titrate upwards β-blockers can mask hypoglycaemic symptoms (carvedilol has least effect on blood glucose, but more hypotension) 	Bradycardia, Bronchoconstriction in nonselective or high dosage, fatigue, hypotension, decrease in libido
[PRESCRIPTION] <i>Entresto</i> Neprilysin Inhibitor combined with ARB (“ARNI”) (<i>Sacubitril + Valsartan Combination</i>)	<p>1) ↓Oedema & Congestion 2) Vasodilation</p> <p>Neprilysin breaks down natriuretic peptide (e.g. BNP). Sacubitril inhibits neprilysin but increases Angiotensin II, thus the combination with ARB. Increasing circulating NP subsequently promotes natriuresis, diuresis, and vasodilation</p>		N/D, hypotension, dizziness, syncope, cough, fatigue, headache, vertigo, hypoglycaemia, hyperkalaemia (also hypokalaemia)
[PRESCRIPTION] <i>Cardiac Glycoside</i> Digoxin (Lanoxin)	<p>1) ↓Oedema & Congestion 2) ↓Tachycardia</p> <p>Digoxin exerts positive inotropic effects (increases contractility & reduces conductivity within the atrioventricular (AV) nodes) via binding to the Na⁺ and K⁺ pump</p>	<ul style="list-style-type: none"> Very old drug with numerous undesirable side effects (narrow therapeutic range) Useful in AF but β-blockers are better and safer 	N/V/D, arrhythmias, conduction disturbances

Treatment Guidelines



4 Management should also include:

Additional medicines based on patient co-morbidities. For example:

Medicine	Co-morbidity
Digoxin	Atrial fibrillation
Anticoagulants	
Intravenous iron	Anaemia and iron deficiency
SGLT-2 inhibitor	Type 2 diabetes

Non-pharmacological support:

- Exercise, as appropriate
- Reduce sodium intake (<2 – 3 g daily)
- Weight loss
- Adequate fluid intake (1.5 – 2 L daily)
- Reduce alcohol/smoking cessation, if relevant
- Influenza/pneumococcal vaccination

See the main text for treatment and monitoring considerations relating to

- 1 Loop diuretics
- 2 ACE inhibitors/ARBs and beta blockers
- 3 Mineralocorticoid receptor antagonists and ARNIs
- 4 Additional medicines for co-morbidities

* If a patient with heart failure has severe symptoms at presentation, they can potentially be cautiously initiated on an ACE inhibitor, beta blocker and spironolactone (i.e. at the same time) according to clinical judgement. However, a beta blocker should not be used unless the patient is euvoemic, and more frequent initial monitoring would be required. See main text for more further information on treatment requirements associated with each medicine or visit the NZ Formulary (NZF) at nzf.org.nz for specific dosing information.

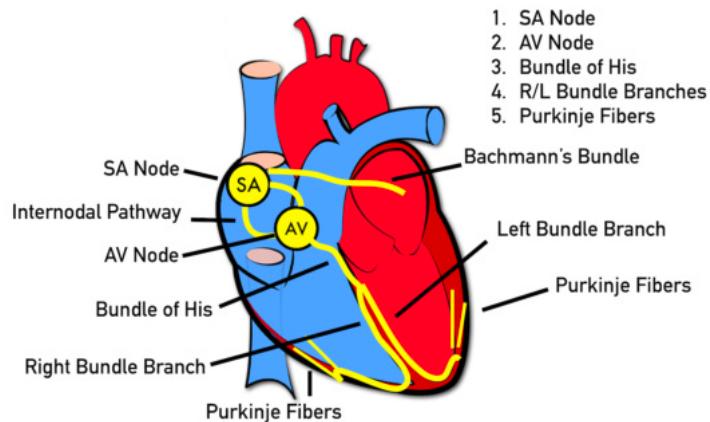
Monitoring

- Daily weight checking. Gain of weight may indicate water retention
- Patient education on diuretic dose and adjustments
- Watch out for dehydration, hypokalaemia, hyperkalaemia (ACEIs, Diuretics), hypotension (postural), hyperglycaemia, hypoglycaemia

ARRYTHMIAS & DYSRHYTHMIAS

The Electrical Activity of the Heart

Before we go into this sub-chapter of the Cardiovascular System, it is important to lay an understanding of the electrical activity of the heart. A very sophisticated process involving pacemaker cells and nodes allows the travel of action potential across the heart to allow the atria and the ventricles to contract (depolarise) ~60 times per minute.

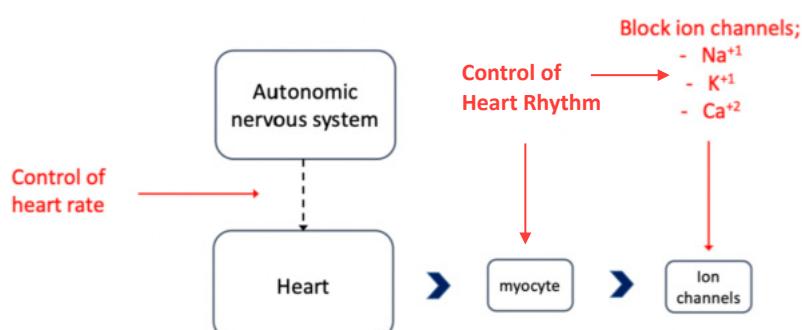


Overview of Arrhythmias

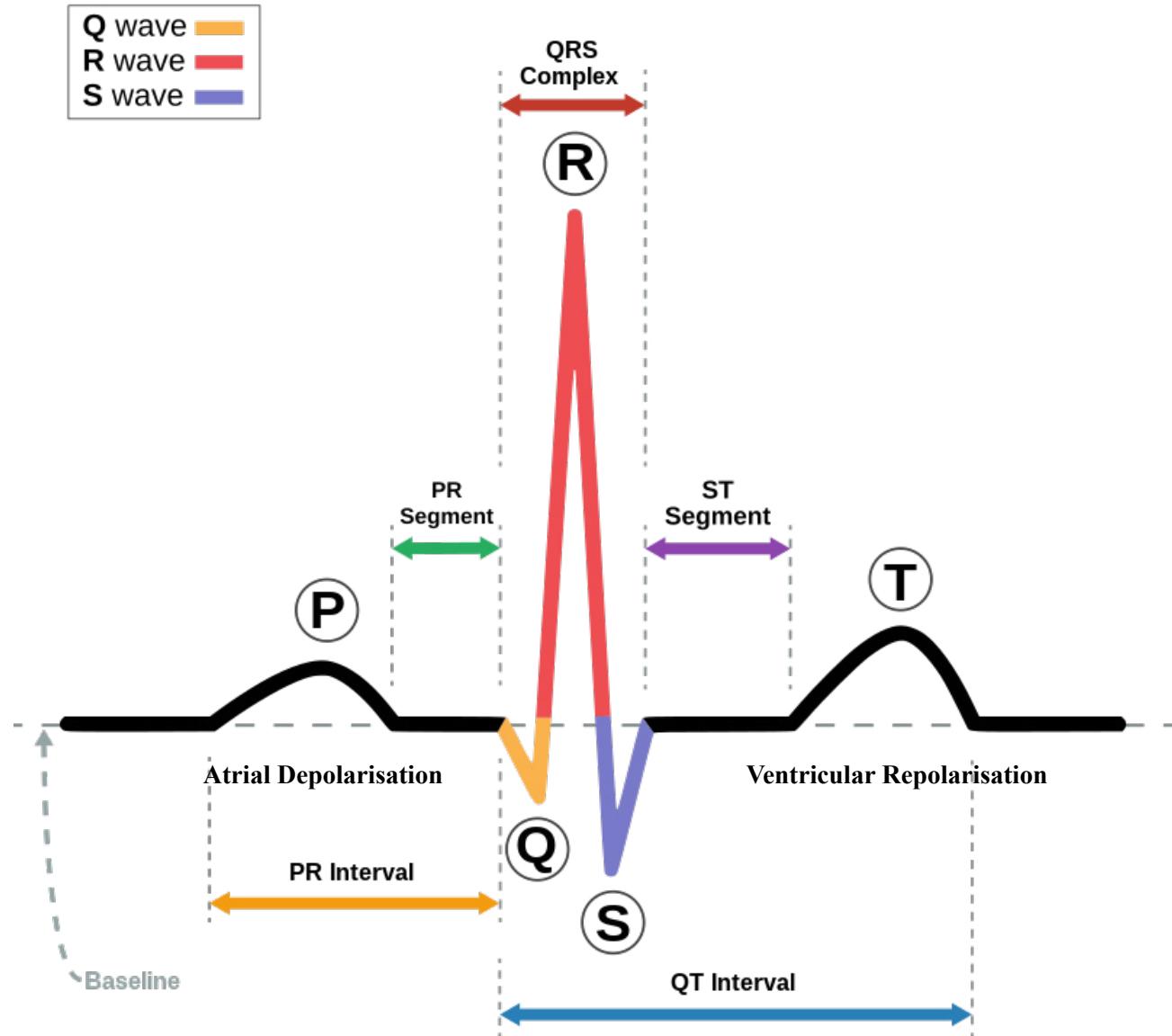
Introduction

Cardiac dysrhythmias or arrhythmias are a disturbance in the **rhythm** (electrical conduction) or **rate** (beats per minute) of those cardiac muscle contractions. The disruption of the cardiac electrical conduction system occurs primarily at two levels:

1. *Autonomic Nervous System (ANS PNS + SNS): SA & AV Node | Heart Rate Determinant*
 - Parasympathetic = Decreased Heart Rate | ACh → M₂ Receptor
 - Sympathetic = Increased Heart Rate + Force of Contraction | NA → β₁ Receptor
2. *Cardiac Conduction System (CCS): Myocytes & Ion Channels | Heart Rhythm Determinant*
 - Movement of ions (Ca, K, Na) across nodal and cardiac membranes create action potentials that cause muscle contractions. The muscles contractions lead to the pumping of blood around the body.



Ventricular Depolarisation + Atrial Repolarisation



Diagnosing Arrhythmias

- Clinical signs and symptoms
- Vital signs
- ECG, ECHO, Holter Monitor

Goal of Treatment for all Arrhythmias

- To prevent mortality
- To prevent complications (e.g. stroke)
- To alleviate symptoms
- To normalise signs (e.g. rhythm, ECHO, ECG abnormalities)
- To control heart rate (e.g. goal is <110 bpm)
- Improve quality of life, give cost-effective treatment
- Minimise ADRs

Signs & Symptoms of all Arrhythmias

Symptoms may last for a short time or persist over time:

- Asymptomatic
- Palpitations, “racing heart”, “fluttering”
- Feeling of pause, dizziness, loss of consciousness
- Shortness of Breath, Anxiety, Cardiac Arrest

Complications: Stroke, HF, MI, dementia

Risk Factors for all Arrhythmias

Damage to the Heart

- Cardiomyopathy
- Myocardial Infarctions (MI)
- Heart Failure (HF)
- High Blood Pressure (HTN)
- Coronary Artery Disease (IHD)
- Diabetes

Other

- Healing process after a cardiac surgery
- Congenital Heart Conditions, Age
- Valve disorders
- Sleep Apnea
- Electrolyte imbalances

Drug-Induced Arrhythmias

- Alcohol, Recreational drugs
- Anti-Psychotics, Antibiotics: macrolides, some quinolones, DMARDs: hydroxychloroquine
- Agents that prolong QT interval (\uparrow TdP): Class 1 (Na) and 3 (K) anti-arrhythmics for rhythm control

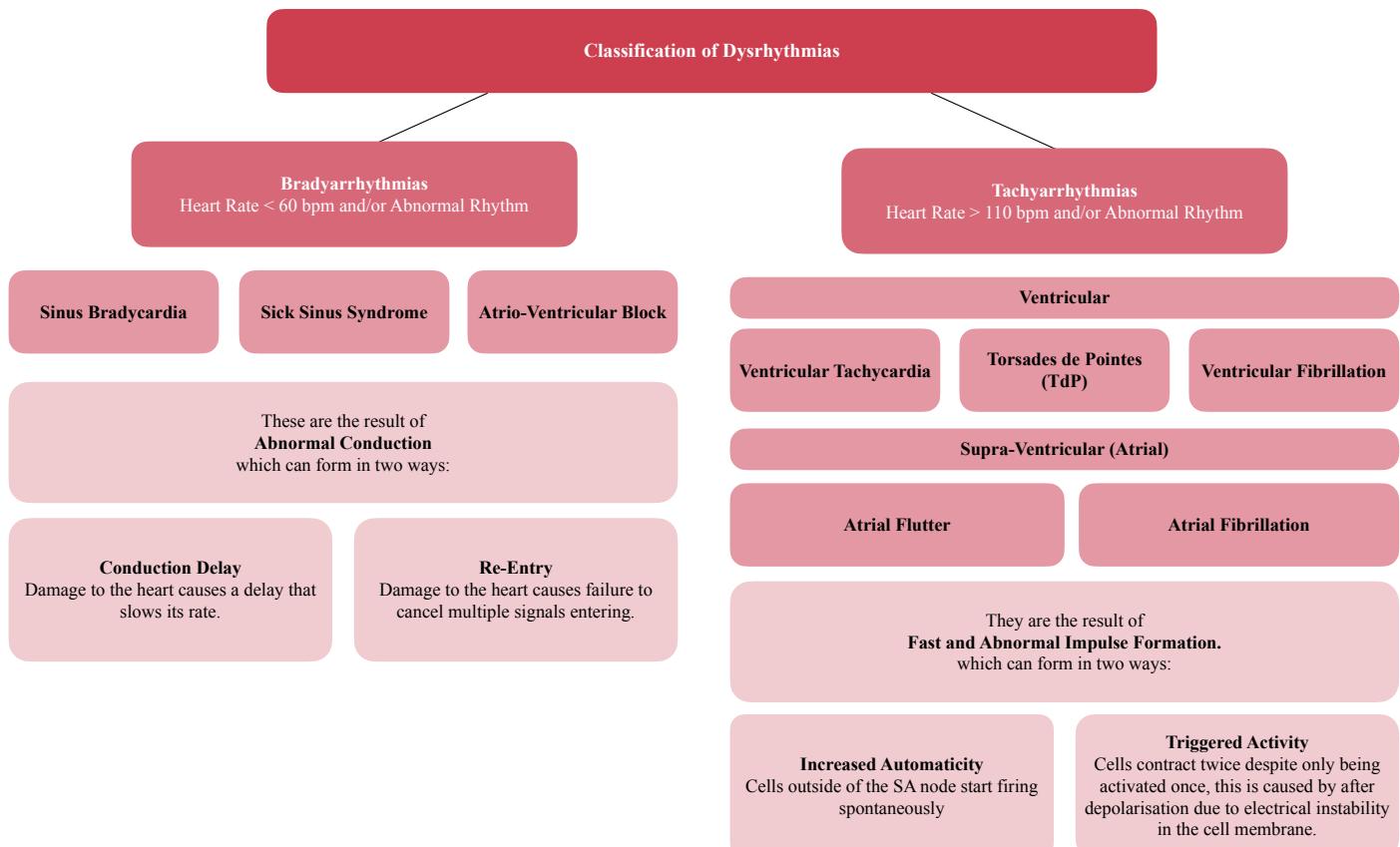


Drugs & QT Prolongation

Drug-induced TdP is rare without risk factors for QT prolongation: Female, structural heart disease, electrolyte disorders or disturbances, interactions between 2 QT prolonging drugs.

Types of Arrhythmias

Arrhythmias can be classified as either bradyarrhythmias or tachyarrhythmias.



Bradyarrhythmias

Slow heart rate < 60 bpm and/or of abnormal rhythm

Sinus Bradycardia

Description

Sinus bradycardia is a type of arrhythmia where the heart rhythm is consistent but firing at a slow rate of < 60 bpm, however the **rhythm is not affected**. It is the result of the SA node firing too slowly to the AV node. It is important to note this condition is commonly observed in the elderly and in endurance runner athletes — if it is, it is of no concern.

Pathophysiology

There are many pathways that can lead to the development of sinus bradycardia:

1. *Increased vagal tone or stimulation (PNS)*
 - Increased ICP can distort the vagus nerve due to the CSF pressure
 - Vomiting and other several GI issues can affect the vagus nerve
 - Myocardial ischaemia or infarctions can lead to the compensatory activation of the vagus nerve.
2. *Hypothyroidism*
3. *Hypothermia*

Causative Drugs

1. β -Blockers (slows impulse generation in SA node)
2. Non-DHP CCBs (slows conduction in SA/AV node)

Sick Sinus Syndrome (SSS)

Description

Sick Sinus Syndrome, also known as Tachy-Brady Syndrome is caused by dysfunction of the sinus node (the heart's natural pacemaker) resulting in a combination of bradycardia and tachycardia (uneven heartbeat) with associations to atrial tachyarrhythmic episodes. Sick Sinus Syndrome can lead to events such as Atrial Fibrillation.

Causative Drugs

1. β -Blockers
2. Non-DHP CCB
3. Digoxin

Atrio-Ventricular Block (AVB)

Description

Atrioventricular (AV) block is type of arrhythmia where there is an interruption or delay of electrical conduction from the atria to the ventricles due to conduction system abnormalities in the AV node or the His-Purkinje system.

Pathophysiology

Impulses generated in the atria are conducted slowly or are partially/totally blocked. This type of arrhythmia is often described as ‘feeling of a pause’. Conduction delay or block can be physiologic if the atrial rate is abnormally fast or pathologic at normal atrial rates.

Causative Drugs

1. β -Blockers
2. CCBs
3. Digoxin

Tachyarrhythmias

Supra-Ventricular & Ventricular | Fast heart rate > 100 bpm and/or of abnormal rhythm

Atrial Flutter (AF)

Description

Atrial flutter is a supra-ventricular dysrhythmia that describes a **rapid** (250 - 350 bpm), but **regular** atrial depolarisation. The concern with atrial flutter is that if atrial impulses are conducted to the ventricles, it may lead to ventricular tachycardia. The ventricles may not be able to cope and a compensatory AV block may occur to protect the ventricles.

Pathophysiology

Atrial flutter is often the result of re-entry into the atrial circuit. The below agents can cause this. The ECG will show 'Saw Tooth Flutter Waves.'

Causative Agents

- Coronary Artery Disease (IHD)
- Thyrotoxicosis
- Cardiac Surgery
- COPD
- Pulmonary Embolism
- Pericarditis

Atrial Fibrillation (Afib)

[NZF AFib](#)

Description

Atrial fibrillation is a supra-ventricular dysrhythmia describes a *rapid* (350 - 600 bpm) and *irregular* atrial depolarisation. It is the most commonly sustained dysrhythmia.

Pathophysiology

Atrial fibrillation is caused by circuit re-entry or random firing (ectopic foci). The impulses are conducted irregularly across the atria and the AV node irregularly filters (blocks) atrial impulses. This leads to fibrillation and therefore irregular and increased ventricular rate.

Causative Agents

- Increasing age

Signs & Symptoms

- Fatigue, SOB, Palpitations
- Syncope (temporary loss of consciousness due to fall in BP)
- Worsening Heart Failure

Complications: [Stroke](#), TIA, HF, MI.

Classifications

1. *First Detected*: Only one diagnosed episode
2. *Paroxysmal*: Recurrent episodes that stop on their own < 7 days | [Rhythm Control](#)
3. *Persistent*: Recurrent episodes that last > 7 days | [Rate & Rhythm Control](#)
4. *Permanent*: Ongoing long-term episode | [Rate Control](#)

Investigations & Acute Interventions

1. *ECG*: 24h ambulatory monitor if suspected paroxysmal Afib
2. *Echocardiogram*: rule out structural abnormalities, influence management strategies
3. *Acute Electrical Cardioversion*: consider if presenting within 48 hours of symptoms onset

Prevention (Stroke)

The main concern with Afib is that the irregular beating can cause areas of the atria to stagnate and this can form red fibrin rich clot. As the atrial thrombus can dislodge (embolus) - a stroke is our greatest concern. We can prevent a stroke by giving anti-coagulants - however not everyone will benefit from anti-coagulants. This is where it becomes important to balance the risk of a clot vs the risk of a bleed.

To do this, there are two scoring tools at our disposition: CHA₂DS₂-VASC and HASBLED.

CHA ₂ DS ₂ -VASC	HASBLED
<i>Assesses risk of a clot - efficacy marker</i>	
Congestive heart failure	Hypertension
Hypertension/current antihypertensive	Abnormal renal/liver function (1 pt each)
Age ≥75 - (2 pt)	Stroke
Diabetes Mellitus	Bleeding
Stroke/TIA/thromboembolism - (2 pt)	Labile INR
Vascular disease	Elderly >65
Age 65-74	Drugs or alcohol (1 pt each)
Sex Category: female	

CHA₂DS₂-VASC (Risk of a Clot)

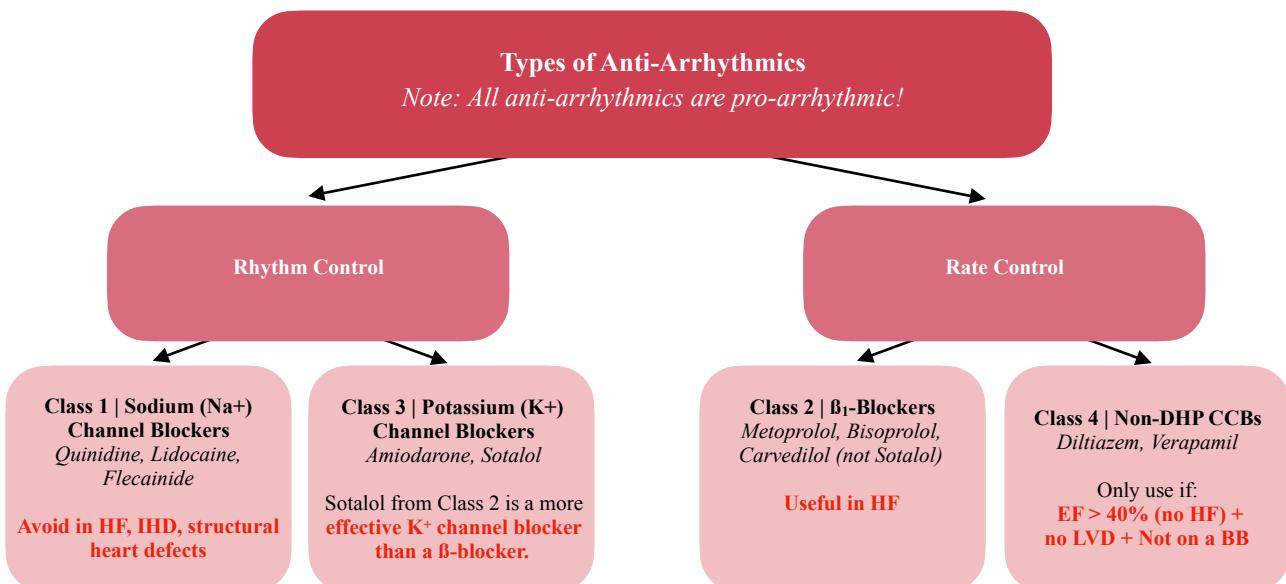
- Assesses ischaemic stroke risk as a complication of Afib using clinical and demographic information
- Anticoagulants are indicated if the score is ≥ 2 (females) or ≥ 1 (males)

HASBLED (Risk of a Bleed)

- Calculates the one-year risk of major bleeding for people on blood thinning drugs for atrial fibrillation
- No specific cut-off for anticoagulant risk

Pharmacological Treatment

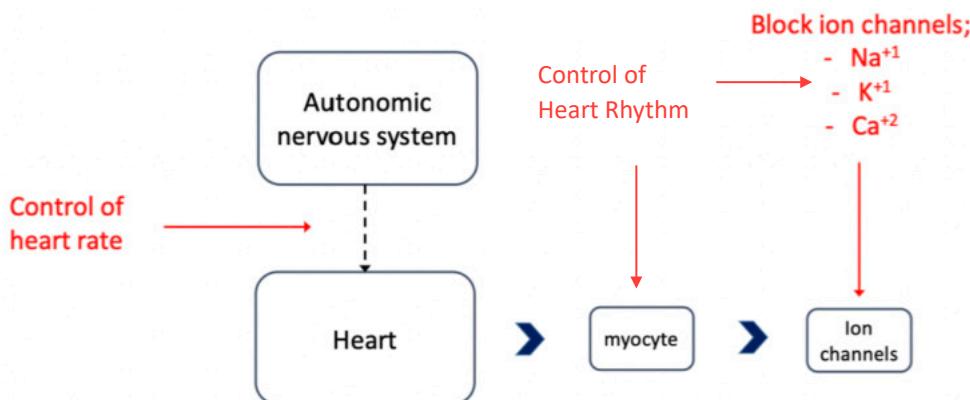
Note: Digoxin is another anti-arrhythmic that exists, however it is kept as line given the ADRs it is associated with.





Rate or Rhythm Control

In order to remember what classes are rate or rhythm — simply remember that ions (Na^+ , K^+ , Ca^{+2}) control the rhythm. CCBs are an exception as non-DHP CCBs are used.



RATE VS RHYTHM CONTROL		
Indication	Treatment	'Criteria'
Rate Control <ul style="list-style-type: none"> Improve symptoms by controlling (decreasing) HR Preferred in primary care Long-term therapy 	<p>Pharmacological</p> <ul style="list-style-type: none"> β-blocker (Class 2) - NOT sotalol Non-DHP CCB (Class 4) - Diltiazem & Verapamil Digoxin <p>Target heart rate:</p> <ul style="list-style-type: none"> <110 bpm <80 bpm if LVD 	<ul style="list-style-type: none"> For persistent or permanent arrhythmia Less symptomatic HTN >65y (as therapy is more long term)
Rhythm Control <ul style="list-style-type: none"> Restore sinus rhythm by electrical or pharmacological cardioversion Usually secondary care Short-term or long-term therapy 	<p>Pharmacological</p> <ul style="list-style-type: none"> Na^+ (Class 1) - Flecainide K^+ (Class 3) - Sotalol & Amiodarone <p>Electrical</p> <ul style="list-style-type: none"> Catheter Ablation (destroys arrhythmia-causing tissue) Cardioversion (if Afib for >48 hours) 	<ul style="list-style-type: none"> For paroxysmal arrhythmia (First Line in paroxysmal Afib, if accompanied by HF) On-going symptoms despite optimal rate control HF exacerbated by arrhythmia <65y (as this therapy is not as long term)
Stroke Prevention	<p>Anticoagulants:</p> <ul style="list-style-type: none"> Warfarin, Dabigatran, Rivaroxaban <p><i>Note:</i> Anti-platelets are no longer recommended (similar bleeding risk but less effective)</p>	

Ventricular Tachycardia

Description

Ventricular Tachycardia is a ventricular dysrhythmia that describes a **rapid** (100 -250 bpm) arrhythmic heart rate. The tachycardia if sustained is it lasts for more than 30 seconds.

Pathophysiology

ECG shows wide and rapid QRS complexes. There are two types of VT that exist:

- *Monomorphic*: All QRS complexes are similar
- *Polymorphic*: QRS complexes change in morphology, amplitude, polarity (normal QT)

Torsades de Pointes (TdP)

Description

TdP is a variance of polymorphic **Ventricular Tachycardia** that has QT prolongation, also known as the ‘twisting of point’. The QRS complexes seem to change axis and amplitude.

Signs & Symptoms

“Feeling of pause”

Causative Agents

- *Drugs*: Anti-Arrhythmics (Class 1a, Class 3), Phenothiazines, Erythromycin
- *Electrolyte Causes*: Hypokalaemia, Hypomagnesemia

Ventricular Fibrillation

Description

Ventricular Fibrillation is a life threatening ventricular dysrhythmia that describes a **rapid (250 -500 bpm)** **arrhythmic (irregular)** heart rate. This type of dysrhythmia often follows an ischaemic event. It is the most frequent cause of sudden death, and is sometimes due to congenital causes.



CHAPTER 9

THE ENDOCRINE SYSTEM



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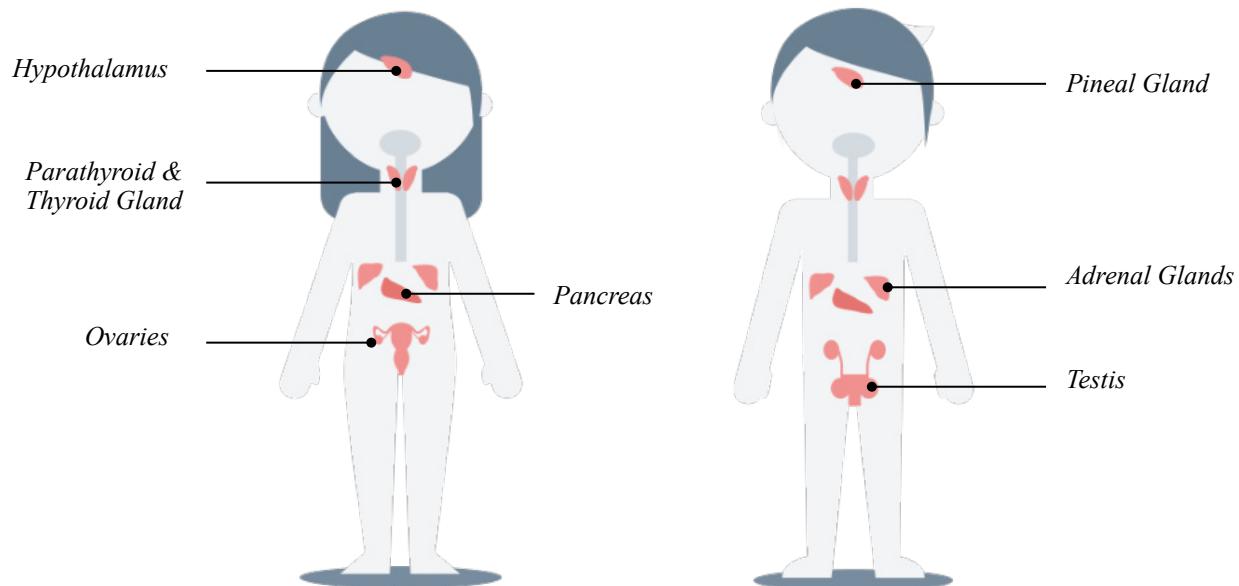
Chapter 9

The Endocrine System

General Overview of the Endocrine System

Introduction

The endocrine system consists of a network of 8 endocrine glands located through the body. These glands secrete hormones that regulate body growth, metabolism, and sexual development and function. This chapter will look into only three types of endocrine disorders: Diabetes, Thyroid & Adrenal disorders.



DIABETES MELLITUS

Overview of Diabetes

Introduction

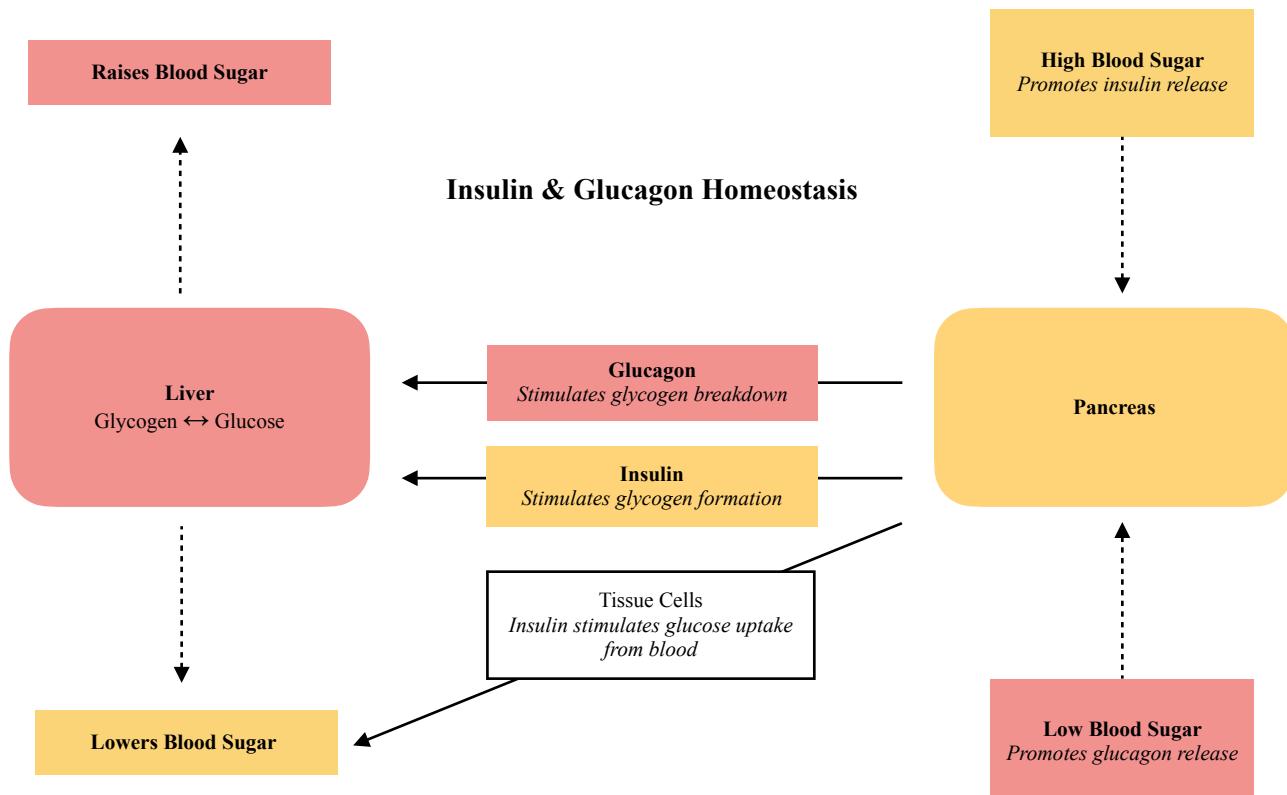
[Diabetes Mellitus & Insulins NZF](#), [Diabetes NZ](#)

Diabetes is a chronic disease that occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces (insulin resistance). Inadequate insulin action results in a rise in blood glucose levels (hyperglycaemia) due to impaired uptake and transport into muscle and fat cells. Persistent hyperglycaemia can lead to damage to the body and failure of organs and tissues. There are two main types of diabetes (T1/T2DM) and one intermediate type (LADA).

The Pancreas - Insulin & Glucagon

Insulin and glucagon are the primary hormones responsible for the regulation of the blood glucose level.

- Pancreatic α-islet cells secrete glucagon in response to low blood glucose
- Pancreatic β-islet cells secrete insulin and adjust this amount very precisely to promote glucose uptake after meals and to regulate glucose output from the liver during fasting.



Hyperglycaemia and Hypoglycaemia

BPAC Diabetes in Elderly

Recognising symptoms of either is important as they may affect adherence to medications - in particular, patients tend to prefer hyperglycaemic events over hypoglycaemic ones, resulting in poor adherence to anti-hyperglycaemics. Please note that illness often causes hyperglycaemia as more hormones are produced when the body is under stress (often food is inadequate).

Hypoglycaemia	Hyperglycaemia
Sweating	Asymptomatic - 3Ts = Thirsty, Tired, Toilet
Shaking	Polyuria & Polydipsia
Hunger	Extreme fatigue (impaired glucose uptake does not meet energy needs)
Confusion/Irritability	Hunger & sudden weight loss (impaired glucose uptake promotes lipolysis)
Loss of consciousness	Poor circulation (reduced blood flow due to plaque formation narrowing blood vessels)
Dizziness, Faint	Recurrent & prolonged infections (particularly urogenital)
Headaches	Blurred vision (lens swelling due to high glucose pulling fluids in)
Fatigue	Headache
Seizures, Coma, Death	Tachypnoea



Hypoglycaemia in the Elderly

Note that hypoglycaemia in elderly can manifest as non-specific neurological symptoms (confusion, dizziness, weakness, visual disturbances) rather than adrenergic symptoms (tremors, sweating).

Complications of Diabetes

Complication		Description	Treatment
ACUTE	Diabetic Ketoacidosis (DKA)	DKA is a medical emergency which occurs when glucose is high and insulin is low. When the body can't use glucose for energy, fats get broken down into ketones which enter the urine and blood — this decreases the pH of blood (i.e. acidosis; pH <7.3 and / or bicarbonate <15mmol/L). DKA is often complicated by dehydration (due to glycosuria) and may lead to kidney failure.	IV Treatment <ul style="list-style-type: none">• Fluids• Insulin• Glucose• Potassium• (Bicarbonate)
	Hyperglycaemia & low insulin	S/S: N/V, dehydration, polydipsia, polyuria, hyperventilation, acetone breath Hyperglycaemia, ketosis , acidosis, hyperkalaemia with a decrease in total K ⁺ (kidneys are failing so K ⁺ spill into blood which gets excreted in urine)	Note: May need to use blood ketone test strips as required
	Hypoglycaemia	Caused by too much insulin, illness and alcohol S/S: hypoglycaemia , Glucose < 4.0mmol/L or < 2.8mmol/L	<ul style="list-style-type: none">• Simple carbs (sugary snack) followed by complex carbs.• IM or SC Glucagon

		Pathophysiology	Signs
Hashimoto's Thyroiditis		Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, is an autoimmune disorder involving chronic inflammation of the thyroid. This condition is often genetic.	Positive thyroid peroxidase (TPO) antibodies
Iodine Deficiency		Without adequate iodine, the thyroid progressively enlarges (goitre) as it tries to keep up with demand for thyroid hormone production.	Low iodine levels
Thyroidectomy		Thyroidectomy is a surgery conducted in the treatment of hyperthyroidism. The overtreatment of hyperthyroidism can induce hypothyroidism.	
Radioiodine ablation		Radio-iodine ablation is radiation therapy in which radioactive iodine is administered to destroy or ablate residual healthy thyroid tissue remaining after thyroidectomy. This can induce hypothyroidism.	
CHRONIC	Macrovascular complications	BRAIN - HEART - PERIPHERY/EXTREMITIES Complications affecting the large blood vessels. Caused by chronic hyperglycaemia, excess free fatty acid, and insulin resistance. Sugar builds up in the blood, eventually causing hardening of blood vessels. These develop earlier and are more severe (50% of patients). <ul style="list-style-type: none">• Brain (stroke), heart (CAD/MI, HLP, arrhythmia), PVD	
	Microvascular complications	EYES - KIDNEY - NERVOUS SYSTEM Complications affecting the small blood vessels. Caused by chronic hyperglycaemia. These develop in 27% of patients. <ul style="list-style-type: none">• Eyes (Retinopathy, blindness), Kidneys (Kidney failure, ESRD), CNS (neuropathy)	
	Co-morbidities	<ul style="list-style-type: none">• Non-Alcohol Fatty Liver Disease• Obstructive Sleep Apnoea• Depression• Increase in all-cause mortality	

Laboratory Investigations of Diabetes

LAB TESTS FOR DIABETES			
Parameter	Description	Normal Value	Diabetic Value
Glycated Haemoglobin (HbA1c)	HbA1c (mmol of HbA1c per mol of Hb) Glucose binds to haemoglobin slowly and irreversibly. Therefore, it reflects the average concentration of blood glucose over the past 2-3 months (chronic exposure).	HbA1c < 40 Normal	<ul style="list-style-type: none"> • HbA1c 41 - 49 mmol/mol Pre-Diabetes • HbA1c > 50mmol/mol = Diabetes • HbA1c < 53 mmol/mol Mild Diabetes • HbA1c 54 - 63 mmol/mol Fair Diabetes • HbA1c 64 - 86 mmol/mol Moderate Diabetes • HbA1c > 86 mmol/mol Severe Diabetes
Fasting Blood Glucose (FBG)	FBG: Fasting Blood Glucose Blood glucose after an overnight fast	Pre-Meal Goal 4 - 7 mmol/L	FBG \geq 7.0 mmol/L
Random Blood Glucose (RBG)	RBG: Random Blood Glucose A random glucose test measures the amount of glucose or sugar circulating in a person's blood (no need to fast beforehand)	Postprandial Goal <7.8 mmol/L or 10 mmol/L 2 hours after eating (postprandial)	RBG \geq 11.1 mmol/L
Post-Glucose Tolerance Test (GTT)	GTT: Post Glucose Tolerance Test Test for T2DM - overnight fast, then consume 100g glucose drink, then take blood glucose measurement.		GTT \geq 11.1 mmol/L

Goal of Treatment & Glycemic Targets

The primary objective is to achieve glycemic control

- Reduce, control and manage long-term microvascular and macrovascular complications
- Preserve β-cell function
- Preventing hyperglycaemia, hypoglycaemia, and ketoacidosis
- Maintaining the patient's overall quality of life

HbA1c Target	Characteristics of patients who may benefit from this target
< 48 mmol/mol	Greatest reduction in risk of microvascular complications. Appropriate if can be achieved without adverse effects. <ul style="list-style-type: none"> • Young e.g. aged < 40 years • Are at low risk of hypoglycaemia (i.e. not on insulin or a sulfonylurea) • Considering pregnancy or are pregnant • Have microvascular complications (particularly retinopathy and nephropathy)
< 53 mmol/mol	Reasonable balance between reduction in risk of microvascular complications with risks of treatment <ul style="list-style-type: none"> • Most patients
< 54 - 70 mmol/mol	Appropriate if benefits from treating to lower levels are outweighed by risk of hypoglycaemia <ul style="list-style-type: none"> • Older patients at risk of falls and fractures • Frailty • Cognitive impairment • Functionally dependent • Hypoglycaemia experienced at lower targets • Live alone and are at risk of severe hypoglycaemia • Short life expectancy • Already have advanced microvascular or macrovascular diabetes complications • Require multiple medicines to achieve lower HbA1c targets and have complications caused by polypharmacy

Monitoring Requirements in Diabetes

[BPAC Type 2 Diabetes Toolbox](#) [BPAC B Quick Type 2 Diabetes Monitoring](#)

Fasting & Random Blood Glucose

Target: Pre-meal goal: 4 - 7 mmol/L | Postprandial goal: <10 mmol/L)

- T2DM: frequently ([1 pack of test strips is funded per script if not on insulin](#))
- T1DM: at least 3 times daily, up to 6-8 times daily (e.g. before/after food, at bed).

Glycated Haemoglobin (HbA1c)

Target: usually < 53mmol/L

- HbA1c: 3-6 monthly until target, then annually
- Diary of any hyper or hypoglycaemic events e.g. DKA

Disease Progression (annual review)

1. Discuss diet and physical activity approaches
2. Discuss medicine use and adverse effects
3. Review management of cardiovascular and renal risk factors
4. Measure weight, waist circumference, BP
5. Examine feet, skin, eyes, nails, deformity, teeth and gums, recurrent infections
6. HbA1c, urinary ACR, serum creatinine, LFT, non-fasting lipids

7. CVD risk, smoking status, alcohol intake, mental health

Meter	Tests	Tests Strips	Eligibility
CareSens Dual	Blood glucose and blood ketones	CareSens PRO and KetoSens	People with: <ul style="list-style-type: none"> • T1DM • Permanent neonatal diabetes • Pancreatectomy • Cystic fibrosis-related diabetes • Metabolic disease or epilepsy under the care of a paediatrician, neurologist or metabolic specialist
CareSens N			People who: <ul style="list-style-type: none"> • Are receiving insulin or sulphonylureas treatment • Are pregnant with diabetes • Are on home total parenteral nutrition at risk of hypoglycaemia or hyperglycaemia • Have a genetic or an acquired disorder off glucose homeostasis, excluding T1DM and T2DM
CareSens N Pop			
CareSens N Primer	Blood glucose	CareSens N	

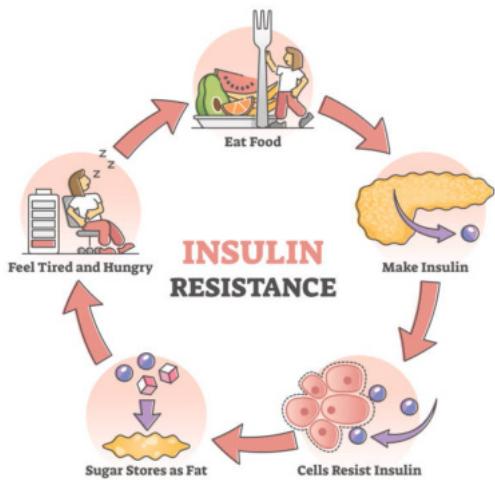
Diabetes Types

Type 2 Diabetes Mellitus (T2DM)

[BPAC Type 2 Diabetes](#)

Description

Type 2 diabetes is a chronic metabolic disorder resulting in hyperglycaemia. Hyperglycaemia here, is the result of reduced insulin sensitivity by cells (insulin resistance - this begins many years **before** the onset of T2DM). The increased secretory demands arising from **insulin resistance leads to β-cell exhaustion**, and the eventual dysfunction & loss of β-cells.



T2DM is therefore the result of insulin resistance happening in the background of β-islet cell destruction — up to 50% at diagnosis.

T2DM is a non-insulin dependent form of diabetes mellitus and accounts for 90-95% of all diabetes. Changes in hormone levels (increased glucagon), impaired response to GLP-1, receptor signalling & insulin production, low grade systemic inflammation all contribute to the pathogenesis of T2DM.

Risk Factors

Genetic

- β-cell dysfunction genes, body adiposity genes
- Ethnicity (e.g. Māori, Pasifika > 30 years old, Indian, Middle Eastern)

Environment

- Age: β-cell function and insulin production declines
- Personal history (pre-diabetes), decreased energy expenditure, increased calorie intake
- Metabolic Syndrome: HTN, HLD, overweight/obese (TOFI with Waist to Hip Ratio > 1, BMI >25 kg/m²), elevated fasting blood glucose

Non-Pharmacological Treatment

A **healthy lifestyle** is the foundation of treatment for all people with T2DM

- Weight loss of 0.5 kg per week recommended (1-4kg per month)
- Regular physical activity: 30 minutes of moderate intensity most days
- Moderation of alcohol consumption, smoking cessation
- Diet: quality and quantity of fats and carbohydrates, whole grains, fruits, nuts, legumes, less processed grains, meats, sweetened beverages

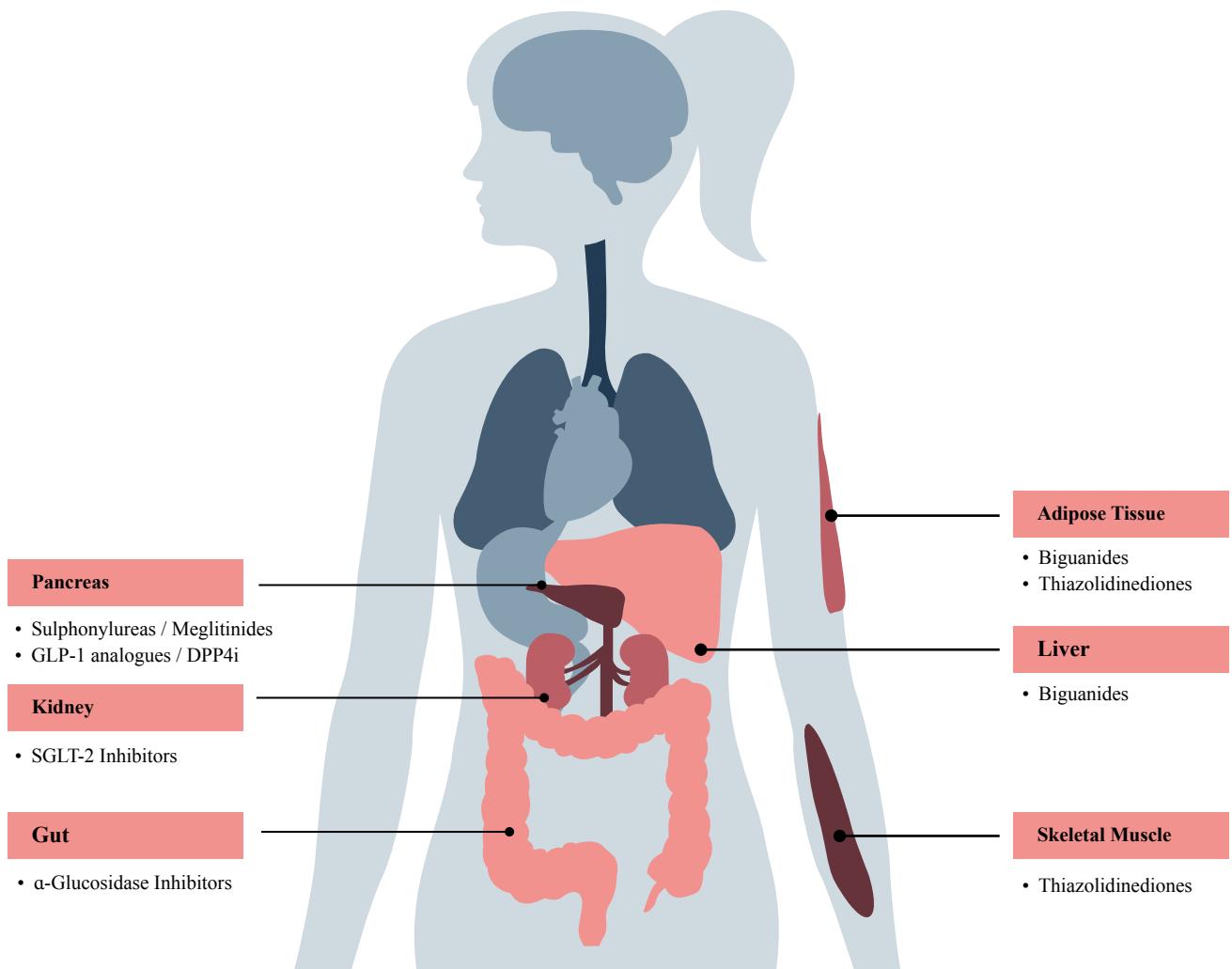
Pharmacological Treatment

[NZSSD Diabetes](#) [T2DM Treatment Guidelines NZSSD](#), [Management of CV Risk Factors in Diabetes](#);

Drug	Mechanism of Action	Side Effects
[PRESCRIPTION] <i>1st Line: Biguanides</i> Metformin (Apotex)	LIVER (& GUT, SKELETAL MUSCLE): ↓ Glucose production and/or secretion • Decreases gluconeogenesis in the liver • Increase peripheral utilisation of glucose (decreases insulin resistance)	Weight loss • Decreased appetite, N/V/D, abdominal pain, taste disturbance, indigestion • May cause B12 deficiency • Take with food
[PRESCRIPTION] <i>2nd Line: SGLT-2 Inhibitors</i> Empagliflozin (Jardiance)	KIDNEY: ↓ Glucose re-absorption SGLT2 is a Na ⁺ glucose co-transporter located in the proximal renal tubule which moves glucose into cells and bloodstream against the concentration gradient. Blocking the receptor decreases blood glucose, reducing renal threshold of glucose exertion from 10 to 2.8 mmol/L.	Weight loss • Increase in UTIs , vaginal thrush, mild diuresis. Effectiveness decreases in kidney disease.
[PRESCRIPTION] <i>2nd Line: GLP-1 Agonists (Incretins)</i> Dulaglutide	PANCREAS: Insulin Secretagogue — Weekly injected on the same day Incretins are GI hormones released after meals (that make you feel full) and stimulate insulin secretion from pancreatic β cells and reduced glucagon secretion from pancreatic α cells. <i>Note: Can switch day of taking if there is a 3 day space between doses.</i>	Weight loss GI disturbances, N & V, decreased appetite A note on Nausea Common within first 4 weeks of treatment initiation. Manage with lifestyle factors
[PRESCRIPTION] <i>3rd Line: DPP-4 Inhibitor</i> Vildagliptin (Galvus)	PANCREAS: Insulin Secretagogue — Require some production of insulin Vildagliptin inhibits DPP-4. As DPP-4 inactivates GLP-1, therefore increasing levels of GLP-1. This results in increased insulin synthesis and secretion from pancreatic β cells, and reduced glucagon secretion from pancreatic α cells.	Weight loss GI disturbances (especially with metformin), peripheral oedema, tremor, asthenia, dizziness, headaches,
[PRESCRIPTION] <i>3rd Line: Sulphonylureas</i> Gliclazide, Glipizide	PANCREAS: Insulin Secretagogue — Require some production of insulin These inhibit β-cell K _{ATP} channel complex (SUR), which then causes insulin secretion. However, the effect declines over with down-regulation of β-cell surface receptors and progression of β cell failure.	Weight gain (do not give if overweight) Hypoglycaemia, less common side effects are N & V, cholestatic jaundice and agranulocytosis.
[PRESCRIPTION] <i>3rd Line: Meglitinides</i> Repaglinide		Avoid in patients with reduced renal function (risk of accumulation and toxicity)
[PRESCRIPTION] <i>3rd Line: Thiazolidinediones (PPAR γ Activators)</i> Pioglitazone (Vexazone)	ADIPOSE & SKELETAL MUSCLE: ↑ cellular uptake of fat and glucose (↑ insulin sensitivity/↓ resistance) TZDs targets the PPAR γ nuclear hormone receptor to reduce blood-glucose concentration by improving insulin sensitivity in adipose tissue and skeletal muscle, and by decreasing hepatic gluconeogenesis. It promotes uptake of fats into adipose and glucose uptake into muscle/adipose tissue.	Weight gain GI disturbances, oedema (may lead to HF with long-term use)

<p>[PRESCRIPTION] <i>3rd Line: Alpha Glucosidase Inhibitors</i></p> <p>Acarbose</p>	<p>GUT: ↓ Glucose absorption Reduces intestinal absorption of starch, dextrin, and disaccharides by inhibiting the action of α-glucosidase in the intestinal brush border. Take before each meal (not absorbed). Not frequently used due to low efficacy.</p>	<p>Not absorbed therefore - malabsorption, flatulence, diarrhoea and abdominal bloating.</p>
<p>[PRESCRIPTION] <i>Last Line: Exogenous Insulin</i></p> <p>Basal Insulin (Isophane or Glargin)</p>	<p>Mimics endogenous insulin ↑ cellular uptake of glucose First line in T1DM but last line in T2DM. Aims to mimic the basal bolus pattern of endogenous insulin. Isophane or glargin at 0.1-0.2 units/kg note.</p>	<p>Weight gain Hypoglycaemia and weight gain due to increased glucose absorption and conversion of excess to fat.</p>

Summary of Anti-Hyperglycaemics



RISK-BENEFIT ANALYSIS OF ANTI-HYPERGLYCAEMICS				
Medicine	Effects on Weight	Risk of hypoglycaemia	Use in patients with renal or hepatic impairment	Other factors and monitoring requirements
Metformin Biguanide	Weight loss of approximately 2-3 kg over 12 months	Low	<ul style="list-style-type: none"> Avoid in CrCl <15 mL/min Reduce dose if CrCl 15-59 mL/min Avoid in severe hepatic disease Use with caution in mild hepatic impairment (reduced lactate clearance can increase risk of lactic acidosis) 	<ul style="list-style-type: none"> Pregnancy/breastfeeding: first line May cause vitamin B12 deficiency GI ADRs: slow titration, take with food Consider temporary cessation of metformin in situations that may lead to lactic acidosis e.g. dehydration due to illness
Empagliflozin SGLT-2<i>i</i>	Weight loss of approximately 2kg over 6 months	Low	<ul style="list-style-type: none"> Contraindicated if eGFR <30 (ineffective) 	<ul style="list-style-type: none"> SGLT2 inhibitors are renoprotective but their efficacy also depends on renal function —Assess renal function annually May cause diabetic ketoacidosis Avoid if history of severe genitourinary infections
Dulaglutide DPP-4	Weight loss of approximately 2-3 kg over 12 months	Low	N/A	<ul style="list-style-type: none"> No additional monitoring requirements ADR: GI disturbance, injection site reactions Avoid if history of medullary thyroid cancer; use in caution in patients with a family history
Vildagliptin GLP-1	No change	Low	<ul style="list-style-type: none"> Reduce dose if eGFR <50 Avoid if hepatic dysfunction e.g. ALT >2.5 x upper limit of normal 	<ul style="list-style-type: none"> Avoid in patients with severe HF Assess liver function prior to initiation, then every 3 months for the first year, then periodically thereafter
Gliclazide Sulphonylureas	Weight gain of approximately 2kg over 12 months	High	<ul style="list-style-type: none"> Other medicines are preferable in patients with risk of hypoglycaemia (including patients with renal or severe hepatic impairment) 	<ul style="list-style-type: none"> Effects on Hb1Ac may not persist as long as other options
Pioglitazone TZD	Weight gain of approximately 2kg over 12 months	Low	<ul style="list-style-type: none"> Avoid in patients with hepatic impairment e.g. ALT levels >2.5 x the upper limit of normal Not commended in patient with renal failure 	<p>Increases risk of:</p> <ul style="list-style-type: none"> Oedema and HF Fractures Bladder cancer; avoid use in patients with risk factors for/history of bladder cancer
Insulin	Weight gain of 3-9 kg over 12 months	High	<ul style="list-style-type: none"> Dose reduction not usually required in patients with hepatic or renal impairment 	<ul style="list-style-type: none"> Injection site reactions are a common ADR

DIABETES TREATMENT GUIDELINES	
Treatment Guideline	Recommendation
Step 1	<p>Metformin (Biguanide)</p> <ul style="list-style-type: none"> • If HbA1c > 64 mmol/mol: consider initiating metformin + another non-insulin medicine • If HbA1c > 80-90 mmol/mol: insulin is recommended
Step 2	<p>ADD a second non-insulin glucose-lowering medicine</p> <ol style="list-style-type: none"> 1. SGLT2 inhibitor: Empagliflozin* — (if CVD / HF / Renal Disease) - SA required 2. GLP-1 inhibitor (incretins): Dulaglutide - SA required 3. DPP-4 inhibitor: Vildagliptin* 4. Thiazolidinediones: Pioglitazone — (if no HF) 5. Sulfonylureas: Gliclazide, Glipizide 6. Meglitinides: Repaglinide 7. Alpha Glucosidase inhibitor: Acarbose <p>* Combination formulations with metformin available</p>
Step 3	<p>ADD insulin</p> <p>Basal insulin is typically recommended: insulin isophane or glargine</p>
Other Medications	<ul style="list-style-type: none"> • Lipid lowering therapy: Statins • BP Control: ACEI/ARB if diabetic + hypertensive/renal disease/HF)

MANAGEMENT ALGORITHM FOR TYPE 2 DIABETES

Expiry date:
30 June
2022



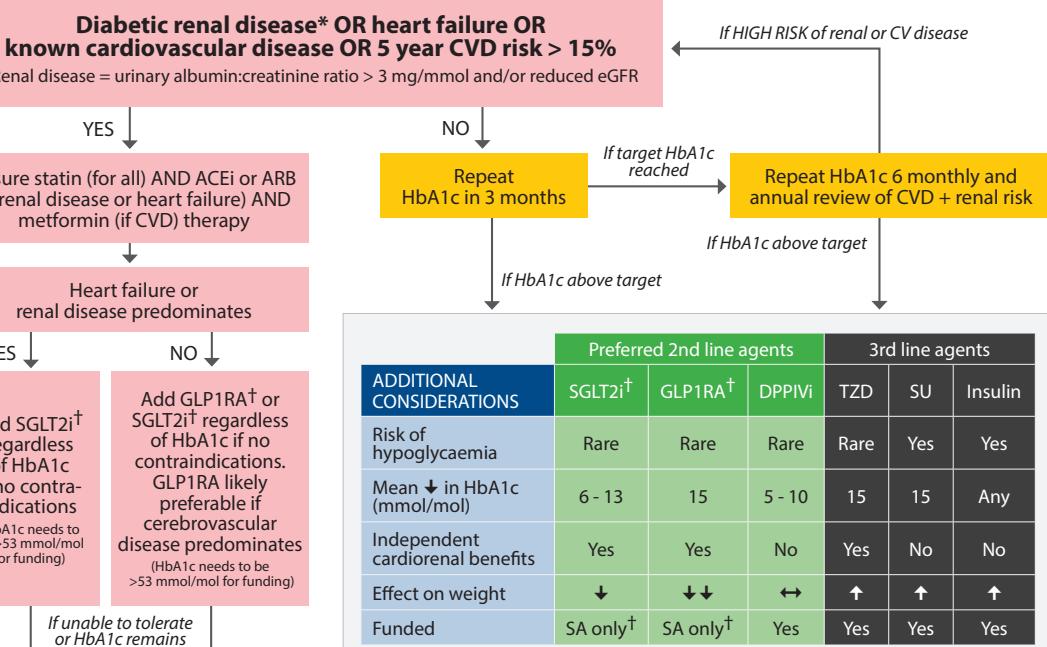
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INITIAL MANAGEMENT

Diagnosis	Lifestyle management	Metformin
Confirm the diagnosis and type of diabetes Determine individualised glycaemic target	Education, support, healthy eating + exercise Essential at all times throughout duration of diabetes	Start unless contraindicated Increase to maximal tolerated dose or 2 g per day

The target HbA1c for most patients with type 2 diabetes is < 53 mmol/mol

- If HbA1c > 64 mmol/mol at diagnosis consider starting additional agent with lifestyle management and Metformin to reach target
 - If cardiovascular and/or renal disease and/or heart failure → preferably SGLT2i or GLP1RA (see below)
 - If no cardiovascular or renal disease and no heart failure → preferably DPPIVi
- Consider starting insulin therapy immediately if:
 - Symptoms of hyperglycaemia/insulin deficiency and/or HbA1c > 90 mmol/mol
 - Suspicion of type 1 diabetes or loss of pancreatic function



GLP1RA† preferred next therapy after SGLT2i†
SGLT2i† preferred next therapy after GLP1RA†
(dual SGLT2i/GLP1RA therapy is not currently funded)

Alternative agents include:

DPPIVi if not on GLP1RA

Thiazolidinediones (TZD) if no heart failure

Sulfonylureas (SU)

Insulin

Escalate therapy + repeat HbA1c every 3 months until target reached

- May require multiple agents including insulin therapy
- Ensure adherence to lifestyle management + medications
- Re-refer for dietitian input if appropriate
- Repeat HbA1c 6 monthly once target reached
- Assess CVD and renal risk at least annually
- Continue standard care to reduce CVD risk e.g. statins, antihypertensives (esp. ACEi in diabetic renal disease) etc.

†SA criteria for SGLT2i and GLP1RA (all required and same for both classes)

- Patient has type 2 diabetes with an HbA1c > 53 mmol/mol despite > 3 months of regular use of at least one glucose lowering therapy (includes metformin)
- The patient is of Māori and/or any Pacific ethnicity OR has known diabetic renal disease OR known CVD OR 5 year CVD risk > 15% OR a high lifetime CVD risk due to onset of diabetes during childhood or as a young adult
- The patient is not on funded SGLT2i and GLP1RA therapy at the same time

Type 1 Diabetes Mellitus (T1DM)

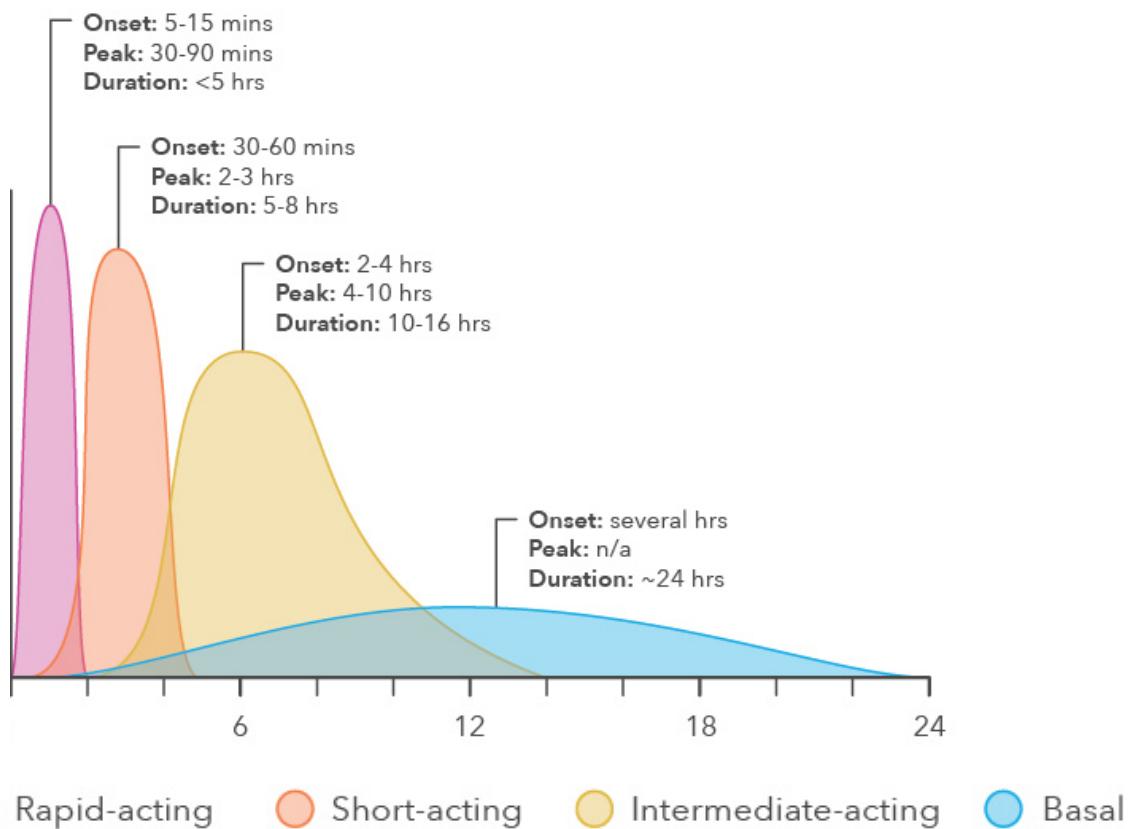
Description

Type 1 diabetes is an autoimmune disorder characterised by the immune destruction of β -islet cells, in which the pancreas produces little or no insulin. It is therefore an insulin-dependent form of diabetes mellitus.

Pharmacological Treatment (Insulin)

[BPAC Type 1 Diabetes Insulin Guidelines](#)

Insulin treatment aims to mimic the endogenous release profile. As a result, 4 types of insulin profiles exist.



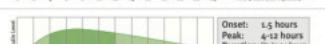
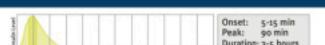
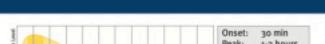
Hypoglycaemia is a common side effect of insulin → Glucagon Administration

1. Call the ambulance and ensure the person is in recovery position
2. Take orange cap off the vial. Take the grey needle cover off
3. Insert the needle through the rubber stopper of the vial
4. Inject all the liquid from the syringe into the vial
5. Without removing the needle, gently shake vial until powder has dissolved and solution is clear
6. Turn the vial upside down and pull back the plunger until all the solution is in the syringe
7. Take out the needle from the vial
8. Inject the glucagon into the person's outer thigh
9. Test the person's blood glucose level
10. Person should wake up in 10-15 minutes. If not, give another injection

Category	Drug	Patient Counselling	Mechanism of Action	Side Effects
Rapid Acting	[PRESCRIPTION] Rapid (Fast) Acting Insulin Aspart (Novorapid) Insulin Glulisine (Apidra) Insulin Lispro (Humalog)	<ul style="list-style-type: none"> Taken directly prior to a meal — have meal within 15 minutes of injection. Take with a long or intermediate acting insulin. Usually given 2-3 times a day. 	Mimics endogenous insulin <i>Onset:</i> 15 minutes <i>Peak:</i> in 1 hour <i>Duration:</i> 2-4 hours	
Short Acting	[PRESCRIPTION] Short (Regular) Acting Human Neutral Insulin (Actrapid, Humulin R)	<ul style="list-style-type: none"> Taken prior to a meal. Take with a long or intermediate acting insulin. Usually given 2-3 times a day. 	Mimics endogenous insulin <i>Onset:</i> 30 minutes <i>Peak:</i> in 2-4 hours <i>Duration:</i> 6-8 hours	Weight Gain Injection Site Reaction
Intermediate Acting	[PRESCRIPTION] Intermediate Acting Insulin Isophane (Humulin NPH) (Protaphane)	<ul style="list-style-type: none"> Mix gently before injecting (roll between hands) Take with a rapid or short acting insulin. Usually given 2 times a day. 	Mimics endogenous insulin <i>Onset:</i> 2-4 hours <i>Peak:</i> in 4-8 hours <i>Duration:</i> 12-18 hours.	
Long Acting	[PRESCRIPTION] Long Acting Insulin Glargine (Lantus) Insulin Detemir (Levemir) Insulin Degludec (Tresiba)	<ul style="list-style-type: none"> Often combined with a rapid or short acting insulin. Usually given once a day. 	Mimics endogenous insulin <i>Onset:</i> several hours after injection <i>Duration:</i> 24 hours.	
Biphasic Insulins	[PRESCRIPTION] Biphasic Insulin Lispro Rapid Acting + Intermediate Acting (Humalog Mix25) (Humalog Mix50)	<ul style="list-style-type: none"> Same time each day roughly, immediately minutes before a meal. 	Mimics endogenous insulin Insulin works 15 minutes after injection, and lasts up to 24 hours.	Weight Gain Injection Site Reaction
	[PRESCRIPTION] Biphasic Insulin Aspart Rapid Acting + Intermediate Acting (NovoMix30)			
	[PRESCRIPTION] Biphasic Isophane Insulin Short Acting + Intermediate Acting (Humalog 30/70) (Mixtard) (Penmix)	<ul style="list-style-type: none"> Same time each day roughly, 30 minutes before a meal. 	Mimics endogenous insulin Insulin works 15 minutes after injection, and lasts up to 24 hours.	

Patient Advice for Insulin	
Storage	<ul style="list-style-type: none"> Inject insulin at room temperature. Opened insulin pens, cartridges, or vials can be kept at room temperature for 4 weeks (6 weeks for protaphane), but should not be exposed to excessive heat or sunlight. Discard any leftover insulin. Unopened insulin should be kept in the fridge between 2°C and 8°C (do not freeze).
Injecting Method	<ol style="list-style-type: none"> (Roll the insulin between your hands until clear if intermediate acting) Inject your insulin into your abdomen (or less commonly into the buttocks, thighs, or upper arms) Pinch the skin and put the needle in at a 90° angle (45° if lower fat content patient) Let go of the skin and push the plunger down slowly. Hold the needle in for 10 seconds to prevent insulin from escaping. Remove the needle at the same 90° angle and dispose into sharps bin. Rotate the site you are injecting insulin into to prevent lipodystrophy from occurring. Before using an insulin pen, you need to prime the pen by performing an 'air shot'. To do this you point the needle at the ceiling and dial up 2 units of insulin then watch the needle tip as the plunger is pushed. Repeat this until more than 2 drops of insulin come out of the end of the needle. When using an insulin pen, depress plunger and hold for 10 seconds before removing.
Adjusting Insulin Dose	<ul style="list-style-type: none"> You may need to change the amount of insulin you use if you become ill, change your diet or amount of physical activity you do —discuss this with your health professional.
Things to avoid & Factors that affect insulin absorption	<ul style="list-style-type: none"> Avoid hot showers or baths within 30 min of an injection Avoid massage at injection site as this increases absorption A thicker layer of subcutaneous fat gives a slower absorption Drinking alcohol decreases your blood glucose. It can also mask warning symptoms of hypoglycaemia (low blood glucose). You may need to change your blood glucose testing and insulin treatment if you are drinking alcohol. Avoid binge drinking and make sure you are eating enough carbohydrates when drinking alcohol.

TYPES OF INSULIN

Product	Name	Type of Insulin	Presentation	Schematic Action Profile*	
Basal					
Lantus®	Insulin Glargine	Long-acting	10ml Vial 3ml Cartridge 3ml SoloSTAR®	 Onset: None Peak: Basal, steady-state Duration: 24 hours Time (hours after injection)	SANOFI
Humulin® NPH	Isophane (NPH)	Intermediate-acting	10ml Vial 3ml Cartridges	 Onset: 1 hour Peak: 4-10 hours Duration: 16-28 hours Time (hours after injection)	LILLY
Protaphane®	Isophane (NPH)	Intermediate-acting	10ml Vial 3ml Penfill®	 Onset: 1-5 hours Peak: 4-12 hours Duration: Up to 24 hours Time (hours after injection)	Novo Nordisk
Rapid Acting					
Apidra®	Insulin Glulisine	Rapid-acting	10ml Vial 3ml Cartridge 3ml SoloSTAR®	 Onset: 5-15 min Peak: 90 min Duration: 3-5 hours Time (hours after injection)	SANOFI
Humalog®	Insulin Lispro	Rapid-acting	10ml Vial 3ml Cartridge	 Onset: 0-15 min Peak: 1 hour Duration: 3-4.5 hours Time (hours after injection)	LILLY
NovoRapid®	Insulin Aspart	Rapid-acting	10ml Vial 3ml Penfill® 3ml FlexPen®	 Onset: 10-20 min Peak: 1-2 hours Duration: 3-5 hours Time (hours after injection)	Novo Nordisk
Short Acting					
Actrapid®	Insulin Neutral	Short-acting	10ml Vial 3ml Penfill®	 Onset: 30 min Peak: 1-2 hours Duration: 8 hours Time (hours after injection)	Novo Nordisk
Premix					
Humulin® 30/70	30% Insulin Neutral / 70% Isophane (NPH)	Premixed Insulin	10ml Vial 3ml Cartridge	 Onset: More rapid than NPH Peak: 2-6 hours Duration: 16-18 hours Time (hours after injection)	LILLY
Humalog® Mix 25®	25% Insulin Lispro / 75% Insulin Lispro Protamine Suspension	Premixed Insulin Lispro	3ml Cartridge	 Onset: 0-15 min Peak: 1 hour Duration: 16-18 hours Time (hours after injection)	LILLY
Humalog® Mix 50®	50% Insulin Lispro / 50% Insulin Lispro Protamine Suspension	Premixed Insulin Lispro	3ml Cartridge	 Onset: 0-15 min Peak: 2 hours Duration: 16-18 hours Time (hours after injection)	LILLY
PenMix® 30 & Mixtard® 30	30% Insulin Neutral / 70% Isophane (NPH)	Premixed Insulin	10ml Vial 3ml Penfill®	 Onset: 30 min Peak: 1-2 hours Duration: Up to 24 hours Time (hours after injection)	Novo Nordisk
NovoMix® 30	30% Insulin Aspart / 70% Insulin Aspart Protamine	Premixed Insulin Aspart	3ml FlexPen®	 Onset: 10-20 min Peak: Up to 2 hours Duration: Up to 24 hours Time (hours after injection)	Novo Nordisk
Basal plus: Basal insulin and rapid acting insulin (meal time insulin)					
Basal plus 1 meal time insulin					
Basal plus 2 meal time insulins					
Basal plus 3 meal time insulins (basal bolus)					

Lantus® SoloStar® pen prefilled with Insulin Glargine. Disposable		Luxura™ pen for Lilly insulin cartridges. Reusable	
Gilber AllStar® Pro pen for Lantus® (Insulin Glargine) cartridges. Reusable		Savvio™ pen for Lilly insulin cartridges. Reusable	
Apidra® SoloStar® pen prefilled with Insulin Glulisine. Disposable With a mealtime icon		Novopen® pen for Novo Nordisk® insulin cartridges. Reusable	
Cobalt/Blue AllStar® Pro pen for Apidra® (Insulin Glulisine) cartridges. Reusable		NovoMix® 30 FlexPen® prefilled with 30% Insulin Aspart / 70% Insulin Aspart Protamine. Disposable	
		NovoRapid® FlexPen® prefilled with Insulin Aspart. Disposable	

Before prescribing, please review the product data sheets. *Duration of action may vary between and within individuals.



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A Trick to Calculate Insulin Vial Supply

Calculating how many vials of insulin to supply can be tricky as prescriptions often list how many units patient need to administer and pharmacists need to work out how many cartridges to give. Here is a shortcut you can use:



A Trick to Calculate Insulin Vial Supply

Total Daily Units x 0.3 = 90 days vial supply or

Total Daily Units x 0.1 = 30 days vial supply

Please visit 'Pharmaceutical Calculations' in *Chapter 23 - Pharmacy Internship* for a full explanation on insulin calculations.

Type 1.5 Diabetes Mellitus (LADA)

[Diabetes NZ - Type 1.5 Diabetes](#)

Description

Latent Auto-Immune Diabetes of the Adult (LADA) is a type of diabetes that has features both from T1 and T2DM. It is an autoimmune disease thus we observe destruction of insulin-producing beta cells of the pancreas, however the person does not present as insulin dependent upon diagnosis, instead exhibiting insulin resistance. Due to this, this type of diabetes is commonly misdiagnosed as Type 2 which results in inappropriate treatment.

Signs & Symptoms

Some features of LADA may include:

- Being slim, or at least not overweight
- A history of autoimmune problems
- No ketoacidosis at diagnosis
- A positive GAD antibody test (blood test)

Pharmacological Treatment

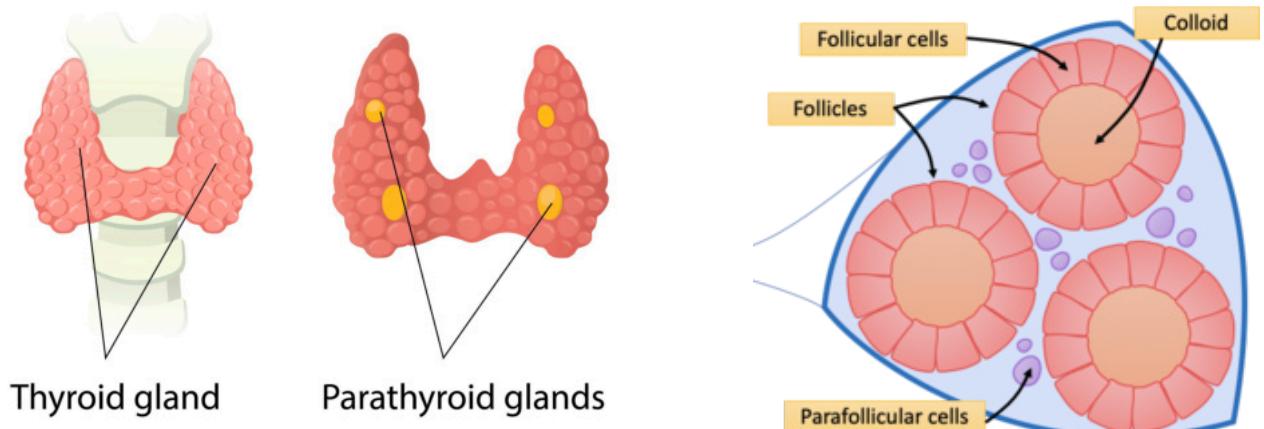
The patient may need insulin relatively soon after initial diagnosis – usually within 3-5 years

THYROID DISORDERS

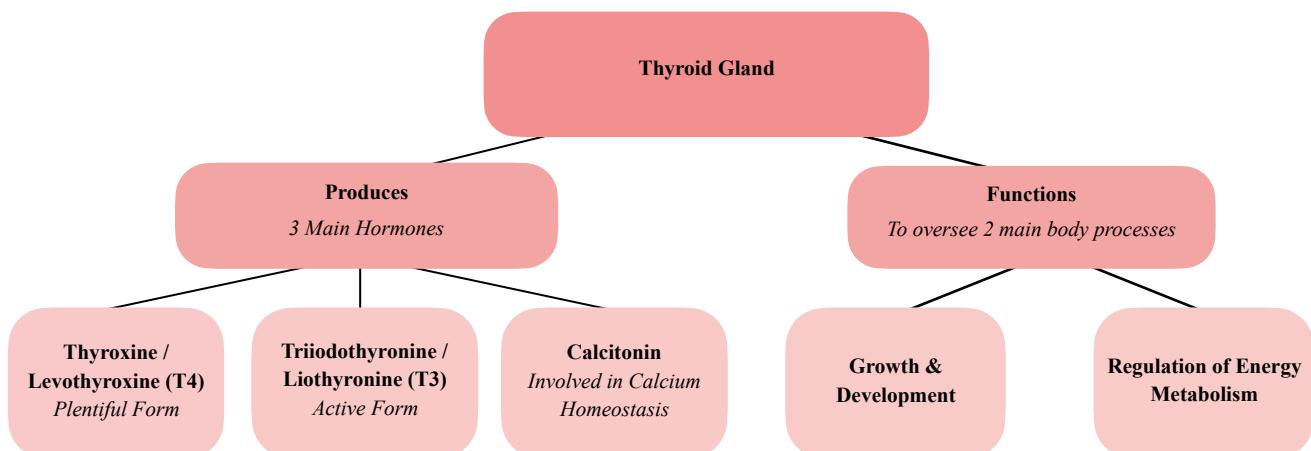
Overview of the Thyroid & Its Disorders

Introduction to the Thyroid Gland

The thyroid is a small gland located anterior to the neck found immediately below the larynx - it is in fact the largest endocrine gland in the human body!



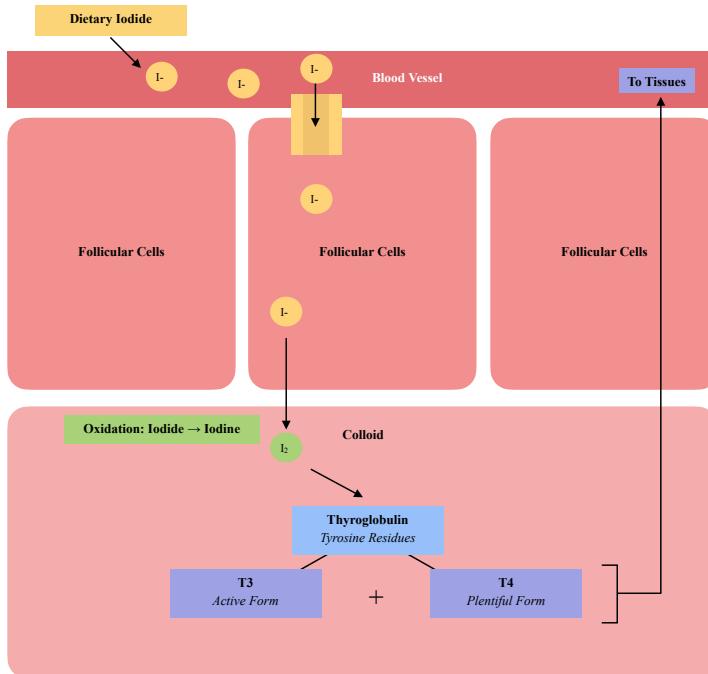
The thyroid gland is composed of follicles which are filled with fluid (colloid). The colloid mainly consists of thyroglobulin and inactive thyroid hormones. Each follicle is surrounded by follicular cells which function as the site of thyroid hormone synthesis. Parafollicular Clear (C) cells found in clusters between the follicles function to make the hormone calcitonin.



Thyroid Hormone Synthesis & Effects

In order to produce thyroid hormones, thyroid cells take up iodide, oxidise it to iodine, and then combine it with the amino acid tyrosine (which is a residue on the thyroglobulin protein) to from T₃ and T₄.

Overview of hormone synthesis in the thyroid follicle



Thyroid Hormone Effects

Following their release into the bloodstream, thyroid hormones are actively transported into target cells, mostly bound to carrier proteins in circulation to have effect on body processes. Due to the versatile functions of this gland, dysfunctions can have severe and widespread consequences.

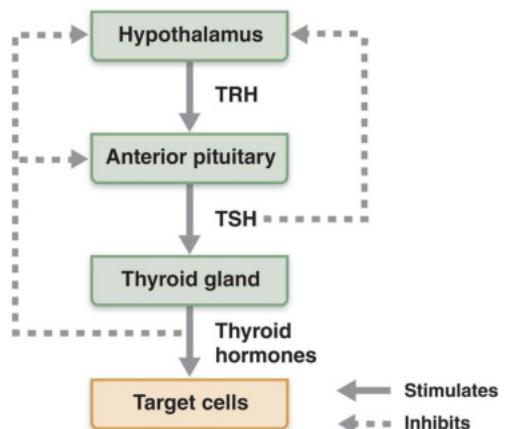
1. Growth & Development

Thyroid hormones increase carbohydrate, fat, and protein metabolism. This causes an increase oxygen consumption and heat production, causing an increase in basal metabolic rate.

2. Regulation of Energy Metabolism

The thyroid is required for the regulation of parathyroid hormone and calcitonin, alertness, skeletal muscle development, normal growth, maturation of the CNS, and sexual development and reproductive function. It also indirectly stimulates growth hormone production, and potentiates the effects of growth hormones on cells.

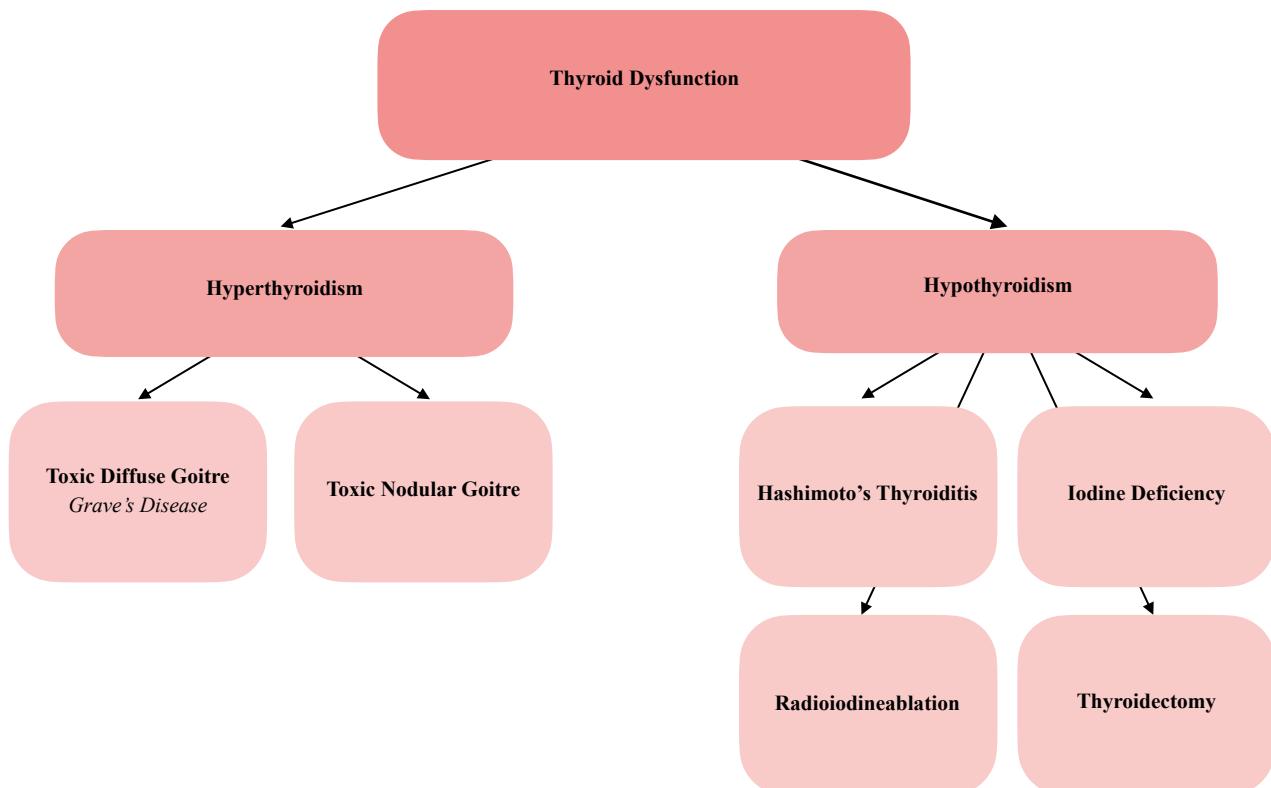
Thyroid Hormone Homeostasis



- TRH is released from the **hypothalamus** in response to stimuli.
- TSH is released from the **anterior pituitary** and acts on receptors in the membrane of thyroid follicle cells to control the steps in thyroid hormone synthesis.
 - High levels of T_3/T_4 suppress TRH and TSH
 - Low levels of T_3/T_4 stimulate TRH and TSH
- TSH has a negative feedback on TRH release

Overview of Thyroid Disorders

Now that we have established an understanding of how the thyroid gland works, let's look into disorders that affect it. The two main types of thyroid disease are *hypothyroidism* and *hyperthyroidism*. Both conditions can be caused by other diseases that impact the way the thyroid gland works.



Hypothyroidism and Hyperthyroidism

Suspicion Level	Hypothyroidism	Hyperthyroidism
High Suspicion	<ul style="list-style-type: none"> • Goitre • Delayed Reflexes 	<ul style="list-style-type: none"> • Thyroid bruit (secondary to increased blood flow) • Lid lag, Proptosis (bulging eyes)
Intermediate Suspicion	<ul style="list-style-type: none"> • Fatigue • Weight gain / difficulty losing weight (low metabolic rate) • Cold intolerances • Dry, rough, pale skin • Constipation • Facial swelling (oedema) • Hoarseness* 	<ul style="list-style-type: none"> • Fatigue • Weight loss & increased appetite (high metabolic rate) • Heat intolerances / sweating / heat intolerance • Fine tremor • Increased bowel movements • Fast heart / palpitations • Staring gaze
Low Suspicion Non-Specific Symptoms	<ul style="list-style-type: none"> • Coarse, dry hair, hair loss • Muscle cramps/muscle aches • Depression, irritability • Abnormal menstrual cycles, decreased libido • Bradycardia • Mental impairment: memory loss, slow speech 	<ul style="list-style-type: none"> • Nervousness • Insomnia • Breathlessness • Light or absent menstrual periods • Muscle weakness • Warm moist skin • Hair loss

*Note: The thyroid secretes hormones onto the larynx, hoarseness is the result of an underactive thyroid and this is usually a red flag.

Risk Factors for all Thyroid Disorders

- Age (especially hypo)
- Pregnancy (especially hypo)
- Female gender
- Drug-induced thyroid dysfunction: Amiodarone, Lithium



Drug Induced Thyroid Dysfunction: Amiodarone & Lithium

Amiodarone (Class 3 anti-arrhythmic) = hypo and hyper

- High iodide content, toxic effect on thyroid
- Decreased peripheral conversion of T₄ → T₃

Lithium (Mood Stabiliser) = hypo

- Decreases synthesis and secretion of thyroid hormones
- Monitor TSH, Free T₄, Free T₃

Diagnosing Thyroid Disorders

Note: Routine screening is not recommended, only test if symptomatic!

- TPO Antibody Test: autoimmune thyroid conditions (Hashimoto's, Grave's Disease)
- Radioactive iodine uptake test
- Patient History, Physical examination, Signs & symptoms
- TSH testing → T₃/T₄ reflex testing

Goals of Treatment for all Thyroid Disorders

- Relieve signs and symptoms
- Increase/Decrease thyroid hormone production
- Achieve euthyroid state
- Prevent complications

Thyroid Conditions

Hyperthyroidism

[NZF Anti-Thyroid Drugs](#) [BPAC Thyroid Dysfunction](#)

Description

Hyperthyroidism describes a thyroid disorder where there is an excessive production of thyroid hormones.

There are two types of hyperthyroidism: Grave's Disease and Toxic Nodular Goitre.

	Pathophysiology	Signs	Symptoms
Grave's Disease (Diffuse Toxic Goitre)	<p>Grave's disease is an autoimmune disease that causes hyperthyroidism due to the overstimulation of the thyroid gland via either:</p> <ol style="list-style-type: none">1. Antibodies to the TSH receptor2. Active mutations of the TSH receptor that imitate signal transduction.	<p>Hyperthyroidism can be subclinical or overt. TSH levels are low (suppressed) due to negative feedback mechanisms.</p> <ol style="list-style-type: none">1. <i>Subclinical (mild form)</i><ul style="list-style-type: none">• TSH: below normal• Free T₄/T₃: normal2. <i>Overt (more symptoms)</i><ul style="list-style-type: none">• TSH: below normal• Free T₄/T₃: above normal	<p>Both types of hyperthyroidism share the same symptoms, however:</p> <ul style="list-style-type: none">• Grave's: autoimmune condition• TNG: no ophthalmologic or dermopathy symptoms
Toxic Nodular Goitre (TNG)	<p>Toxic nodular goitre involves an enlarged thyroid gland that contains masses (nodules) which produce too much thyroid hormone.</p>	<p>Complications: Loss of bone density, CVD, Grave's ophthalmopathy, dermopathy (red swollen skin)</p>	<ol style="list-style-type: none">1. <i>Goitre</i><p>The overstimulation of the gland eventually produces the characteristic goitre we observe, in which the thyroid gland grows and continues to produce thyroid hormones.</p>2. <i>Grave's Ophthalmology</i><p>Immunologically mediated inflammatory reactions occur in the extrinsic muscles and fats of the eye, causing exophthalmos (bulging eyes).</p>3. <i>Grave's Dermopathy</i><p>Rare skin reactions may occur too</p>

Complications: Thyroid storm is a life-threatening health condition that is associated with uncontrolled hyperthyroidism combined with a trigger such as illness. During thyroid storm, an individual's heart rate, blood pressure, and body temperature can soar to dangerously high levels. Without prompt and aggressive treatment, thyroid storm is often fatal.

Pharmacological Treatment

1. First Line:

- Thionamides (immunosuppressants): Carbimazole → methimazole (MMI), Propylthiouracil (PTU)
- Non-invasive alternative: Radioactive iodine I¹³¹

2. Last Line:

- Potassium Iodate (KI)
- Partial Thyroidectomy (Surgery) + Lugol's Solution

3. Symptomatic relief of adrenergic symptoms:

- β -blockers: Propanolol, Nadolol

4. Treatment of exophthalmos (eyes): Grave's Disease

- Guanethidine eye drops
- Glucocorticoid (prednisolone or hydrocortisone) eye drops

	Drug	Mechanism of Action	Guidelines	Side Effects
Anti-Thyroid Drug Thionamides	[PRESCRIPTION] <i>1st Line Thionamides</i> Carbimazole (MMI - AFT)	↓ TPO = ↓ I- oxidation/binding = ↓ T ₄ /T ₃ synthesis Carbimazole (prodrug) is metabolised to its active metabolite, methimazole/thiamazole. • Inhibits TPO, therefore interfering with the synthesis of thyroid hormones. As this medicine does not interfere with the actual release of hormones, it takes 4-6 weeks for levels to deplete due to the long half life of T ₄ and current hormone stores.	<i>Block & Replace Method</i> High doses of carbimazole are given to completely block thyroid function. Levothyroxine is then added and titrated until euthyroid is achieved (~ 18 months). <i>Carbamazole — first line over PTU</i> • Contraindicated in pregnancy (palates cutis risk) • Single daily dose • Better overall safety profile (less hepatotoxicity risk) • Subsidised	Minor: Rash, Fever, GI upset (N/V) Moderate: hypothyroidism Serious (discontinue treatment!): Bone marrow suppression (agranulocytosis within first 3m), hypo-prothrombinhaemia
	[PRESCRIPTION] <i>1st Line Thionamides</i> Propylthiouracil (PTU)	↓ TPO AND ↓ T ₄ → T ₃ Propylthiouracil works more rapidly: • Inhibits TPO AND • Reduces peripheral conversion (deiodination) of T ₄ (plentiful) to T ₃ (active).	<i>Propylthiouracil — only use if carbimazole is contraindicated</i> • Can be used in pregnancy • Preferred during thyroid storms as it works faster but it can cause severe liver injury • Section 29 unapproved medicine!	Counselling: Report any signs of fever, sore throat, infection or dark urine (BMS)
Anti-Thyroid Drugs Iodine Treatment	[PRESCRIPTION] <i>Alternative First Line</i> Radioactive Iodine	Cytotoxic effect on the Thyroid (thyroid ablation without surgery) • Orally administered as a sodium salt in a single dose • Radioactive iodine is taken up in the same way as dietary iodide. However, upon incorporation into thyroglobulin, it emits β and γ radiation. • The short range of β particles allow absorption by local tissues to exhibit a cytotoxic effect, permanently destroying the thyroid gland. 80-90% of patients achieve a euthyroid state after a single dose. • Due to their short t _{1/2} of 8 days, the radiation effectively disappears by 2 months. • However, as the thyroid has been permanently destroyed, patient will need to take replacement hormones such as levothyroxine.	Avoid in pregnancy or breastfeeding <i>Patient groups:</i> all ages, where medical compliance is an issue, where patients have cardiac disease.	Risk of relapse after partial thyroidectomy. Risk of permanent hypothyroidism Risk of infertility, haematopoietic suppression and other consequences of radiation toxicity.
	[PRESCRIPTION] <i>Last Line</i> Potassium Iodate (Lugol's Solution)	↓ Iodination of Thyroglobulin → ↓ T ₄ /T ₃ synthesis Lugol's solution (KI) presents I- to the body in its stable form. An increase in iodine uptake temporarily inhibits the production and release of thyroid hormones and TPO activity by negative feedback mechanisms. • Reduces symptoms in 1-2 days with maximum effect in 10-15 days — short term use only	Avoid in pregnancy or breastfeeding (iodine-induced hypothyroidism in neonates) • LS is given preoperatively as an adjuvant treatment in Graves' disease planned for thyroidectomies to minimise intraoperative blood loss during surgery • Indication for treatment of severe thyrotoxicosis and thyroid storm.	Thyroid gland can adapt and resume hormone synthesis. Rash, drug fever, metallic taste, bleeding disorders, irritation of gastric mucosa (take with food), anaphylactic reactions
Symptomatic Relief	[PRESCRIPTION] <i>β-Blockers</i> Propranolol & Nadolol Initiate ASAP	Adrenergic Symptoms AND ↓ T₄ → T₃ • Symptomatic relief of palpitations, anxiety, heat intolerances • Can also inhibit peripheral de-iodination of T ₄ to T ₃ .	• Initiate at diagnosis of hyperthyroidism • Maintain until a euthyroid state is achieved.	GI upset, bradycardia, HF, hypotension, coldness of the extremities
	[PRESCRIPTION] <i>Eyes Drops</i> Guanethidine	Endocrine Exophthalmos in Grave's Disease Tx <i>Guanethidine</i> Antihypertensive drug which reduces the release of catecholamines, such as norepinephrine		N/A
	[PRESCRIPTION] <i>Glucocorticoid Eye Drops</i> Prednisolone, Hydrocortisone	Endocrine Exophthalmos in Grave's Disease Tx Particularly before radioactive iodine treatment		N/A
Surgery	[PRESCRIPTION] <i>Last Line</i> Partial Thyroidectomy	(Partial) removal of thyroid gland	<i>Indication:</i> if evidence of past medical treatment failure, intolerances to anti-thyroid medications, pressure from the goitre on the trachea or oesophagus, cosmetic issues (in young women)	Risk of permanent hypothyroidism.

Monitoring

- Carbimazole: Full blood count once a week during the first 6 weeks of treatment
- Radioactive iodine: Lifelong monitoring of TSH

Drug Interactions

- The addition of an antithyroid drug (e.g. carbimazole) may necessitate an increase in the warfarin dose.

Hypothyroidism

Thyroid and Anti-Thyroid Drugs NZF

Description

Hypothyroidism is a condition in which the thyroid gland doesn't produce enough thyroid hormone. It is the most common and frequently occurring form of thyroid disorders. There are four main causes:

Pharmacological Treatment

If Iodine deficient:

1. Iodine — if hypothyroidism is not the result of an iodine deficiency, iodine is not required as your thyroid does not have the ability to absorb it.

If Thyroid Hormone deficient: synthetic analogues of thyroid hormones

1. Levothyroxine (Thyroxine, T4)
2. Liothyronine (Tri-Iodothyronine, T3)

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Thyroid Hormone Replacement T₄ (Thyroxine)</i> Levothyroxine (Eltroxin, Synthroid, Mercury Pharmacy)	Supplies T₄ → T₃ peripheral deiodination Levothyroxine is a synthetic form of T ₄ . It is converted to T ₃ by deiodination in peripheral tissue, therefore the levels of T ₃ in the body consequently become entirely dependent on the exogenously administered T ₄ . Start low and increase dose slowly due to increase in metabolic activity → ↑ cardiac activity → angina, arrhythmia, MI. • Be careful in elderly and IHD.	Take dose once daily before breakfast (on empty stomach or 4 hours after food) The following drugs will increase levothyroxine dose requirements: <i>Decrease gut absorption</i> Calcium, iron supplements, aluminium hydroxide (antacids), cholestyramine <i>CYP Inducers (Metabolism)</i> Phenytoin, Carbamazepine, Estrogen (HRT), Rifampicin <i>Drug-Food Interactions</i> Soy, high fibre diet	At excessive doses, the drug can cause symptoms of hyperthyroidism: <i>GI Problems</i> diarrhoea, headache, flushing, sweating, heat intolerance, fever, increased appetite <i>Heart Problems</i> tachycardia, arrhythmia, palpitations, HTN, restlessness, excitability, insomnia
[PRESCRIPTION] <i>Thyroid Hormone Replacement T₃ (Liothyroxine)</i> Triiodothyronine	Much more rapid onset of action due to a shorter half life compared to T ₄ . • Supplies level of T ₃ hormone that the thyroid would normally produce under healthy working conditions. Section 29 Drug — Unfunded	T ₃ is indicated for 2 conditions: 1. Severe hypothyroidism (oral) 2. Hypothyroid coma (IV): Myxedema coma is a life threatening condition that can be caused by infection, heart failure, stroke, surgery.	<i>Muscle Problems</i> muscle weakness, tremor <i>Hormonal Problems</i> Menstrual irregularities, impaired fertility
[PRESCRIPTION] <i>Iodine (if deficient)</i>	Iodine intake if iodine deficient . Does not help with autoimmune disease.	N/A	N/A

Monitoring

Warning: Brands are **non-interchangeable** (same active ingredient but different excipients and bioavailability) without consultation with GP.

TSH in Levothyroxine Dose Adjustments

Titrate according to blood tests results.

- Monitor TSH every 6-8 weeks following treatment initiation until stable (due to long T₄ half life)
- Monitor every 6-12 months once stable

- Monitor TSH every 6 weeks if brand change occurs.

Drug Interactions

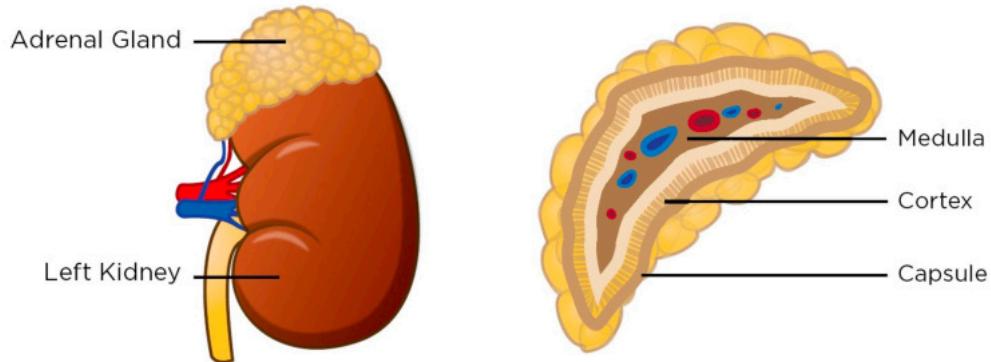
- In people with hypothyroidism who are also taking warfarin: the addition of thyroxine usually results in an increased anticoagulant effect and a reduction in the dose of warfarin is necessary.

ADRENAL DISORDERS

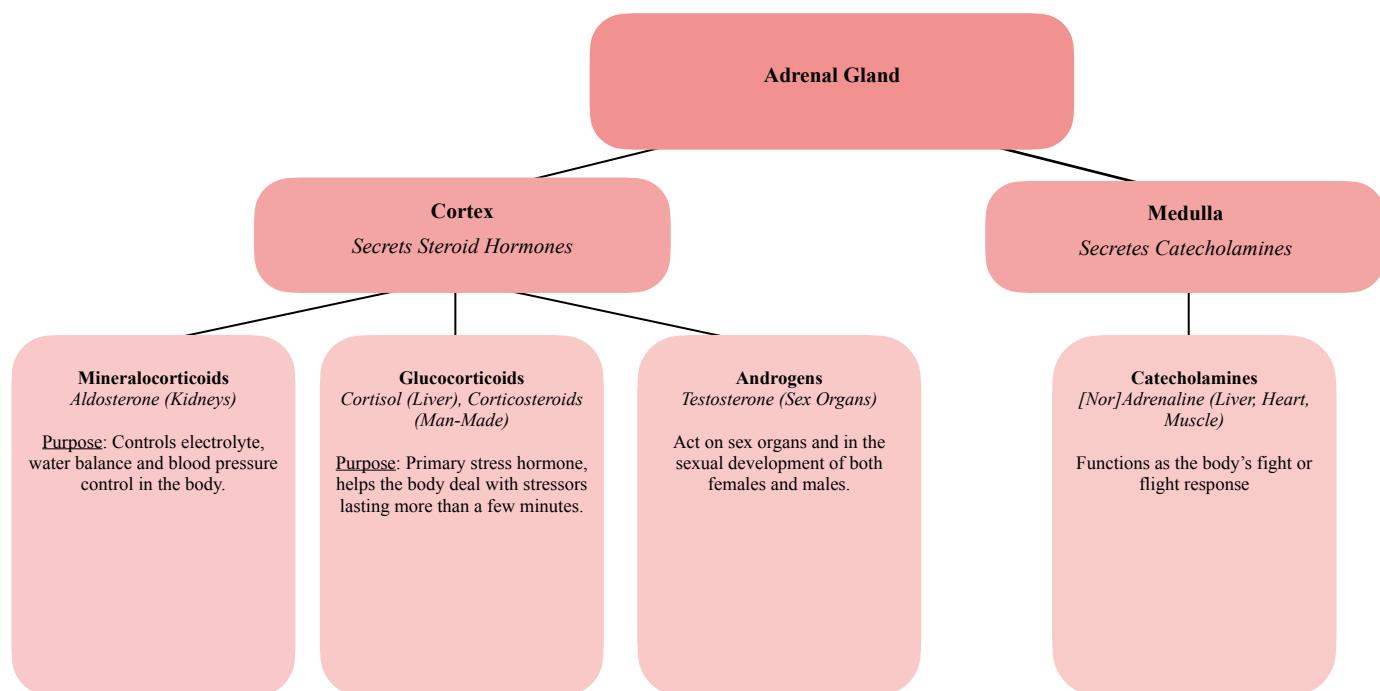
Overview of the Adrenal Glands & the HPA Axis

Introduction to the Adrenal Glands

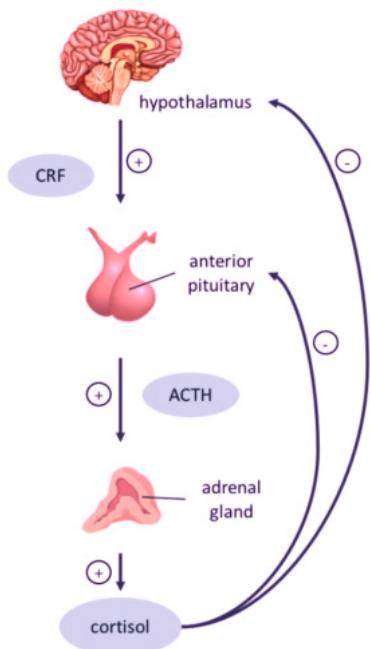
The adrenal glands are a pair of endocrine glands situated on top of both kidneys.



Each gland consists of two main parts: cortex (the outer region) and medulla (the largest region) which respectively secrete steroid hormones and catecholamines. These hormones help regulate your metabolism, immune system, blood pressure, response to short-term and long-term stress, and other essential functions.



The Hypothalamic-Pituitary-Adrenal Axis (HPAA)



The hypothalamic pituitary adrenal (HPA) axis is our body's central stress response system. It describes the interaction between the aforementioned structures to produce the primary stress hormone, cortisol.

Hypothalamus (CRF) → AP (ACTH) → Adrenal Glands (Cortisol)

The purpose of cortisol is to help the body deal with stressors lasting longer than a few minutes e.g. wound healing and minimising injury pain.

Under stress, our initial response is immediately mediated by the sympathetic nervous system and thus adrenaline. However, 10 seconds later, the HPA axis is activated.

A Focus on Cortisol

In Stress

In order to aid the body through a stressful situation, it exerts the following effects:

- Increase BP and cardiac output: provides more blood to skeletal muscles if physical exertion is required
- Increase blood glucose: increased availability for tissue repair
- Curbing of functions that are nonessential or harmful in a fight-or-flight situation e.g. reproductive activity

Day-to-Day

Cortisol also helps in our day-to-day life by:

1. Controlling sleep cycle
2. Regulating immune response
3. Stimulates fat and carbohydrate metabolism

Long Term Risks of HPAA Activation

While the proper functioning of the HPAA is essential for stress-responses, overstimulation, and thus consistently elevated cortisol levels, can cause problems. Although many things can cause repeated HPAA activation - there is a predominant association with T2DM, obesity and CVD.

- Suppression of immune system response
- Detrimental effects on memory and cognition
- Mood disorders (depression)
- Increased anxiety
- Metabolic effects (increases appetite, excess fat deposition, insulin resistance)

Long Term Risks of Glucocorticoids (Exogenous Corticosteroids)

1. HPA Axis Suppression

Glucocorticoids are often prescribed for their pronounced anti-inflammatory effects. However, with prolonged use, negative feedback mechanisms cause temporary suppression of the HPA axis. This causes a complete arrest in the production of endogenous steroids, resulting in the body becoming reliant solely on the exogenous supply.

As this impairs the body's ability to respond to stress, **tapering of oral* glucocorticoids is critical** when stopping these medications in order to allow the body's mechanism to return to normal. Failure to do this can result in complications such as opportunistic infections, poor host defence, morbidity and death.



Topical Corticosteroids

Very potent topical corticosteroids can cause temporary HPA axis suppression after a few week's treatment due to systemic absorption. However, this resolves upon cessation of the topical corticosteroid, without the need for dose tapering

2. Side Effects

Topical Corticosteroids	Oral Corticosteroids
Effects on Skin (if inappropriately used)	Effects on Carbohydrate, Protein and Fat metabolism
<ul style="list-style-type: none">• Skin thinning• Stretch marks• Easy bruising• Enlarged blood vessels• Susceptibility to skin infections• Localised increase in hair thickness and length• Allergy	<ul style="list-style-type: none">• Promotes gluconeogenesis• Can precipitate hyperglycaemia (diabetics need to monitor)• Skeletal muscle wasting• Hypertension (mineralocorticoid effects)• Redistribution of body fat ('moon face', 'buffalo humps')• Elevation of mood• Skin thinning (striae)• Acne• Bruising

Adrenal Conditions

Adrenal Insufficiency

Description

Adrenal insufficiency is a disorder that occurs when your adrenal glands don't produce enough of certain hormones. The different types are characterised by the cause of the insufficiency.

Type	Cause	Pathophysiology
Primary (Addison's Disease)	Autoimmune Condition	The adrenal glands produce insufficient levels of cortisol and aldosterone <ul style="list-style-type: none">This causes high ATCH, low cortisol levels, and low aldosterone levels (low Na⁺, high K⁺). Symptoms develop slowly and often go unnoticed until stressors worsen these symptoms.Patients are likely to have other accompanying autoimmune diseases.
Secondary	Pituitary dysfunction	Adrenal insufficiency caused by a problem with the pituitary (secondary) <ul style="list-style-type: none">May be caused by tumours, surgery, or radiation.
Tertiary	Hypothalamus dysfunction	Adrenal insufficiency caused by a problem with the hypothalamus (tertiary) <ul style="list-style-type: none">May be caused by tumours, surgery, or radiation.
Steroid-Induced	Synthetic corticosteroids	Adrenal insufficiency caused by abrupt cessation of long-term synthetic corticosteroid use <ul style="list-style-type: none">Can be severe and life-threateningIt is caused by suppression of the hypothalamic-pituitary-adrenal (HPA) axis due to the negative feedback loop. While the timing of recovery is variable, it can take anywhere from 6-12 months for the adrenal axis to operate again.

Signs & Symptoms

- Non-specific: Weakness, fatigue, hyperpigmentation (darkening of skin), nausea, dizziness upon standing, weight loss, decreased appetite.

Complications: Untreated adrenal insufficiency can eventually lead to **Addisonian crisis**. As the glands naturally function to produce two to three times the amount of cortisol in response to high-stress situation (injury, infection or illness), the inability to do so leads to a crisis.

Pharmacological Treatment

1. Addison's Disease

- Replace absent hormones (e.g. Glucocorticoids: hydrocortisone, fludrocortisone)
- Note:* Adverse effects of high-dose glucocorticoids **should NOT** occur in Addison's disease.

2. Steroid-Induced Adrenal Insufficiency

- Saline and glucose (for volume depletion, hypoglycaemia, dehydration)
- Corticosteroid (hormone replacement)

Note: Patients may require glucocorticoid replacement therapy (**tapering of doses**) after the chronic use of corticosteroids in periods of stress such as trauma, surgery or acute illness until the full recovery of adrenal function.

Adrenal Crisis

Description

The body has limited or no aldosterone and cortisol production. It is often a complication of adrenal insufficiency or caused by rapidly stopping corticosteroid medicines. The body needs more cortisol than usual during times of physical stress (e.g. illness, serious injury, surgery). This can lead to shock and cardiac arrest, and ultimately death if not treated right away.

Signs & Symptoms

- Sudden, severe pain in lower back/abdomen/legs, N/V/D, weakness, confusion, loss of consciousness
- From lack of cortisol: **Life-threatening low BP**, low blood glucose, low plasma Na⁺, high plasma K⁺.

Cushing's Syndrome & Disease (Hypercortisolism)

Description

Cushing's is a disorder that occurs when the body is exposed to high levels of cortisol for prolonged periods of time due to an excessive production (either endogenous or exogenous).

- Cushing's Disease (endogenous): The body produces too much cortisol e.g. pituitary or adrenal tumour
- Cushing's Syndrome (exogenous): The usage of large amounts of corticosteroids medications.

Signs & Symptoms

Early osteoporosis, myopathy, easy bruising, fat distribution, moon face, stretch marks, thin skin, high BP, high blood glucose, stomach ulcers.

Complications: Diabetes, cardiac problems, life-threatening illness, irreversible organ damage, early death

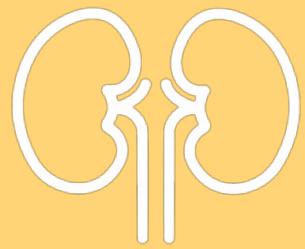
Treatments

Cushing's Disease

- Surgery (curative): removing the tumour
- Medication
- Radiotherapy

Cushing's Syndrome

- Gradual reduction of steroid drug dose (aiming for a **1 for 1 titration duration**)
 - Eg. if the patient was on the steroid treatment for 8 weeks, titrate the dose over 8 weeks



CHAPTER 10

THE RENAL SYSTEM



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Chapter 10

The Renal System

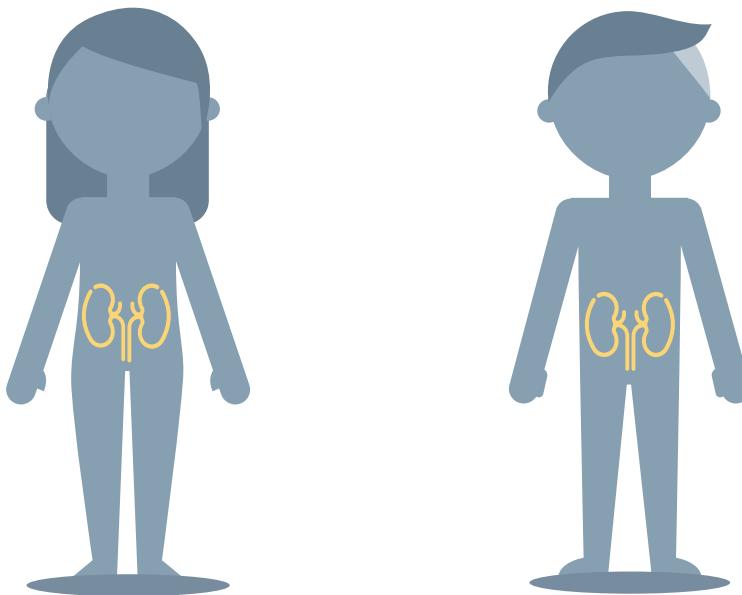
General Overview of the Kidneys

Chapter Resources

The [Renal Drugs Handbook](#) is a great resource to use for this Chapter.

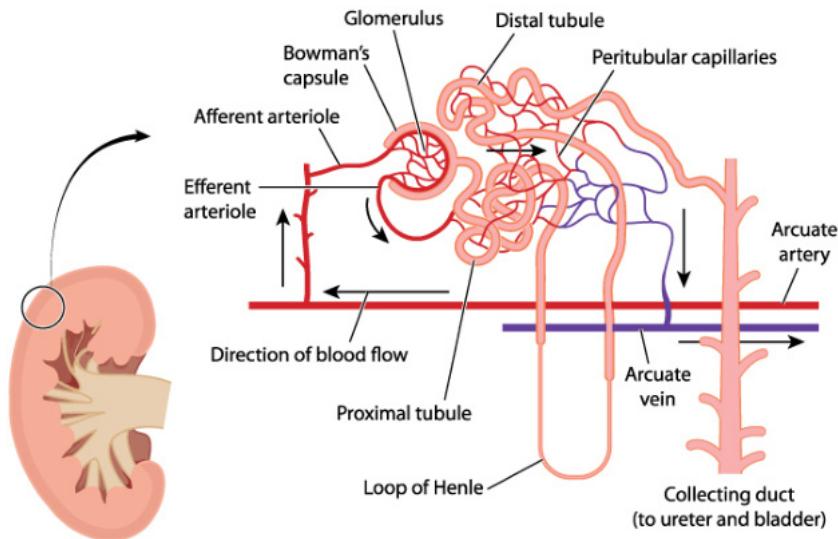
Introduction

The kidneys are a pair of bean-shaped organs situated in the retroperitoneal cavity on either side of the spine — with the left kidney being positioned a little higher than the right.



Each kidney has around approximately a million nephrons (tiny filters). Each nephron comprises:

1. Renal corpuscle (*glomerulus*)
2. Renal tubules:
 - a. *PCT*: resorbs water, glucose, electrolytes
 - b. *Loop of Henle*: resorbs H_2O , Na^+
 - c. *DCT*: controls Na^+ , K^+ , H^+ , HCO_3^-



Kidney Function

So what do the kidneys actually do? The kidneys aim to maintain a stable internal environment (homeostasis)

- they have four main functions, with their respective impairments shown in red



Blood Filtering

The purpose of the kidneys can be essentially simplified to 'blood filtering.' A third of the heart's pumped blood is sent to the kidneys to remove waste, control the body's fluid balance, and maintain the right level of electrolytes. Once filtered, the blood returns to the body and the waste is excreted as urine.

1. Excretory Function → Cardiovascular Module

- Water (**oedema**)
- Metabolic Waste (**reduced waste clearance**)
- Xenobiotics (**reduced clearance**)

2. Regulatory Function → Cardiovascular, Endocrine & Respiratory Module

- Extracellular Fluid Volume
- Electrolyte Balance (**electrolyte disturbances**)
- Osmolality, pH (**impaired pH control**)
- Urine volume and composition

} Drugs that impact the RAAS system } Drugs that impact diuresis

3. Endocrine Function

- EPO production = increase RBCs) (**anaemia**)

4. Metabolic Function

- Vitamin D, bone health (**metabolic bone disease**)

Renal Laboratory Investigations

Measuring Kidney Function

In order to measure kidney function - we can either look at the excretory function or the regulatory function.

- Renal Blood Flow: ~ 1200-1500mL/min
- Glomerular Filtration: ~ 100mL/min
- Urine Output: 1-2 mL/min

Function	Variable	Function	Lab Value	Limitations / In CKD
Excretory Function	Glomerular Filtration Rate (GFR)	The GFR shows how well the kidneys are filtering - we can obtain it through three ways: <ol style="list-style-type: none"> 1. Calculations - GFR Estimations <ul style="list-style-type: none"> Cockcroft Gault Equation: eCrCl MDRD + CKD-EPI: eGFR Please see the next page for more information on eCrCl vs eGFR and when to use either. 2. 24h Urine Samples - GFR True Value 3. Clearance of other items: <ul style="list-style-type: none"> Cystatin C Clearance Xenobiotic Clearance (inulin, radioisotopes) 	eGFR normalised to BSA (1.73m ²) <i>Adult Male:</i> 50-110 umol/L <i>Adult Female:</i> 45 - 90 umol/L	We will focus on the limitations of the calculations: Limitations of CrCl (Cockcroft Gault Equation) Creatine is a muscle waste-by product- we use it to estimate the GFR as it is filtered and not reabsorbed. However it is not a good marker of renal function: <ul style="list-style-type: none"> It is influenced by muscles, mass, age, sex, diet. It overestimates the GFR in the elderly and obese. Is a poor predictor of GFR in the malnourished, those with low muscle mass, <18 and in those with rapidly changing renal function. It is tubularly secreted in addition to being filtered - making the CrCl is always slightly higher than true GFR We can combat a few of these limitations by choosing between Ideal Body Weight (IBW) or the Actual Body Weight (ABW). Use the lesser of either e.g if the actual body weight is less than the IBW, use this value. Limitations of eGFR (CKD-EPI Equation) <ul style="list-style-type: none"> eGFR is normalised to a BSA of 1.73m² - adjust for individual patients.
		• Urea is the end product of protein metabolism. Amino acids are catabolised in the liver and the amino group is removed through the urea cycle, and urea is excreted renally	<i>Adults (All)</i> 3.2 - 7.7 mmol/L	• Although almost all urea is filtered by the glomerulus, about 50% is reabsorbed in the tubules - this increases in dehydration. Due to this it is not an ideal marker. • Furthermore many other non-renal conditions can increase urea (e.g. hypovolaemia, shock, burns, dehydration, HF)
Regulatory Function	Potassium (K ⁺)	<ul style="list-style-type: none"> Concentrated in ICF, is free filtered in the kidney but then <u>completely</u> reabsorbed. ACEIs, ARBs, Diuretics (drugs used to control proteinuria in CKD) can dangerously lower the GFR and exacerbate the hyperkalaemic response which explains the purpose of potassium monitoring in renal injury. 	<i>In plasma:</i> 3.2 - 5.2 mmol/L	<ul style="list-style-type: none"> Renal elimination controlled by aldosterone via distal tubular secretion. CKD impairs K⁺ homeostasis, causing its accumulation - due to the RAAS response, secretion of K⁺ ions due to aldosterone means that K⁺ lab tests may look normal up until CKD 1-3 with hyperkalaemia being more likely observed in CKD 4 or 5 (> 5 mmol/L causes muscle weakness, fatigue, nausea)
	Sodium (Na ⁺)	<ul style="list-style-type: none"> Concentrated in the ECF, is free filtered but reabsorbed primarily with water in the proximal tubule. Major regulatory control sites are the distal tubule and the collecting ducts. 	<i>In plasma:</i> 135 - 145 mmol/L	<ul style="list-style-type: none"> CKD impairs Na⁺ homeostasis, normally only 1-3% being excreted but progressive renal failure can cause fluid retention, volume expansion, high blood pressure and oedema. Consequently, hypernatraemia and hyperkalaemia result from renal failure.

Regulatory Function	Arterial Blood pH	<ul style="list-style-type: none"> Blood pH (7.36 - 7.44) is tightly controlled between the renal and respiratory system. Many metabolic functions produce an excess of acidic compounds which leads to acidosis. In this case, bicarbonate is resorbed back. The lungs and kidney produce a ratio of HCO_3^- and CO_2 which regulates tightly the arterial pH - where bicarbonate is reabsorbed in the tubule in exchange of H^+ ions. 	<i>Arterial:</i> 7.36 - 7.44 <i>Bicarbonate:</i> 22 - 28 mmol/L	<ul style="list-style-type: none"> Low/high CO_2 = respiratory alkalosis/acidosis Low/high HCO_3^- = metabolic acidosis/alkalosis CKD causes fluid retention which reduces H^+ excretion, causing a tendency towards acidosis. This contributes to loss of bone, muscle wasting, hyperparathyroidism, increased mortality, and accelerated progression of CKD.
	Proteinuria	<ul style="list-style-type: none"> Measured using a spot urine test and ACR (Albumin: Creatinine Ratio) The glomerulus filters plasma proteins, such as albumin (MW: 67 kDa) which is reabsorbed by the proximal tubules. 	<i>Macroalbumin</i> 30 - 300 mg/24h <i>Macroalbumin</i> >300 mg/24h	<ul style="list-style-type: none"> Reabsorption process is halted in kidney failure and consequently, leakage of albumin & proteins in the urine is a risk factor for the progression of kidney disease and CV morbidity and mortality. Note: Albuminuria can occur acutely after exercise, fever, UTIs and manifests in early diabetes.

A note on eCrCl and eGFR

As we've established there are two calculations available to us to estimate the Glomerular Filtration Rate (GFR) of kidneys:

1. Cockcroft Gault Equation (calculates Creatinine Clearance - which estimates the GFR)
2. CKD-EPI Equations (calculates the estimated GFR)

While both equations aim to estimate the GFR, **they are not equal!** CrCl measures the excretion of waste while eGFR measures fluid filtration. They thus have different limitations and serve different purposes - for example CrCl is used to guide drug dosing while eGFR is used to guide CKD staging. Please find a table below on which equation might more be more suitable based on patient characteristics.

Impact of Patient Characteristics on estimates of Renal Function		
Patient Characteristic	eCrCl	eGFR
Reduced GFR	May be less accurate	May be more accurate
Actual BSA >1.73 m ²	Depends on body weight only, height is not incorporated	Actual GFR is >30% higher for taller or heavier individuals
Older age (>70 years)	Acceptable	Acceptable
Younger Age (<40 years)	May be less accurate	May be more accurate
Obesity (BMI > 30kg/m ² or weight >120 kg)	Overestimates GFR (use adjusted ideal body weight)	Underestimates GFR, use deindexed eGFR
BMI <18.5 kg/m ² or weight <60 kg	Acceptable, use ABW	Overestimates GFR, use deindexed eGFR

Please visit 'Pharmaceutical Calculations' in *Chapter 23 - Pharmacy Internship* for a full explanation on how to use these equations or alternatively, use an online calculator: [MDCalc](#)

The Renin-Angiotensin-Aldosterone System (RAAS)

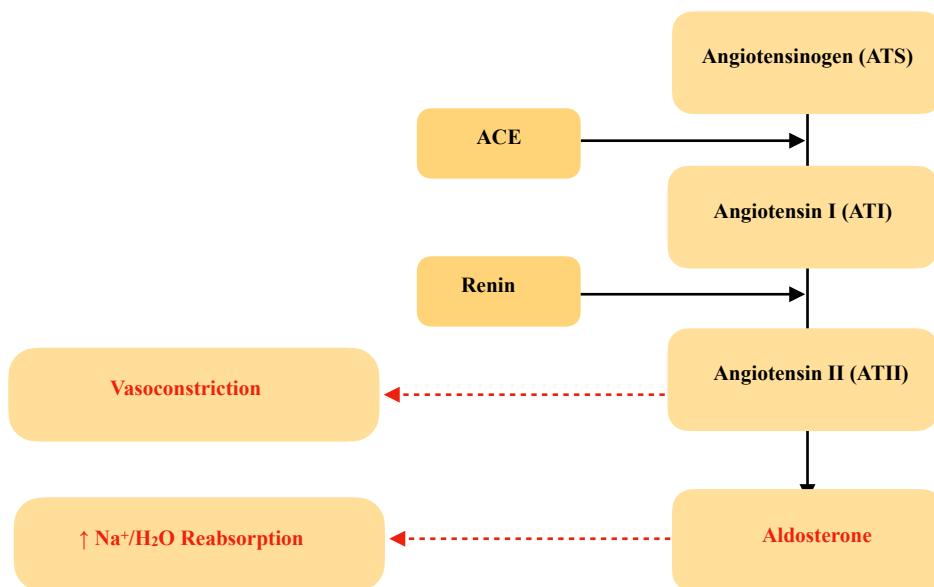
Function of the RAAS

The RAAS, much like the kidneys, also functions to maintain homeostasis:

- *CV System*: Regulation of Blood Pressure
- *Renal System*: Regulation of Extracellular Fluid Balance, Electrolyte Balance

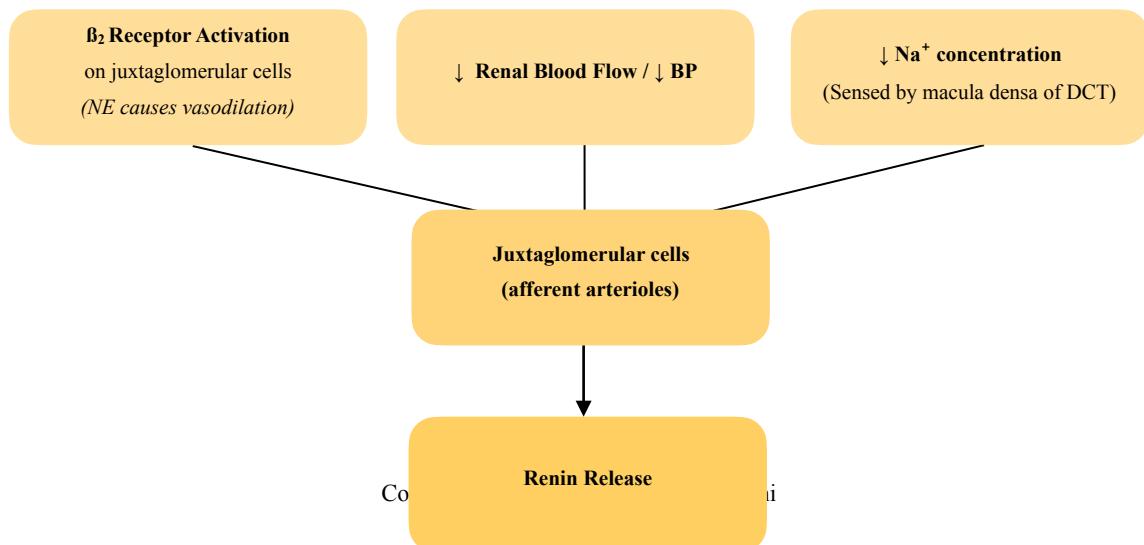
The RAAS thus plays a major role in multiple important pathologies (CKD, HTN, HF, MI, Diabetic nephropathy) - this is because when it becomes impaired in renal disease, the following can occur:

1. Impaired potassium homeostasis (excess K^+)
2. Impaired sodium/water homeostasis (excess Na^+ / H_2O)
3. Hypertension (excess aldosterone)
4. **Cardio-Renal Syndrome** (co-morbid cardiac & renal disease where each exacerbates the other; HF/CKD)



Focus on the Renin Component of the RAAS

Renin is a protease secreted by and stored in the juxtaglomerular cells within the afferent arterioles of the kidneys. The primary purpose of renin is to regulate blood pressure - there are 3 determinants for its release:



Overview of Pharmacological Interventions

Targeting the RAAS System

We can thus target various parts of the RAAS System in order to achieve effects on blood pressure, fluid/electrolyte balance and so forth.

Drug	Description
[PRESCRIPTION] ACEIs/ARBs Enalapril, Candesartan	↓ BP, ↑ Renal Blood Flow via predominantly EFFERENT arteriole dilation, ↓ Systemic Vascular Resistance <i>Indication: HTN, CVD, HF, Diabetic nephropathy</i> Renoprotective as vasodilation reduces the pressure on the glomerulus which in turn reduces proteinuria (main causes of renal failure due to the inflammatory reaction that occurs upon protein re-absorption). However, paradoxically can cause renal injury if too much pressure is taken off.
[PRESCRIPTION] NSAIDs	↓ Renal Blood Flow due to AFFERENT vasoconstriction Vasoconstriction reduces blood flow, which can lead to kidney injury
[PRESCRIPTION] Loop Diuretics Furosemide, Bumetanide	↑ Rate of Urine Flow via Natriuresis (water follows sodium), ↓ ECF, ↓ Body Weight Maximal Effect is ~ 20 - 25 % <i>Indication: HTN (although not anti-hypertensives themselves), HF, Renal Failure (reduces ECF)</i> • Loop Diuretics inhibit the Na/K/2Cl (NKCC2) co-transporter in the thick ascending loop of Henle . By the time the filtrate reaches this part, around ~75% of filtered sodium has been reabsorbed in the body; maximum effect is 20 - 25 % • However, this effect may seem paradoxical as loop diuretics also inhibit NKCC2 at the macula densa cells (distal tubule). These cells will sense a reduction in sodium and thus stimulate renin release to increase BP. <u>Diuretic Breaking</u> Loop diuretics have a steep dose response with a large maximum natriuretic effect. Progressive renal impairment will reduce the diuretic effect, requiring a higher dose of diuretics.
[PRESCRIPTION] Thiazide Diuretics Bendrofluorothiazide	↑ Rate of Urine Flow via Natriuresis (water follows sodium), ↓ ECF, ↓ Body Weight Maximal Effect is ~ 5 % <i>Indication: Treatment of HTN (although not anti-hypertensives themselves), HF, Renal Failure (reduces ECF)</i> • Thiazide Diuretics inhibit the activity of the NaCl (NCCT) co-transporter in the distal convoluted tubule . Over 95% of the filtered Na ⁺ load has already been reabsorbed by the time filtrate reaches the DCT; maximum effect is 5%. <u>Diuretic Breaking</u> In contrast to loop diuretics, thiazides have a flat dose response and a much lower maximum effect, beyond which increasing the dose will only increase side effects — Contraindicated in CKD
[PRESCRIPTION] K ⁺ Sparing Diuretics Triamterene	↑ Rate of Urine Flow via Natriuresis (water follows sodium), ↓ ECF, ↓ Body Weight Maximal Effect is ~ 2 % <i>Indication: Treatment of HTN (although not anti-hypertensives themselves), HF, Renal Failure (reduces ECF)</i> • Potassium Sparing Diuretics inhibit the activity of epithelial sodium channels in the late distal convoluted tubule and collecting duct . It has very limited effectiveness since >98 % of the filtered Na load has already been reabsorbed by the time filtrate reaches the collecting duct; maximum effect is 2%.
[PRESCRIPTION] Aldosterone Antagonists & K ⁺ Sparing Diuretics Spironolactone	↑ Rate of Urine Flow via Natriuresis (water follows sodium) ↓ ECF, ↓ Body Weight Maximal Effect is ~ ? % <i>Indication: Treatment of HTN (although not anti-hypertensives themselves), HF, Renal Failure (reduces ECF)</i> • Aldosterone Antagonists competitively inhibit the binding of aldosterone to the mineralocorticoid receptor . These are the only class of diuretics that do not enter the tubule cell from the apical (tubular) side. • Spironolactone is potassium-sparing as it doesn't act on potassium directly, thereby preventing hypokalaemia
Other	β-Blockers, Vasodilators, Centrally Acting Sympatholytics (methyldopa, clonidine)



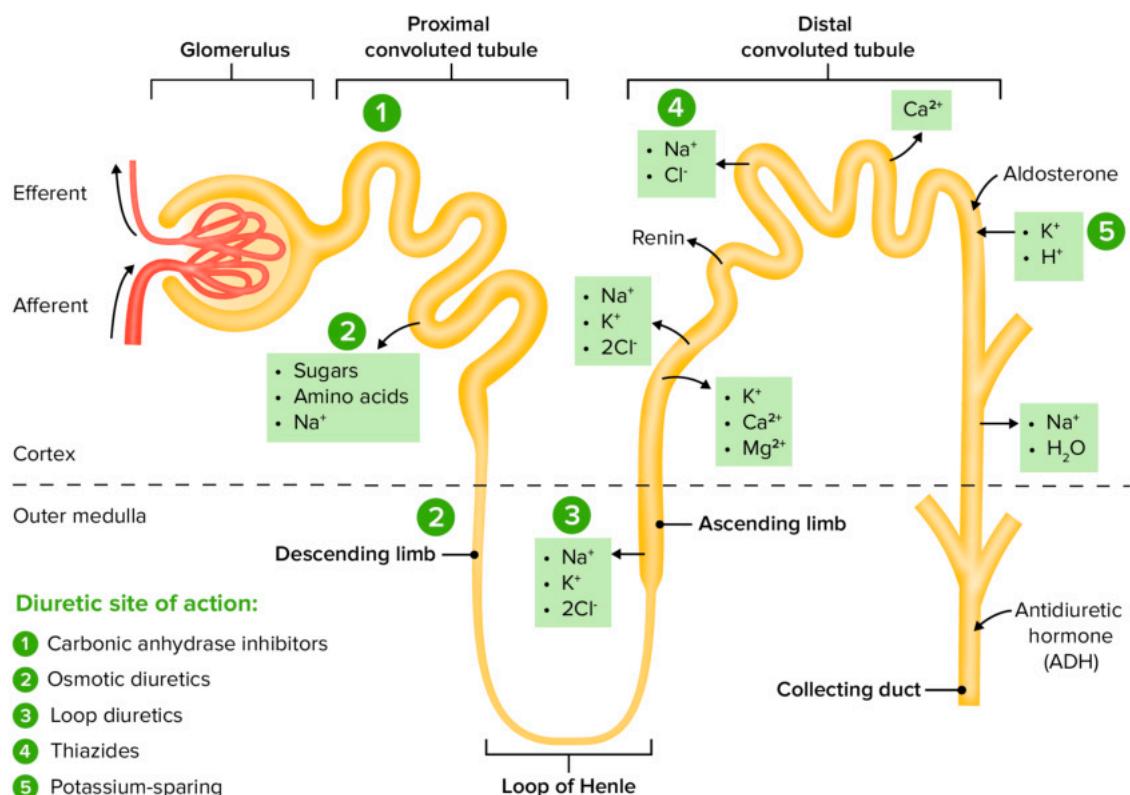
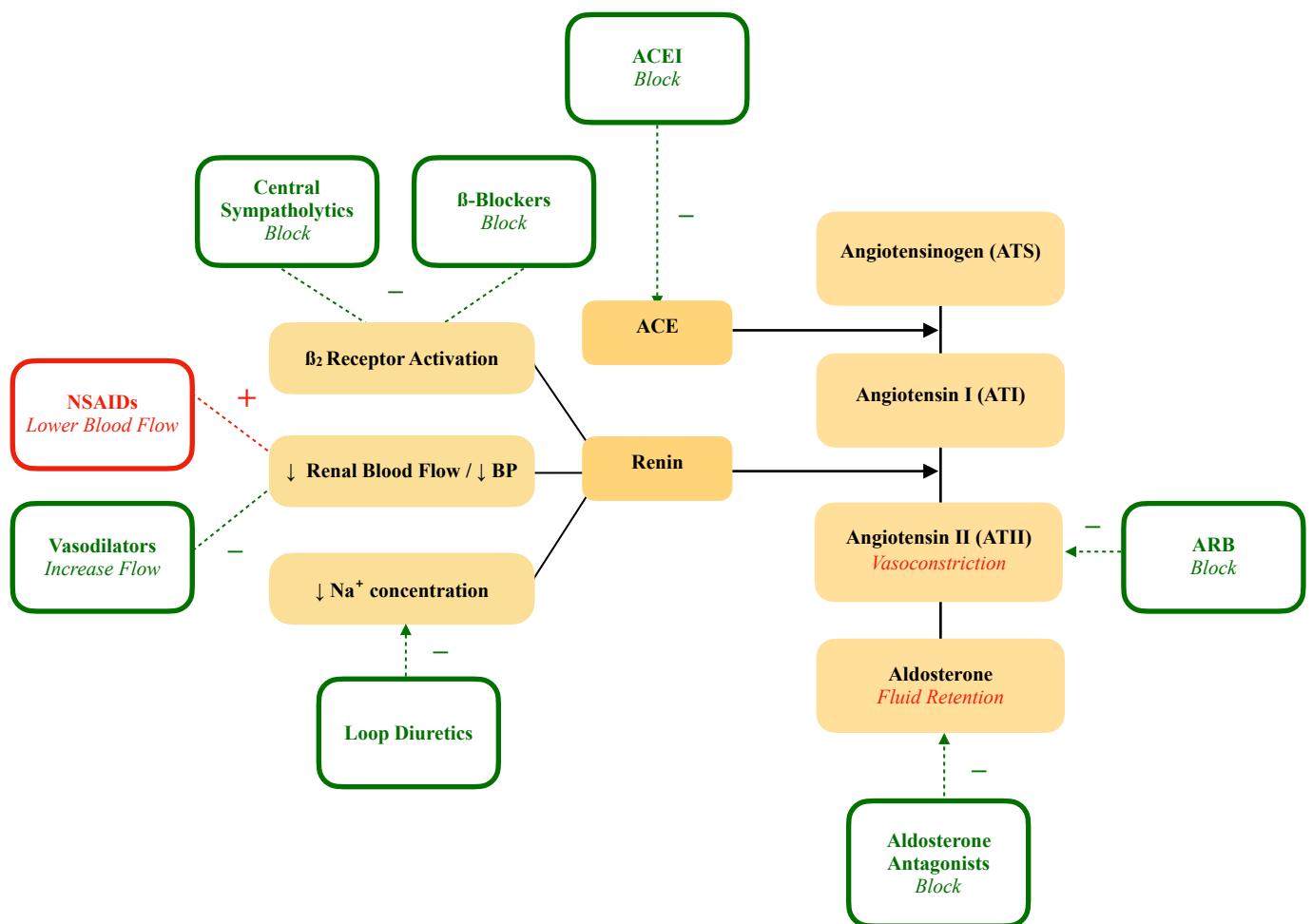
Diuretic Breaking

Diuretic breaking is defined as a decrease in a patient's response to a diuretic after receiving the first dose. This is because the time course of diuretics is finite due to the renal compensatory mechanism (e.g RAAS) re-establishing the Na⁺ balance.

A Note: Triple Whammy (ACEI/ARB + NSAID + Diuretic)

Out of the above listed medications - 3 of them should not be combined due to the potential for severe kidney injury. Pharmacists should be wary of prescriptions containing these medications at the same time and should screen patients purchasing OTC NSAIDs.

1. ACEI/ARB: **vasodilation** of efferent arterioles decrease glomerular capillary pressure & reduce GFR
2. NSAIDS: **vasoconstriction** of afferent arteriole reduces blood flow to nephron & reduces GFR
3. Diuretics: decrease blood volume

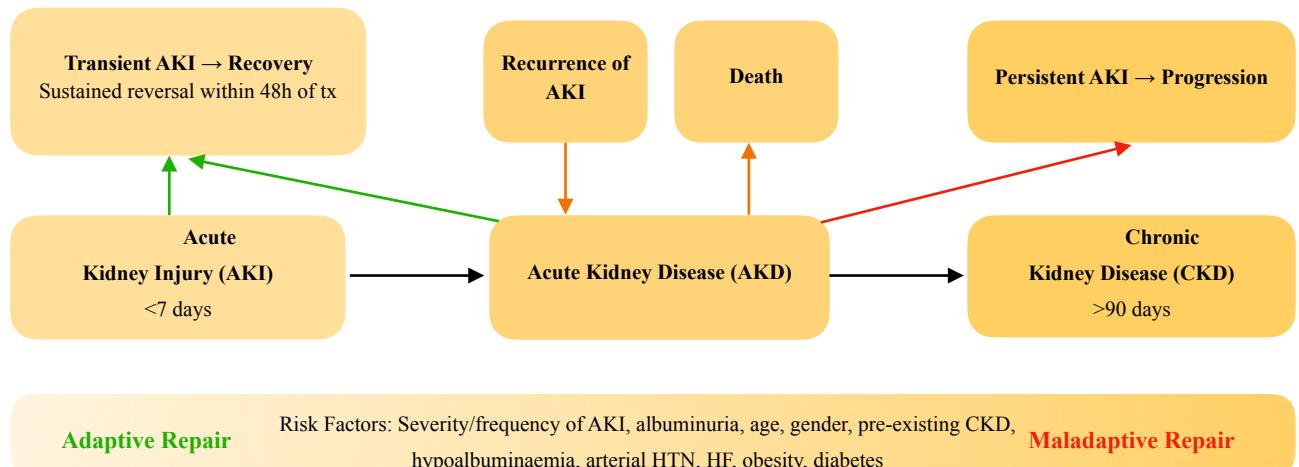


RENAL INJURIES

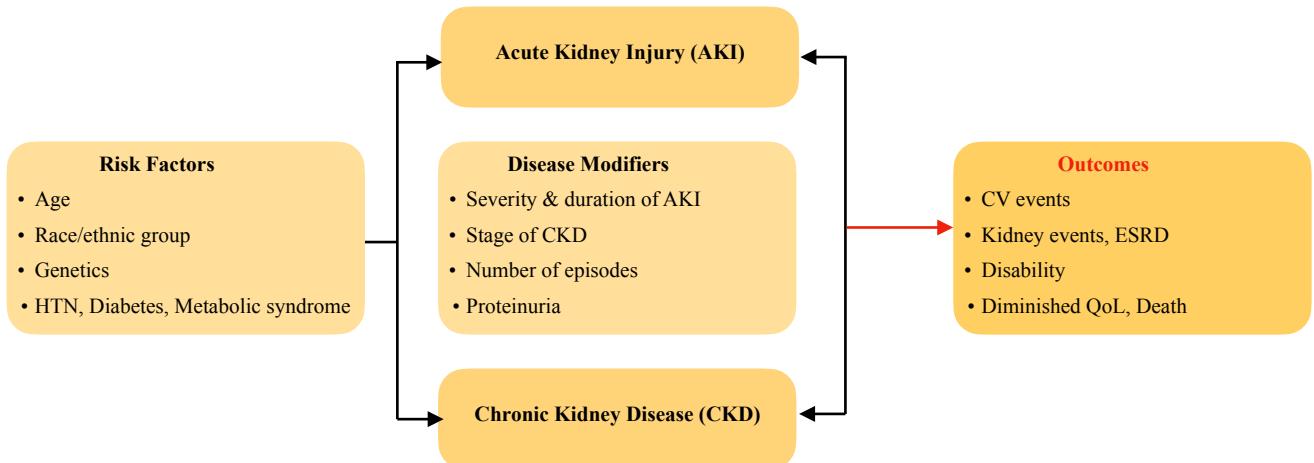
Introduction

Injury to the kidneys can cause many downstream complications, therefore prompt recognition and management is important. Note that AKI and CKD are often not discrete but a *continuum*.

[AKI → AKD → CKD → ESRD → TKD]



Risk Factors and Outcomes associated with Renal Disease



Non-Pharmacological Treatment for AKI/CKD

- Dietary sodium restriction
- Protein restriction if GFR <30ml/min (balance with risk of malnutrition)
- Weight reduction if overweight or obese
- Regular physical activity
- Moderation of alcohol consumption
- Smoking cessation

Preventing Complications

1. Renoprotection therapy with ACEI/ARB to slow progression of renal disease

As renal function declines, angiotensin II is required to maintain the hyperfiltration state of the remaining functioning nephrons. Angiotensin II has a preferential vasoconstrictor effect on efferent arterioles, which increases glomerular capillary pressure, expanding the pores between podocytes. This enables protein to pass into the tubules and cause damage. Therefore, ACEI/ARB are used to prevent this vicious cycle.

2. Treatment of co-morbid conditions

- Diabetes, HTN

3. In more advanced renal disease (ESRD)

- Managing complications associated with declining renal function

Acute Kidney Injury (AKI)

Description

Acute Kidney Injury (AKI) is a term used to describe an abrupt decrease in kidney function over a period of ≤ 7 days. Typically, reduced renal blood flow (ischaemia) initiates AKI. The function decreases to the point that the body accumulates waste products and becomes unable to maintain electrolyte, acid-base, and water balance. This can cause CV events, renal disease, disability/death, and CKD.

Risk Factors

The following can cause renal ischaemia and reduce the number of intact and functional nephrons

- Infection, sepsis, trauma
- Severe dehydration, excessive vomiting, diarrhoea
- Bleeding
- Nephrotoxic agents
- Medications (**Triple Whammy: ACEI/ARB + Diuretic + NSAID**)

Signs & Symptoms

Largely asymptomatic, therefore late diagnosis is common.

1. Serum Creatinine Levels — *not specific*
2. Decreased Urinary Output / Volume
3. Fluid Retention causing swelling & oedema

Goal of Treatment

The focus of management of acute kidney injury is to:

1. Restore renal blood flow
2. Treat urinary obstructions
3. Review medicine use

Pharmacological Treatment

Most patients recover from AKI if diagnosed early. However, the need for dialysis is associated with much worse outcomes including slow recovery and higher mortality rates.

1. Adjust really excreted medications (calculate CrCl) e.g. NSAIDs
2. Withdraw drugs with active metabolites
3. Diuretics to treat fluid retention
4. ACEI/ARB for renoprotection

Drug	Mechanism of Action	Side Effects
[PRESCRIPTION] <i>ACEIs/ARBs</i> Cilazapril (Zapril) Candesartan (Candesartan Cilextil)	↓ BP, ↑ Renal Blood Flow via predominantly EFFERENT arteriole dilation, ↓ Systemic Vascular Resistance Are renoprotective as the vasodilating effect reduces the pressure on the glomerulus which in turn reduces proteinuria (main causes of renal failure due to the inflammatory reaction that occurs upon their re-absorption). However paradoxically, it can cause renal injury if an immense amount of pressure is taken off.	Dry cough, GI disturbance (N/V/D), constipation, dyspepsia, abdominal pain), hypotension, headache, dizziness, fatigue, renal impairment, hyperkalaemia
[PRESCRIPTION] <i>Loop Diuretics</i> Furosemide, Bumetanide (s.29)	↑ Rate of Urine Flow via Natriuresis (water follows sodium) ↓ ECF, ↓ Body Weight Maximal Effect is ~ 20 - 25 % Loop Diuretics inhibit the activity of the Na/K/2Cl ⁻ (NKCC2) co-transporter in the <u>thick ascending loop of Henle</u> . By the time the filtrate reaches this part, around ~75% of filtered sodium has been reabsorbed in the body. Therefore maximum effect is 20 - 25 %.	Loop Diuretics have a steep dose response with a large maximum effect. Progressive renal impairment will reduce the diuretic effect, requiring a higher doses. Thiazides have a flat dose response and a much lower maximum effect. Beyond which, increasing the dose will only increase side effects. Contraindicated in CKD.
[PRESCRIPTION] <i>Thiazide Diuretics</i> Bendro Fluorothiazide	↑ Rate of Urine Flow via Natriuresis (water follows sodium) ↓ ECF, ↓ Body Weight Maximal Effect is ~ 5 % Thiazide Diuretics inhibit the activity of the NaCl (NCCT) co-transporter in the distal convoluted tubule . Over 95% of the filtered Na load has already been reabsorbed by the time filtrate reaches the distal convoluted tubule - therefore maximum effect is 5%.	The time course of diuretics is finite due to the renal compensatory mechanism (e.g RAAS) which re-establishes Na ⁺ balance. Electrolyte disturbances (hyponatraemia, hypokalaemia, hypocalcaemia, hypochloraemia, hypomagnesaemia), mild GI disturbances.

Chronic Kidney Disease (CKD)

Description

Chronic Kidney Disease (CKD) describes abnormalities in kidney structure or function that persist for > 90 days — it is the result of the gradual loss of kidney function over time and it can be caused by AKI. As CKD is a progressive disease, it eventually leads to End Stage Renal Disease (ESRD) which is chronic renal failure caused by a progressive decline in all kidney functions, eventually ending in terminal kidney damage.

Pathogenesis

Nephrons naturally reduce in function over time (atrophy). However, this is worsened by genetic and environmental factors. Due to the decreasing number of nephrons, hypertrophy of the few remaining nephrons occurs to compensate. However, podocytes cannot cope and detach, leading to loss of barrier functions, sclerotic lesions, impaired filtration, and proteinuria. Further, this leads to inflammation, fibrosis, and scar formation, and eventually to ischaemia and more nephron damage — i.e. a vicious cycle. The resulting reduced kidney function leads to fluid retention and accumulation of toxins.

Signs & Symptoms

Similar to AKI, CKD is largely asymptomatic until later stages due to its relatively slow onset, therefore late diagnosis is common.

- Fluid & electrolyte imbalances, anaemia, mineral bone disorder, metabolic acidosis, hyperuricaemia, hypertension, dyslipidaemia, CVD, endocrine dysfunction.
- Severe renal impairment: pruritus, taste disturbances, N/V, muscle pain, fatigue, bleeding abnormalities, changes in urine volume and consistency, ‘foaming’ of urine (indicative of proteinuria), oedema

Risk Factors

HTN and CKD can cause/exacerbate each other!

Development of the Disease

- Underlying disease: **diabetes, HTN**
- Hyperglycaemia, Dyslipidaemia
- Advanced Age
- Glomerulonephritis (associated with autoimmune conditions e.g. lupus)

Disease Progression

- Proteinuria
- HTN, HLD, Hyperglycaemia
- AKI, Smoking
- Medications: NSAIDs, triple whammy, aminoglycosides

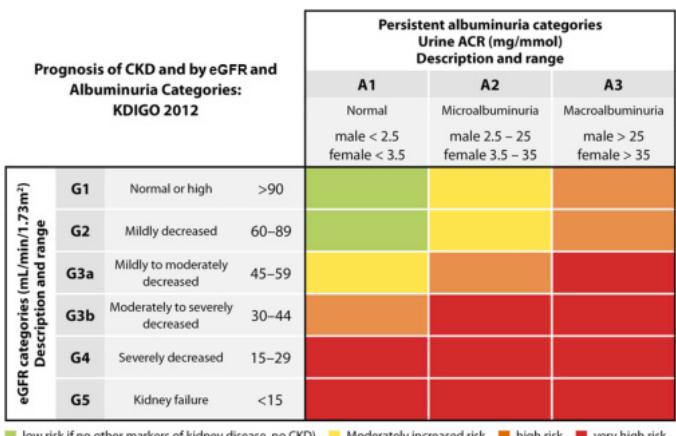
Diagnosis

Detected by screening those at risk

- Structural Abnormalities: Albuminuria, Albumin:creatinine ration (ACR), Haematuria or casts in urine sediment, Electrolyte and other abnormalities, Histology or imaging
- Functional Abnormalities: Decline in glomerular filtration rate (GFR): $<60\text{ml/min}/1.73\text{m}^2$

Classification/Stages of CKD (GFR mL/min/1.73m²)

- Normal (CKD 1): GFR $>90\text{ mL/min}$
- Mild (CKD 2): GFR 60-90 ml/min
- Moderate (CKD 3): GFR 30-60 ml/min
- Severe (CKD 4): 15-30 ml/min
- End-Stage (CKD 5): $<15\text{ ml/min}$**



Goal of Treatment

- Prevent or slow progression
- Decrease risk of CVD
- Decrease CKD complications
- Decrease the need for renal replacement therapy (i.e. dialysis)

Management Focus

- CKD2 - CK4:** Focus is on **preserving kidney function/reducing decline rate** - these stages are often asymptomatic
- CKD 5 (ESRD):** Focus is on managing **complications/symptoms** - this stage becomes increasingly symptomatic and is associated with dependence on dialysis or transplants.

Non-Pharmacological Treatment - [BPAC - The Detection and Management of CKD](#)

- Reduce weight
- Exercise
- Good diet e.g. low salt intake, intake of fresh vegetables and fruit, fish, milk, unprocessed meats, normal protein intake
- Limit alcohol
- Smoking Cessation

Pharmacological Treatment

- Adjust renally excreted medications e.g. NSAIDs
- Withdraw drugs with active metabolites
- Diuretics to treat fluid retention (Thiazides & Loops)
- Blood Pressure Control - ACEI/ARB for renoprotection
- Blood Sugar & Blood Lipids (if relevant)

Monitoring for all CKD patients — [BPAC Making a Difference in CKD](#)

- Annual cardiovascular risk

2. Blood pressure
3. Weight
4. Urinalysis (PCR should be measured annually if there is persistent proteinuria)
5. Serum creatinine/eGFR
6. Electrolytes: potassium
7. Other: Any underlying medical conditions e.g. diabetes, gout.
8. Any signs & symptoms

Key Parameters		
	Parameter	Target
Annual Cardiovascular Risk	5-year risk	
Blood Pressure		<ul style="list-style-type: none"> • Target $\leq 130/80 \text{ mmHg}$ if diabetes, proteinuria or high ACR otherwise $\leq 140/90$
Creatinine Clearance	Serum creatinine / eGFR	
Urinalysis	Visual & Microscopic examination, Chemical dipstick test	<ul style="list-style-type: none"> • Screening & diagnostic test
Electrolytes	Potassium	<p><i>In plasma (potassium)</i> 3.2 - 5.2 mmol/L</p> <p><i>In plasma (sodium)</i> 135 - 145 mmol/L</p>
Lifestyle	Weight	<ul style="list-style-type: none"> • Reducing BMI to at least $\leq 30 \text{ kg/m}^2$ with an ideal target of $\leq 25 \text{ kg/m}^2$ • Waist circumference for males $< 102 \text{ cm}$ and a circumference $< 88 \text{ cm}$ for females
	Diet	<ul style="list-style-type: none"> • Reduce salt intake to $\leq 6 \text{ g/day}$ • Protein intake of 0.75 – 1 g/kg/day
	Exercise	Moderate intensity physical activity $\geq 30 \text{ minutes/day}$
	Alcohol	<p>Need 2 alcohol free days a week +</p> <ul style="list-style-type: none"> • Females: max of 2 daily standard drinks and 10 weekly ones. • Males: max of 3 daily standard drinks and 15 weekly ones.
Additional Monitoring (PLUS key parameters)		
CKD Stage	Frequency	Investigations
1 & 2	6-12 monthly (Less frequently if eGFR is stable and risk factors are controlled)	Serum creatinine, ACR or PCR, serum electrolytes, serum urate, HbA1c, and lipids
3	3-6 monthly	<i>In addition to the above</i> <ul style="list-style-type: none"> • CBC, FBC, serum ferritin, calcium, phosphate, Alk Phos, PTH
4	3 monthly (6 monthly once stable)	<i>In addition to the above</i> <ul style="list-style-type: none"> • Plasma bicarbonate
5	Monthly (3-6 monthly once stable)	

End Stage Renal Disease (ESRD)

[The Renal Drug Handbook](#) [Cari Guidelines](#) [Australian Medicines Handbook](#)

[Dialysis of Drugs \(Bailie and Mason\)](#) [Oxford Handbook of Dialysis](#) [Merck Manual - Aspects of RRT](#)

Description

End Stage Renal Disease is the 5th stage of CKD, in which a person's kidneys cease functioning on a permanent (irreversible) basis, leading to the need for a regular course of long-term dialysis or kidney transplant to maintain life.

Risk Factors

- **Diabetes, obesity, hyperglycaemia**
- **Hypertension (can cause CKD)**
- Advanced age
- Proteinuria
- CKD and/or AKI history
- Māori Ethnicity
- Social Deprivation

Diagnosis

CKD Stage 5 (GFR < 15ml/min)

Differential Diagnosis

- **AKI:** acute kidney injury described as the dramatic sudden decline in kidney function
- **CKD:** gradual loss of renal function over time — eventually will lead to ESRD
- **ESRD:** irreversible kidney failure and eventual complete cessation in function

Signs & Symptoms

- Unlike other stages of CKD, this stage is blatantly and increasingly **symptomatic**
- N/V, loss of appetite, fatigue and weakness, sleep problems, bleeding abnormalities, changes in urine volume, “foaming” of urine (indicative of proteinuria), increasing incidence of pruritus, taste disturbance, muscle pain, fatigue, bleeding abnormalities, oedema

Complications

1. Fluid overload/oedema
2. Anaemia
3. Decreased clearance of drugs (dose adjustments)
4. Electrolyte disturbances
5. HTN
6. Impaired pH control (acidosis)
7. Hyperparathyroidism, calcitriol deficiency, hyperphosphataemia, hypocalcaemia, metabolic bone disease

Goal of Treatment

- To prolong life and improve its quality
- To prevent complications of ESRD e.g. uraemia & CVD complications
- To prevent complications of dialysis

- Provide adequate management of signs/symptoms e.g. BP, volume overload
- Adjust dialysable medications

Pharmacological Treatment

The focus is on **managing symptoms and complications** of ESRD instead of slowing down disease progression as in CKD. Sub-optimal management can mean a poor prognosis e.g. progressive uraemia, hyperkalaemia, acidosis, malnutrition, altered mental functioning.

END STAGE RENAL DISEASE COMPLICATIONS OVERVIEW		
System Impacted	Complications	Management/Intervention
Excretory Function	<p>Fluid Overload/Oedema, Proteinuria, Uraemia, ↓ Clearance A decrease in excretory function results in fluid accumulation in the interstitial space, which is why ESRD patients produce little to no urine. There are two theories as to why this occurs:</p> <ol style="list-style-type: none"> 1. <i>Proteinuria (nephrotic syndrome)</i> <ul style="list-style-type: none"> Kidney failure causes proteins to 'leak' into the urine. A profound loss of proteins can cause hypoalbuminaemia, which in turn decreases plasma oncotic pressure. This subsequently causes a shift of fluid to the interstitial space. RAAS is activated as a compensatory mechanism, to cause sodium and water retention. However, this causes increase in plasma volume. 2. <i>Electrolyte imbalance</i> <ul style="list-style-type: none"> Sodium retention theory competes to be the primary cause. 	<p>Pharmacological Treatment: Loop Diuretics <i>e.g. Furosemide, bumetanide</i></p> <ul style="list-style-type: none"> Failing kidneys will require progressively higher effects of diuretics, making thiazides ('flat dose response') less effective in ESRD than loop diuretics. <p>Dosing based on response:</p> <ul style="list-style-type: none"> Inadequate response: increase dose every 1-3 days If refractory: IV diuretics or addition of thiazide diuretics, potassium-sparing diuretics, or metolazone
	<p>Decreased Drug Clearance A decrease in excretory function will also cause accumulation and toxicity of renally cleared drugs. Therefore, these must be adjusted to renal function.</p> <ul style="list-style-type: none"> Traditionally, we would start low go slow (however clinical benefit is delayed). However, it may be more practical to adjust dose with the assumption that kidney drug clearance will decrease in proportion to GFR/CrCl (maintenance dose is proportional to drug clearance) 	<p>Dose Adjustment of Renally Cleared Drugs</p> <ul style="list-style-type: none"> ACEI/ARB, NSAIDs... <p>In RRT — See Dosing Diuretics following RRT</p> <ul style="list-style-type: none"> Intermittent Haemodialysis: May cause sub-therapeutic levels post-dialysis
Regulation (ECF volume, electrolytes and osmolality, pH)	<p>Electrolyte Disturbances & Hypertension Fluid retention from failing kidneys results in a failure to maintain electrolyte balance, which results in the following:</p> <ol style="list-style-type: none"> 1. <i>Hypernatraemia/HTN</i>: Kidneys are unable to alter sodium excretion. This can cause volume overload (activation of sympathetic system and alteration of RAAS) and consequently hypertension. ADRs (if > 180/120mmHg): headache, nosebleed, blurred vision 2. <i>Hyperkalaemia</i>: Kidneys are unable to remove excess potassium. ADRs: nausea, cramps, fatigue, numbness, paralysis, cardiac arrest. 3. <i>Hyperphosphataemia</i>: Reduced elimination of phosphate and its unchanged intestinal absorption can cause increased levels. ADRs: cramps, spasms, mouth tingling/numbness, weak bones, itchy skin & rashes. 4. <i>Hypocalcaemia</i>: Retention of phosphorus can decrease calcium levels in the blood. ADRs: seizures, arrhythmia, cardiac failure, muscle spasms 	<p>Non-Pharmacological Treatment</p> <ul style="list-style-type: none"> Diet <p>Hyperkalaemia Management</p> <ol style="list-style-type: none"> 1. <i>If mild (<6mmol + no ECG abnormalities)</i> <ul style="list-style-type: none"> Minimise K⁺ intake Stop/reduce K⁺ elevating drugs Add loop diuretic to maximise excretion 2. <i>If moderate (6-6.5mmol/L)</i> <ul style="list-style-type: none"> Insulin + glucose rapid infusion Sodium bicarbonate 3. <i>If severe</i> <ul style="list-style-type: none"> Sodium polystyrene sulfonate Haemodialysis <p>Hyperphosphataemia/Hypocalcaemia Management: Phosphate Binders — Cari Guidelines (Serum Phosphate)</p> <ol style="list-style-type: none"> 1. <i>Calcium-based antacids (with meals)</i> <ul style="list-style-type: none"> Calcium carbonate, calcium acetate 2. <i>Alternative (if risk of hypercalcemia)</i> <ul style="list-style-type: none"> Sevelamer carbonate, lanthanum carbonate, sucroferric oxyhydroxides, ferric citrate 3. <i>Additional (if AKI, severe hyperphosphataemia)</i> <ul style="list-style-type: none"> Aluminium-based phosphate binders (with meals) 4. <i>Dietary phosphate restriction</i> <ul style="list-style-type: none"> 0.8-1g/day in eGFR < 60ml/min

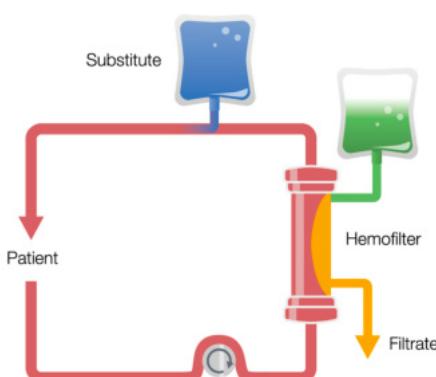
		<p>Hypertension Management: Target < 130/80 mmHg</p> <ol style="list-style-type: none"> ACEI: enalapril 2.5mg OD & titrate (given post-dialysis) ARBs: candesartan 2mg & titrate Diet <ul style="list-style-type: none"> Decrease salt intake to < 1.5-2g per day Decrease fluid intake to no more than 1.5L per day Monitor electrolytes (particularly potassium)
	<p>Acid-base balance: Metabolic Acidosis (Impaired pH Control)</p> <p>Kidneys function to remove acid from the body through urine. In ESRD, H⁺ excretion is reduced, causing a build-up of acid in the blood. This initially buffered by bicarbonate, however this falls overtime resulting in metabolic acidosis.</p> <ul style="list-style-type: none"> Diagnosis: Low bicarbonate levels (< 22 mmol/L) Symptoms: Long and deep breaths, tachycardia, headache, confusion, weakness, tiredness, N/V, loss of appetite Complications: Bone resorption, insulin/growth hormone resistance, muscle protein catabolism, systemic inflammation, hypotension 	<p>Alkali Therapy & Diet</p> <ol style="list-style-type: none"> Sodium Bicarbonate: neutralises acid and maintains serum bicarbonate in the normal range (23-29 mEq/L) Sodium Citrate: metabolised to sodium bicarbonate - given to those with contraindications to sodium bicarb. Avoid in those taking Aluminium Antacids. Calcium Carbonate: used in conjunction to help increase serum bicarbonate levels Diet: restrict sodium intake, avoid high potassium containing foods (hyperkalaemia risk) or high dietary acid (e.g. animal protein), increase fruit and vegetable intake, fluid restriction is not required, consider multivitamins (e.g. vitamin D)
Endocrine (e.g. EPO)	<p>Normocytic Anaemia (See Oncology Chapter)</p> <p>EPO is a hormone produced by the kidneys which stimulates RBC production in the bone marrow. Production is reduced in failing kidneys, causing RBC deficiency (anaemia → decrease in O₂ delivery). As a compensatory response, cardiac output increases, however this increases the risk of LVH and CVD.</p> <ul style="list-style-type: none"> Diagnosis: Hgb < 130g/L (men), < 115-120 g/L (women) Symptoms: Fatigue, SOB, exercise intolerance, headache, loss of libido, weakness, dizziness, lightheadedness. 	<ol style="list-style-type: none"> Iron Supplementation <ul style="list-style-type: none"> Oral or IV EPO Stimulating Agents (if Hgb remains persistently low or is <100 g/L) <ul style="list-style-type: none"> Epoetin alfa (funded in NZ) Darbepoetin alfa
Metabolic (e.g. low Vit D)	<p>Metabolic Bone Disease, Calcitriol Deficiency, Hyperphosphataemia, Hypocalcemia, Hyperparathyroidism</p> <p>As kidneys fail, changes in minerals and hormones occur.</p> <ul style="list-style-type: none"> Active Vitamin D (Calcitriol): Healthy kidneys change vitamin D to an active form. This is important to form new bones and to keep blood calcium levels balanced (vit D helps with calcium absorption from the gut) Calcium and Phosphate: These are used to maintain bones. The kidneys are important in keeping blood levels of calcium and phosphate balanced. Parathyroid hormone (PTH): PTH glands function to increase calcium levels to maintain homeostasis in the blood. Failing kidneys cause hypocalcaemia (due to high phosphate). PTH moves calcium from the bones into the blood, promote resorption in the kidneys, and promote activation of vitamin D to increase calcium absorption from the gut. However, excess stimulation of PTH enlarges the gland and excess calcium can lead to skin, blood vessels, heart problems, and kidney stones. 	<p>(See Osteoporosis Chapter)</p> <ul style="list-style-type: none"> Diet: low phosphorus foods such as egg whites, apples and broccoli, high calcium foods such as dairy, soybeans, calcium fortified products. Low Vit D: Calcitriol (+/- alendronic acid) Hyperphosphataemia/hypocalcaemia: Phosphate binders e.g. calcium carbonate, aluminium hydroxide Secondary hyperparathyroidism: Calcitriol, Cinacalcet, PTH Gland Removal Surgery
Peritonitis from Peritoneal Dialysis	<p>Peritonitis</p> <p>ISPD Peritonitis</p> <ul style="list-style-type: none"> Leading cause of morbidity in PD Cause: mainly gram+, less commonly gram- Symptoms: Cloudy peritoneal fluid, abdominal pain, ↑ WBC in effluent, fever, N/V Treatment: empiric antibiotics with gram +/- coverage — can be administered interperitoneally (IP) Prevention: Keep pets away from dialysis equipment room 	<p>Pharmacological Treatment (Antibiotics)</p> <p>Empiric treatment is necessary! Add chosen antibiotics to dialysis bag. See Guidelines.</p> <ul style="list-style-type: none"> Prophylaxis: Mupirocin ointment to catheter exit site Gram +: vancomycin or 1st gen cephalosporin (cefazolin) Gram -: 3rd gen cephalosporin (ceftazidime) or aminoglycoside Alternative monotherapy: 4th gen cephalosporin (cefepime) <p>Inter-peritoneal (IP) Pharmacokinetics</p> <ul style="list-style-type: none"> 65-100% of antibiotic dose administered IP is absorbed systemically Peritonitis alters the permeability of the peritoneal membrane, leading to increased systemic absorption Poor systemic clearance in PD patients leads to drug accumulation — potential toxicity of renally eliminated antibiotics e.g. gentamicin

In some patients, RRT or a kidney transplant may be indicated — [BPAC](#)

1. Renal Replacement Therapy (RRT)/Dialysis: Haemodialysis (35%) or Peritoneal Dialysis (10%)
2. Kidney transplant (25%)

RENAL REPLACEMENT THERAPY (RRT)							
Definition	A generic term for any mechanism that replaces the excretory function of the kidneys — it serves to remove waste products, excess water and electrolytes						
Clinical Use	<p><i>Recommend planning:</i> CKD 4 (GFR < 30ml/min) <i>Indication:</i></p> <ol style="list-style-type: none"> 1. GFR < 10-15ml/min 2. A.E.I.O.U: <ul style="list-style-type: none"> • Acid Base Problems e.g. severe metabolic acidosis • Electrolyte problems e.g. uncontrollable hyperkalaemia • Intoxications e.g. overdose • Overload fluid e.g. pulmonary oedema • Uremic symptoms e.g progressive uremic encephalopathy or neuropathy 						
Goals of RRT	<ol style="list-style-type: none"> 1. Restore acid-base status 2. Correct electrolyte abnormalities 3. Remove toxic metabolites to decrease uremic symptoms 4. Maintain volume status 5. Improve quality of life 6. Decrease the morbidity and mortality associated with ESRD 						
Types of RRT	<p>1. Haemodialysis (HD) (most common) This type of dialysis filters the blood. Plasma is passed outside of the body into a dialyser, it is then separated from the “dialysate” by fibres (creates large surface area for diffusion). Substances are exchanged across the membrane between the plasma and the dialysate by diffusion and convection (H_2O ultrafiltration, Na^+ convection)</p> <p>2 types:</p> <ul style="list-style-type: none"> • Intermittent HD (e.g. 3 times a week for 4 hours) • Sustained low-efficiency dialysis (SLED) <p><i>Complications of HD</i></p> <ul style="list-style-type: none"> • Hypotension • Thrombosis <p>2. Peritoneal Dialysis (PD) A type of dialysis where sterile fluid is instilled into the peritoneal cavity (peritoneal membrane acts as a filter). This allows for large solutes to be exchanged by diffusion between the blood and dialysate. Dialysate “dwells” for a specified length of time, then is drained and replaced. The continuous nature of PD mimics endogenous kidney function and limits fluctuations in intravascular fluid balance</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;"><i>Advantages of PD</i></td><td style="padding: 5px;"><i>Disadvantages of PD</i></td><td style="padding: 5px;"><i>Complications of PD</i></td></tr> <tr> <td style="padding: 5px;"> <ul style="list-style-type: none"> • More haemodynamic stability (BP) • Mimics endogenous kidney function • Better preservation of residual renal function • Convenient IP route of administration of drugs • Suitable for elderly and very young patients • Freedom from the ‘machine’ </td><td style="padding: 5px;"> <ul style="list-style-type: none"> • Protein and amino acid losses through the peritoneum and reduced appetite • Risk of peritonitis • Patient burnout (large volumes and frequent exchanges) </td><td style="padding: 5px;"> <ul style="list-style-type: none"> • Increased risk of infections (e.g. peritonitis) • Sclerosis of the peritoneal membrane • Discomfort associated with catheter/installation of fluid • Metabolic problems (glucose and fluid load), electrolyte imbalances, albumin and protein loss </td></tr> </table> <p>Other types of RRT</p> <ul style="list-style-type: none"> • Haemofiltration (HF) • Haemodiafiltration (HDF) 	<i>Advantages of PD</i>	<i>Disadvantages of PD</i>	<i>Complications of PD</i>	<ul style="list-style-type: none"> • More haemodynamic stability (BP) • Mimics endogenous kidney function • Better preservation of residual renal function • Convenient IP route of administration of drugs • Suitable for elderly and very young patients • Freedom from the ‘machine’ 	<ul style="list-style-type: none"> • Protein and amino acid losses through the peritoneum and reduced appetite • Risk of peritonitis • Patient burnout (large volumes and frequent exchanges) 	<ul style="list-style-type: none"> • Increased risk of infections (e.g. peritonitis) • Sclerosis of the peritoneal membrane • Discomfort associated with catheter/installation of fluid • Metabolic problems (glucose and fluid load), electrolyte imbalances, albumin and protein loss
<i>Advantages of PD</i>	<i>Disadvantages of PD</i>	<i>Complications of PD</i>					
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Haemodialysis

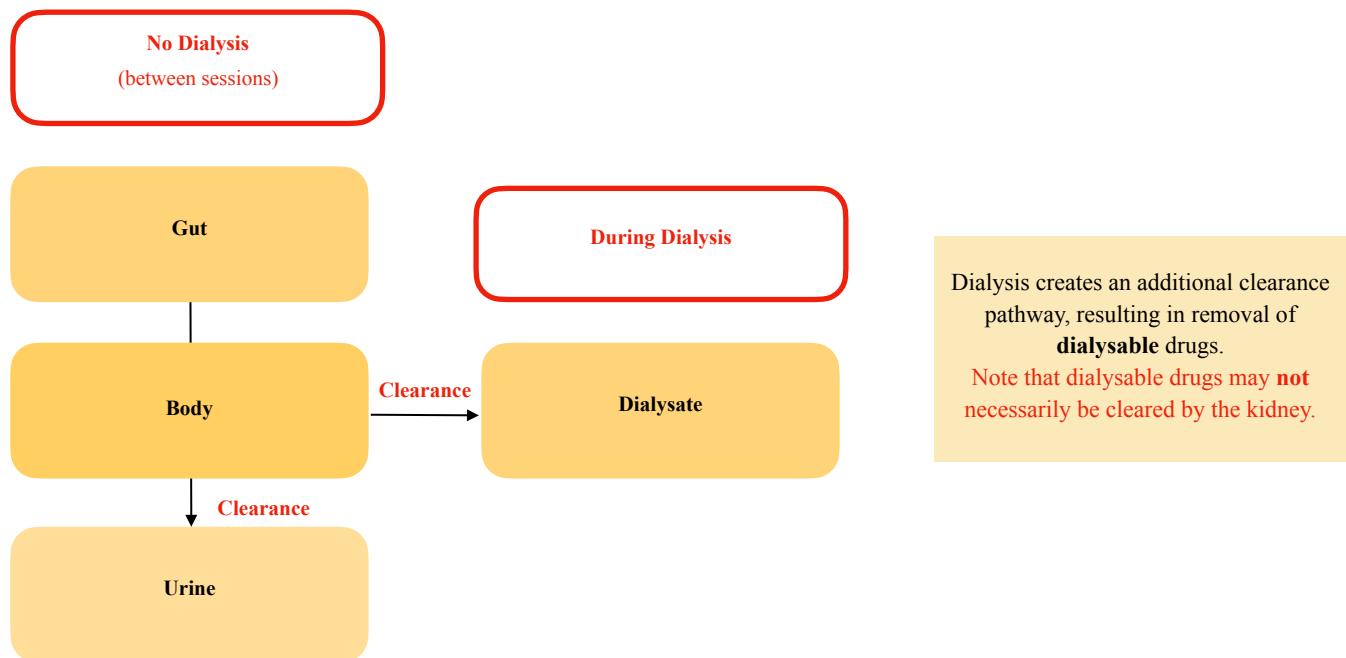


Peritoneal Dialysis



Drugs & Dialysis

An important consideration during dialysis is the additional clearing mechanism that occurs for drugs that are dialysable. Failure to account for it means that the dramatic drop in drug exposure results in sub-therapeutic plasma concentrations. Due to this, dosing adjustments must be put in place so that following dialysis sessions, the patient can receive therapeutic levels of their medications.



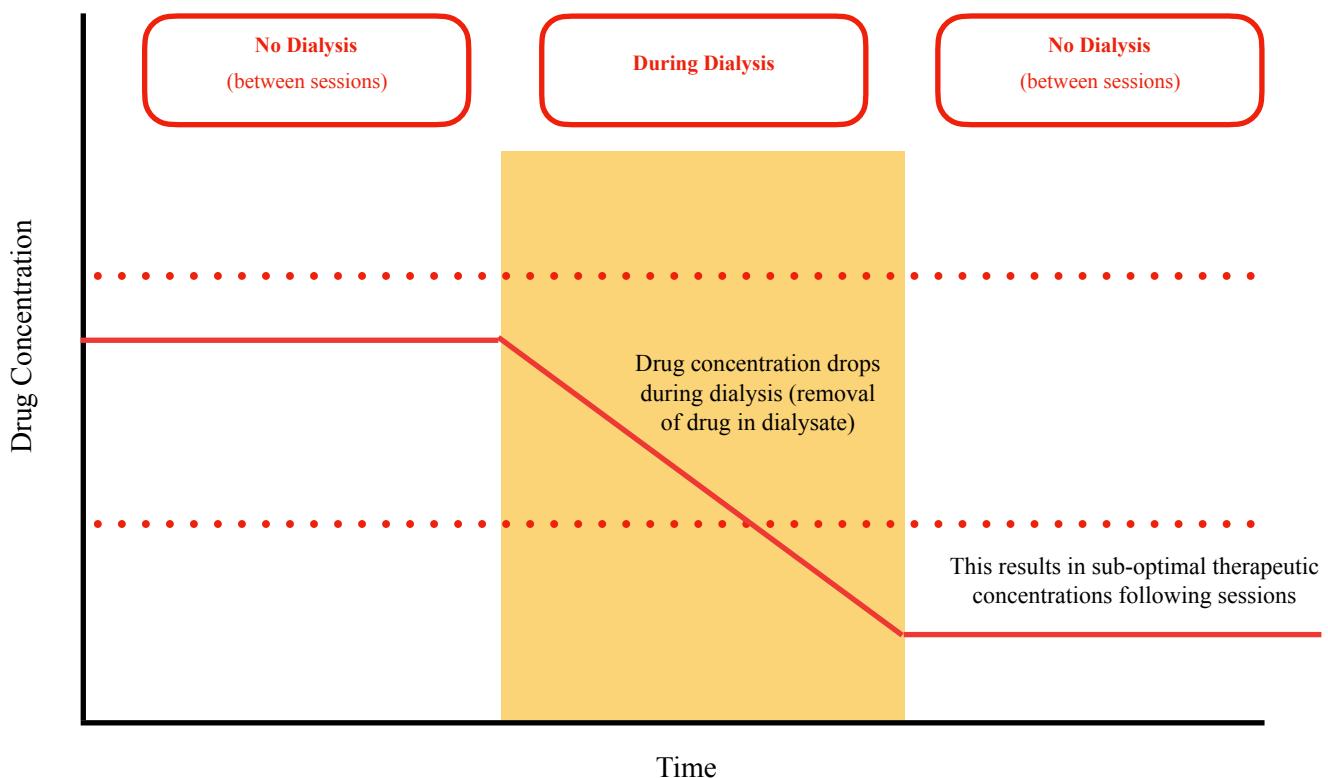
Features of Dialysable Drugs

1. *Molecular size*: smaller molecules are more easily dialysed
2. *Protein binding*: only free drug can be dialysed
3. *Volume of distribution*: increased V_d may mean lower levels of drug dialysed. If distributed mainly in the tissues, the drug is more likely to be lipophilic, and have relatively low concentrations in the plasma.
4. *Hydrophilic drugs*: more readily dialysed

Drug Dosing in (Intermittent) Haemodialysis

Refer to [Renal Drugs Handbook](#) for dosing recommendations of dialysable drugs

- Dose **POST**-dialysis after **each** dialysis session. If sub-therapeutic concentrations are detrimental: give small supplementary (“top-up”) dose mid-way through dialysis
- An **EXCEPTION** is **aminoglycosides (e.g. gentamycin)**: Dose **PRE**-dialysis to optimise C_{max} /bacterial killing, and reduce overall exposure. If dosed post-dialysis, drug won’t be cleared until next dialysis, therefore toxic concentrations (narrow therapeutic range) will occur over a longer period.

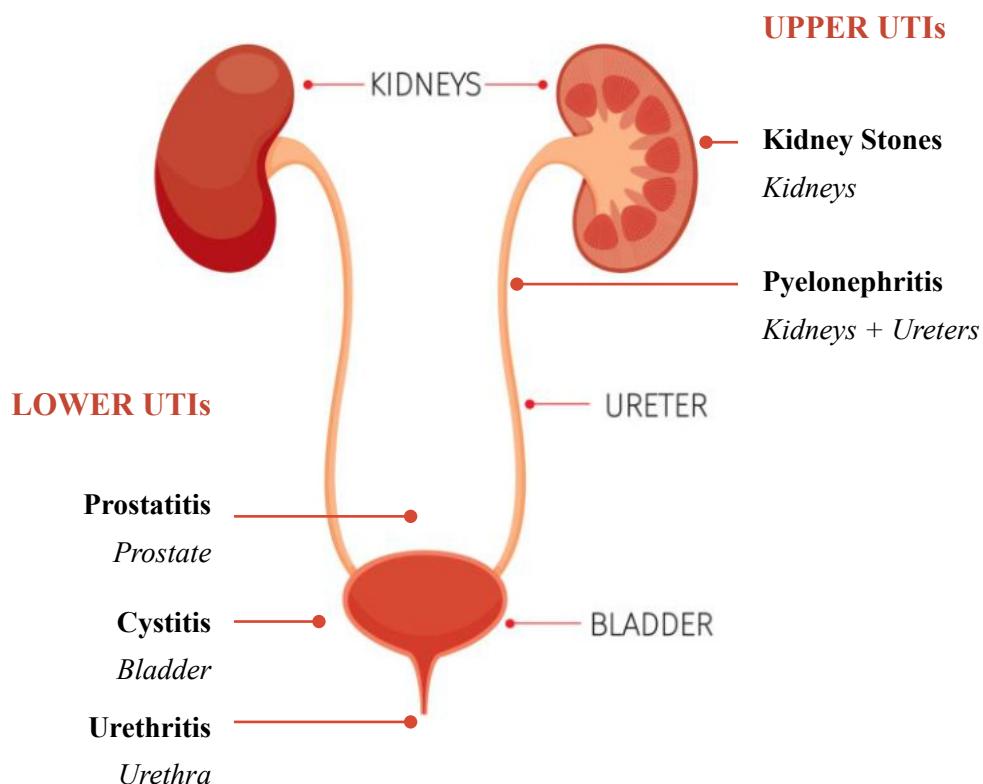


URINARY TRACT INFECTIONS (UTIs)

Overview of the Urinary System & Its Infections

Introduction - NZF Genito-Urinary Infections

Urinary-tract infections (UTIs) are common infections that can affect any part of the urinary tract and are a common presentation to community pharmacies — they can be categorised into 2 kinds: upper and lower UTIs. However, before we go any further into UTIs, it is important to first understand the urinary system.



The Urinary System

The urinary system's function is to filter blood and pass urine as a waste by-product. It is composed of:

Component	Description
Kidneys	Create the urine from filtering blood
Ureters	Tubes that carry urine from the kidneys to the bladder, ureter wall muscles continually force the urine downwards, away from the kidneys.
Bladder	Relaxes/expands to store urine, and contract/flattens to empty urine through the urethra.
Urethra	A tube that allows urine to pass out of the body.
Sphincter Muscles	Circular muscles around the opening of the bladder that prevent urine leakage.
Bladder Nerves	Signal when it is time to urinate.
Prostate	Produces semen in males. Located below the bladder wrapped around the urethra, it is the tube that carries urine + semen.

Infections of the Urinary Tract

Urinary infections are caused by bacteria, virus, or fungi (candida). The urinary tract is usually kept sterile through 2 defence mechanisms; immune system & regular passing of urine. UTI's are classified into 2 types:

1. *Ascending infections (95%)*: start at urethra and moves up (e.g. pyelonephritis which began as cystitis)
2. *Descending infections (5%)*: work their way down (e.g. bacterial sepsis in the blood going to kidneys)

Causative Agents of UTIs

Implicated pathogens often originate from the perirectal area.

1. **E-coli**: > 80% of uncomplicated UTIs and < 50% of complicated UTIs
2. Gram -ve: Klebsiella pneumonia, Proteus spp.
3. Gram +ve: Staphylococcus and Enterococcus species from GIT
4. *Candida albicans*: rare but may occur in hospitalised patients who are immunocompromised or have indwelling catheter in urethra.

Risk Factors for all UTIs

1. Females: shorter urethra, opening near vagina and anus (rich microbiota)
2. Age: children <1 years (nappies), pre-menopausal women, elderly men (prostatic hyperplasia), immunocompromised, old age, urination issues.
3. *Other*: dehydration, **diabetes** (glucose promotes pathogen growth), pregnancy (hormone changes), obstructive objects (catheters, kidney stones), urine composition (presence of microbial inhibitors)
4. Medications: NSAIDs, allopurinol, danazol, cyclophosphamide
5. **Unprotected Sex**: Vaginal, anal or oral sex without a condom, sex play



Diabetes & UTIs

Diabetes requires an immediate referral as both uncontrolled blood sugar as well as the fact that diabetes causes antibiotic resistance means that pharmacist-supplied antibiotics won't be effective.

Clinical Presentation of UTIs

UTIs can present as either complicated or uncomplicated infections

	Uncomplicated UTIs	Complicated UTIs
Example	Urethritis	Pyelonephritis
Location	Usually lower UTIs	Usually upper UTIs
Risk Factors	• Commonly in women of child-bearing age • Lower risk in men due to longer urethra. Fluid from prostate gland also has antibacterial properties	Structural / functional abnormalities: elderly, children , males, pregnant women
	Can occur in people with normal immunity & normal urinary tracts	Abnormal immunity & abnormal urinary tracts, people with a urinary catheter
		Medical conditions: diabetes, renal failure
		People living in residential care facilities

		Persistent or recurrent cystitis (> 3/ year) or atypical symptoms
Cause of Recurrence	Due to new infection	Due to relapse from previous infection
Response to Antibiotics	Responds to antibiotic therapy (cotrimoxazole)	Infection may not respond to antibiotic therapy i.e. antibiotic resistance

Signs & Symptoms of UTIs

Refer UTIs that last longer than 5-7 day due to the high risk of developing pyelonephritis

Uncomplicated AND Complicated UTIs	
Urinary frequency, nocturia	Suprapubic pain
Urinary urgency	Discomfort
Dysuria	Painful ejaculation
<i>Additionally for Complicated UTIs (Systemic S/S)</i>	
Fever, Chills	N/V
Flank pain	Elevated WBC count

Note: Older patients may **NOT** present with these usual signs and symptoms due to their naturally impaired immune system. They may present with: altered mental status, poor appetite, involuntary urination (incontinence)

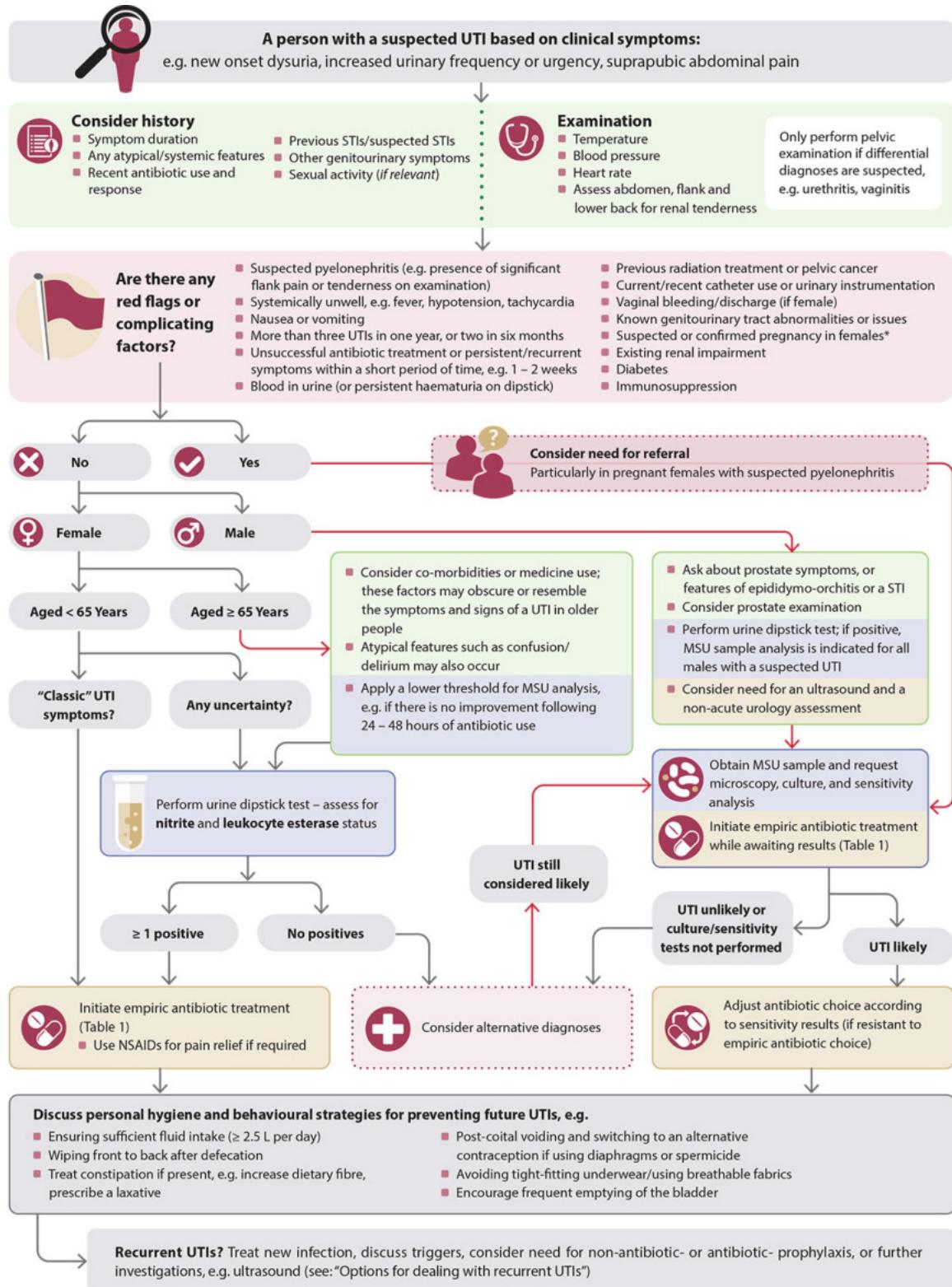
Diagnosis & Management of UTIs

There are four ways to diagnose a UTI. However 2-4 provide very little diagnostic value — it is best to rely on signs, symptoms and urine bacterial counts.

1. Self Diagnosis (of recurrent infections): Reliable — “If you think it is a UTI it probably is.”
2. OTC Test Kits: Measure protein levels on midstream urine (MSU)
3. Lab Based MSU Urinalysis: Provides with very little additional diagnostic value
4. Direct Microscopy or Culture of MSU: Not very helpful

Please Note:

- For females with **uncomplicated** cystitis, the causative bacteria and antibiotic sensitivity profile are often **predictable**. As such, requesting microscopy, culture and sensitivity testing is not necessary as it is unlikely to influence treatment decisions, therefore we initiate empiric antibiotics (BPAC).
- In males (adult) and pregnant females, antibiotic treatment for LUTIs is extended to **7 days**.



Goals of Therapy in UTIs

1. Eradicate the causative pathogen
2. Prevent or treat consequences of infection (e.g. progression of UTI, renal damage)
3. Administer appropriate empiric antimicrobial therapy or targeted therapy based on culture results
4. Optimise drugs to minimise side effects and development of resistance
5. Prevent recurrence of infection
6. Monitor patient response by urinalysis (in some UTIs e.g. cystitis)

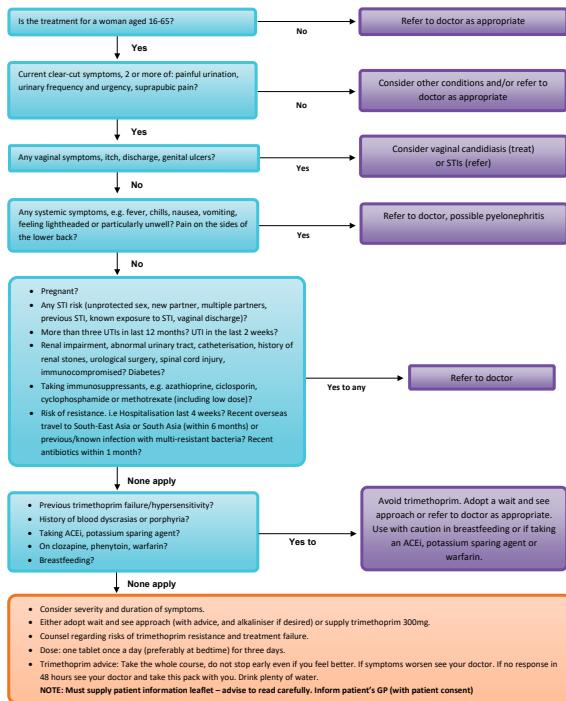
Non-Pharmacological Treatment Summary

Behavioural	Limited Evidence
Wipe from front to back	Cranberry juice
Drink plenty of water	D-Mannose (sugar)
Do not resist the urge of urination	Alkalinisers (Ural)
Take showers instead of baths	Potassium citrate
Cleanse the genital area before sexual intercourse	
Avoid using feminine hygiene sprays which may irritate the urethra	
Avoid acidic drinks (e.g. fruit, fizzy drinks) and spicy foods (may irritate bladder in some people)	

Pharmacological Treatment Summary

Anti-microbial therapy is the cornerstone of treatment. See 'Pharmacist Only Medicines' Section from *Chapter 23 - Pharmacy Internship* for the guidelines on pharmacist supply of Trimethoprim.

Trimethoprim for UTIs Algorithm



Consultation Record – UTI Assessment

Name		Address	
Anatomically Female: YES/NO		Age (between 16 and 65 years)	Diabetic NO / YES = refer
Pregnant (or possibly pregnant) NO / YES = Refer		Trimethoprim allergy/hypersensitivity NO / YES = refer	
		YES/NO	Notes
SYMPTOMS:			
Urinary Tract: Two or more of Painful urination, urinary frequency and/or urgency, suprapubic pain			
Vaginal: Any of Itch/irritation, discharge Consider vaginal candidiasis (treat) or STI – (see criteria for referral below)			
Systemic: Any of Fever, chills, nausea, vomiting, very unwell, pain in sides or lower back		Refer – do not supply	
CRITERIA FOR REFERRAL:			
<ul style="list-style-type: none"> • UTI in the last 2 weeks or more than three UTIs in last 12 months • Immunocompromised • Risk of resistance, i.e. <ul style="list-style-type: none"> ▪ Antibiotic within last 30 days ▪ Previous immunosuppression failure ▪ Previous/known infection with multi-resistant bacteria ▪ Hospitalisation last 4 weeks ▪ Travel to South-East Asia (within last 6 months) • STI risk (unprotected sex, new partner, multiple partners, previous STI, known exposure to STI) • Other: Renal impairment, abnormal urinary tract, catheterisation, history of renal stones, urological surgery, spinal cord injury 		Refer – do not supply	
DRUG INTERACTIONS:			
<ul style="list-style-type: none"> • Warfarin – not contraindicated but possible theoretical rise in INR – advice re bleeding possibility • ACE/ARB – theoretical possibility of hyperkalaemia. Avoid TMP if possible, however short course of 3 trimethoprim tablets unlikely to cause this in age group being treated! 		May supply – give advice	
Contraindications:			
<ul style="list-style-type: none"> • Clozapine – risk of blood dyscrasias • Immunosuppressants e.g. <ul style="list-style-type: none"> ▪ Azathioprine – increased risk of haematological toxicity ▪ Cyclosporine – increase serum creatinine levels ▪ Methotrexate (including low dose) – bone marrow depression ▪ Phenytoin – Phenytoin serum concentrations can be increased by TMP 		Refer – do not supply	
BREASTFEEDING – compatible – refer if baby is premature or otherwise unwell			
PHARMACIST MANAGEMENT PLAN			
<input type="checkbox"/> 3 x Trimethoprim 300mg tablets <input type="checkbox"/> Treated for vaginal candidiasis <input type="checkbox"/> Referred to doctor		<input type="checkbox"/> Advice: Self-care measures, follow up with doctor if symptoms persist or worsen (antibiotic resistance – different treatment), provide patient information sheet <input type="checkbox"/> Notify patient's GP (send this form with patient consent)	
		Patient consent YES/NO	
GP Name and Practice			
Pharmacist		Date	

1. Medicines Adverse Reaction Committee. <https://www.medicines.govt.nz/committees/marc/reports/178-3.2.1%20UseofTrimethoprim.pdf>

Uncomplicated UTIs

- Nitrofurantoin, trimethoprim*, cefalexin — *usually a 3-5 day course*
 - Best taken at night so the antibiotic can have time to take effect without regular passing of urine

Complicated UTIs

- Empiric therapy + urine culture

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Trimethoprim (TMP)</i> <i>Trimethoprim-Sulfamethoxazole (Trisul)</i>	A folate antagonist, reversibly inhibits dihydrofolate reductase to prevent conversion of dihydrofolate to tetrahydrofolate (a necessary step in bacterial DNA synthesis). Trimethoprim is usually bacteriostatic but may be bacteriocidal depending on organism and growth conditions. *Pharmacist can supply a 3 day course if accredited	<ul style="list-style-type: none"> Short course (3 days) of trimethoprim or trimethoprim-sulfamethoxazole Best taken at night First line in females with uncomplicated UTIs Urine culture testing not recommended as it doesn't improve outcomes 	GI upset (N/V), pruritus, rash
[PRESCRIPTION] <i>Nitrofurantoin</i> (Macrobid, Nifuran)	Nitrofurantoin, a bactericidal antibiotic, is reduced by bacterial flavoproteins (mainly in the acidic environment of urine) to reactive intermediates which interfere with bacterial ribosomal proteins and other macromolecules. This causes inhibition of several bacterial biochemical processes (including aerobic energy metabolism), and the syntheses of bacterial cell wall, proteins, DNA, and RNA. Macrobid is long acting (BD dosing) Nifuran is to be taken every 6 hours (QID) *Liquid formulation available for children	<ul style="list-style-type: none"> Take with or just after food, or a meal. Swallow whole, do not crush or chew (Macrobid) Avoid antacid preparations containing magnesium trisilicate 	May colour your urine yellow or brown.
[PRESCRIPTION] <i>Cephalosporins</i> (Cephalexin)	Cephalosporins are antibiotics that attach to penicillin binding proteins to interrupt cell wall biosynthesis, leading to bacterial cell lysis and death.		N/V/D, abdominal discomfort
[GENERAL] <i>Prevention</i> <i>Methenamine hippurate</i> (Hiprex)	Methenamine hippurate is hydrolysed to formaldehyde and hippuric acid in an acidic environment (e.g. the urine). Formaldehyde is a nonspecific bactericidal agent. Hippuric acid maintains urinary acidity and may have bacteriostatic activity.		GI disturbances, bladder irritation, rash

OSCE Points

- Check for flank pain, blood in urine, pregnancy status, age of person, possibility of menopause, risk of diabetes, any vaginal discharge

Lower Urinary Tract Infections (LUTIs)

Description

[BPAC \(Be Quick\) Lower UTIs Guidelines](#)

Infections of the bladder (cystitis), urethra (urethritis) or prostate (prostatitis) are known as lower UTIs.

Urethritis

Description

Urethritis is a bacterial or viral infection of the urethra, commonly due to sexually transmitted organisms (chlamydia, gonorrhoea) or infection from GI organisms.

Non-Pharmacological Treatment

- STI checking and testing (urine and urethral swab) for gonorrhoea and chlamydia
- Contact and treat sexual partners

Pharmacological Treatment (Females)

[BPAC \(Be Quick\) Urethritis](#)

1. *First Line:* Nitrofurantoin
2. *Alternative:* Trimethoprim, Cefalexin

Pharmacological Treatment (Males)

[BPAC Urethritis Non Specific Male Antibiotic Guidelines](#), [Urethritis in Males - NZSH](#)

Urethritis in males is considered usually complicated.

1. *First Line:* Doxycycline (7 days)
2. *Alternatives:* Azithromycin (STAT)

Cystitis

Description

Cystitis is an inflammatory infection (bacterial, viral or fungal) of the bladder.

Pathogens

1. *Bacterial:*

- E. coli (> 90% of uncomplicated cystitis), uropathogenic E. coli (UPEC) (> 75% of recurrent infections)
- GI organisms: Staphylococcus saphrophyticus, Enterobacter, Klebsiella

2. *Fungal:* Candida

3. *Viral:* Adenovirus

Pharmacological Treatment (Children > 6 months)

Children Cystitis BPAC Antibiotic Guidelines

1. *First Line:* Trimethoprim + sulfamethoxazole (trisul/co-trimoxazole)

2. *Alternative:* Cefalexin, amoxicillin + clavulanic acid

Pharmacological Treatment (Adults)

Adult Cystitis BPAC Antibiotic Guidelines

1. *First Line:* Nitrofurantoin

2. *Alternative:* Trimethoprim, Cefalexin

Prostatitis

[Health Navigator Prostatitis](#)

Description

Prostatitis is an infection or inflammation of the prostate gland (**complicated UTI**). The prostate can be infected from the backflow of urine from the bladder. This is the most common urological diagnosis in men under the age of 50 (> 25%). Usually caused by E.coli or Klebsiella.

Signs & Symptoms

Acute (<3 months): Lower abdominal pain, fever, frequency, urgency, pain on urination, foul smelling urine

Chronic (>3 months): intermittent cystitis, urinary symptoms, painful ejaculation

Risk Factors

- Recurrent cystitis, STIs
- Obstructed urine flow (kidney stones, catheters), Injury
- Immunocompromise, immune system disorder, congenital abnormalities

Diagnosis

Urinalysis & Digital Rectal Examination (DRE)

Non-Pharmacological Treatment

- Hot baths
- Avoid caffeine, alcohol and spicy food
- Avoid hard bowel motions and constipation which can put pressure on the prostate and cause more pain
- Use of condoms during sexual intercourse to prevent future episodes

Pharmacological Treatment — [The Pink Book Prostatitis](#)

Note: Nitrofurantoin is **not** appropriate treatment of prostatitis due to poor tissue penetration

1. Acute (Spontaneous) Prostatitis — Oral Antibiotics (4 weeks)
 - *First Line*: Trimethoprim + Sulfamethoxazole
 - *Alternative*: Ciprofloxacin
2. Complicated Prostatitis — IV Antibiotics (minimum 4 weeks)
 - *First Line*: Gentamicin AND Amoxicillin + Clavulanic Acid
 - *Mild Penicillin Allergy*: Gentamicin AND Cefuroxime
 - *Severe Penicillin Allergy*: Consult infectious diseases/clinical microbiology
2. Other
 - *a-blockers (relax bladder neck/muscle fibres)*: Doxazosin, tamsulosin, prazosin, terazosin
 - *Pain relief*: Paracetamol, NSAIDs
 - *Surgery*: but risk of dry ejaculation

Upper Urinary Tract Infections (UUTIs)

Pyelonephritis

[NZF Pyelonephritis](#)

Description

Pyelonephritis is an upper urinary tract/renal infection causing inflammation of the kidney(s) and ureter(s). It is an infection that is most likely to begin in the bladder, but can be due to an infection spread from the blood. Commonly caused by E.coli and candida. Uncommon in the community, but common in the hospital due to catheter use.

Signs & Symptoms

Acute: Flank pain, fever, N/V, fatigue, dysuria, frequency, urgency, foul smelling urine, blood/pus in urine

Chronic: Low grade pain, fever, urinary symptoms, weight loss, malaise, fatigue

Complications: AKI/CKD, renal failure

Risk Factors

- Recurrent Cystitis
- Obstructed Urine Flow (kidney stones, catheters)
- Immunocompromise
- Congenital Abnormalities (utererale reflux — backflow of urine from bladder to kidneys)

Diagnosis

- Urinalysis
- Abdominal examination (CT scan)

Pharmacological Treatment

[BPAC Pyelonephritis Antibiotic Guidelines](#) [The Pink Book Pyelonephritis](#) (for known cultures)

Acute: Oral antibiotics (10 days)

1. *If mild:* Trimethoprim + sulfamethoxazole
2. *If severe:* IV gentamicin (hospital; use IBW)
3. *Alternatives/additional:* Amoxicillin + clavulanic acid, Cefalexin

Chronic: Treat underlying cause

1. Long term and prophylactic therapy

Monitoring

- Gentamicin is associated with ototoxicity and nephrotoxicity (narrow therapeutic range)

Complications of Urinary Tract Infections

Kidney Stones

Description

Kidney stones are the accumulation of mineral salts found in urine that form in the kidney and ureters. They themselves aren't a UTI but are risk factors for one or can be the result of one. They also share the same symptoms as complicated UTIs.

Types of Stones

- Calcium (75-85%)
- Uric Acid (5-8%)
- Cystine (<1%)
- Struvite (10-15%) — caused by infections (e.g. recurrent cystitis)

Risk Factors

- Bacterial infection
- Dehydration / drinking too little water
- Eating food with too much salt or sugar
- Exercise (too much or too little), obesity, weight loss
- Surgery

Signs & Symptoms

Asymptomatic

N/V, fever, chills, tenderness in abdomen region, blood in urine, frequency, urgency, dysuria

Diagnosis: *only ~10 % of people will have kidney stones diagnosed*

- Urinalysis
- Imaging (Ultrasound, CT)

Non-Pharmacological Treatment

- ~ 86 % of stones will pass spontaneously (but pain relief may be required)
- Hydration

Pharmacological Treatment

- Pain relief
- Treat infection & prevent recurrent cystitis
- Surgical procedures if stones:
 - Do not pass after a reasonable period of time and cause constant pain
 - Too large to pass on their own and cause obstruction
 - Cause too many ongoing UTIs
 - Damage kidney tissue

- Cause constant bleeding
- Have grown larger as seen on X Ray.



Surgical Procedures

Include: open surgery, ureteroscopic & nephroscopic techniques (stones shattered using shockwaves or removed), extracorporeal shockwave lithotripsy (non-invasive)

Asymptomatic Bacteria Infection (ABU)

Description

ABU is defined as ‘two positive consecutive clean catches (mid-stream) specimens with **NO symptoms**’

It is a type of urinary tract (UT) bacterial colonisation that is often **mistaken for an UTI**, however it isn’t an infection that requires treatment. They themselves do not progress to a symptomatic UTI and in fact, their treatment is associated with an increased risk of infection with drug resistant E.coli — studies have shown that young women treated for ABU were more likely to develop a symptomatic UTI.

This is because they act as a protective local microflora, especially in prevention of symptomatic recurrence. ABU microbe is used to treat UTI because it was found to out-compete drug-resistant pathogenic strains and subjects reported fewer UTIs with the achievement of long term colonisation. These are very common and their prevalence increases with age, diabetes, and pregnancy.

Recommendation

“It doesn’t cause any harm so don’t look for it!”

- Do **not** screen or treat pre-menopausal, non-pregnant women (diabetic or not)
- May screen & treat pregnant women due to increased risk of pyelonephritis, premature delivery, and birth of low birth weight babies.
- It is no longer recommended to perform routine pre-operative urine testing in those undergoing major surgery as ABU isn’t a risk factor for haematogenous bacterial spread.

Urinary Incontinence

[NZF Urinary Incontinence in women](#) [BPAC Urinary Incontinence](#)

Description

Urinary incontinence is a heterogenous condition that causes dribbling to continuous involuntary loss of urine or stool in sufficient amounts or frequency to constitute a social and/or health problem.

While 80% of urinary incontinence can be cured or improved, this condition is unfortunately very much under-diagnosed and under-treated as patients do not report it and health care professionals do not routinely ask about it.

TYPES OF URINARY INCONTINENCE	
Overflow Urinary Incontinence (OUI)	<p>Bladder doesn't empty fully and/or properly Overflow urinary incontinence describes the frequent or constant dripping of urine from the urethra due to bladder overdistention.</p> <p><i>Bladder Outlet Blockage</i></p> <ul style="list-style-type: none">BPH, Strictures, Cystocele, Fecal impaction <p><i>Non-Contractile Bladder</i></p> <ul style="list-style-type: none">Hypoactive detrusor, Atonic Bladder, Diabetes, MS, Spinal injuryMedications: Drugs with anticholinergic effects
Stress Urinary Incontinence (SUI)	<p>Pressure on the bladder results in urine leaking Stress incontinence is the result of a relaxed pelvic floor and increased abdominal pressure (coughing, laughing, exercising, lifting heavy things). This is the most common cause of involuntary leaking and the most common type in women < 75 years</p> <p><i>Hyper-motility of the bladder neck and urethra (85% of cases)</i></p> <ul style="list-style-type: none">Associated with ageing, hormonal changes, childbirth trauma, pelvic surgery <p><i>Intrinsic Sphincter Problem (15% of cases)</i></p> <ul style="list-style-type: none">Pelvic surgery, radiation, trauma, neurogenic causes
Urgency Urinary Incontinence (UUI)	<p>Uncontrollable need to go the bathroom (usually idiopathic) Most common in men. Urge incontinence is the sudden intense urge to urinate followed by an involuntary loss of urine. This occurs due to detrusor muscle overactivity. Many things can render the bladder over-sensitive:</p> <p><i>Infections</i></p> <ul style="list-style-type: none">Infections, tumor, atrophic vaginitis or urethritis <p><i>Neurological Disorders</i></p> <ul style="list-style-type: none">Strokes, Parkinson's disease, dementia, spinal injury
Overactive Bladder Syndrome	<p>Urgency incontinence with no known cause — (managed the same way as urgency incontinence) Overactive bladder syndrome is a largely idiopathic urological condition comprising urgency, frequency and, often, nocturia — the loss of neurological control of the detrusor muscle activity (detrusor overactivity) is thought to contribute to the condition. However, in people with overactive bladder, urgency and frequency can occur without any resulting incontinence. The frequency of voiding will generally be more than eight times per day.</p>
Functional Urinary Incontinence (FUI)	<p>This type of incontinence does NOT involve the lower urinary tract Physical, cognitive or mental impairment keeps you from making it to the toilet in time</p> <p><i>Example</i></p> <p>Severe arthritis means you can't unbutton your pants quickly enough, wheelchair-bound</p>
Mixed Urinary Incontinence (MUI)	<p>A combination of stress and urgent incontinence Person experiences more than one type of urinary incontinence. Usually defined as urgency that occurs without or without urgency urinary incontinence and usually with frequency and nocturia.</p>

Pathophysiology

The lower urinary tract has two functions:

- Filling and storage of urine*

- Increase in volume while maintaining low pressure
- Sensation of bladder filling
- Bladder outlet that remains closed when subjected to pressure
- Absence of involuntary contraction

2. *Emptying of urine*

- Coordinated bladder contraction with relaxation of the outlet
- No physical obstruction
- Physiologic bladder contraction is mediated by ACh at (M₃)

The Process of Micturition

The micturition reflex starts when the bladder begins to fill, which is sensed by stretch receptors and relayed to the brain (express a conscious/voluntary desire to urinate) and to the sacral region of the spinal cord (allow contraction of the bladder). The greater the stretch, the greater the frequency of the signals between the bladder and the sacral segment.

If urination is not possible at the time

The micturition reflex is inhibited via voluntary contraction of the external sphincter

When urination is possible

The micturition reflex is stimulated and the external sphincters relax while the bladder muscle (detrusor) contracts. It is important to note that **estrogen** holds a hormonal effect over the bladder — in older women, atrophy of tissue and muscle (associated with declining estrogen) causes poor bladder control.

In normal people, drinking approximately 2L of water should result in bathroom visits of no more every 3-4 hours. In incontinence, control over the urinary sphincter is either lost or weakened, resulting in reduced outlet resistance.

A note on pregnancy

Pregnancy can cause abnormal contractions (overactive bladder or detrusor overactivity) resulting in incontinence. Estrogen also has a hormonal effect on the bladder. In older women, bad bladder control is associated with declining estrogen (because it causes atrophy of tissue and muscle)

Risk Factors

Age & Gender

- Children (e.g. nocturnal enuresis)
- Older adults
- Being female (pregnancy, menopause)

Environment

- Functional impairment (restricted mobility)
- Barriers to toilet access

- Diet (drinking little water, caffeine, alcohol)

Medical Conditions

- Psychological/endocrine disorders, BPH
- Dementia, delirium, diabetes, MS, spinal injury
- Atrophic vaginitis/urethritis, kidney infections

Medications

- Diuretics, sedatives/hypnotics, narcotics, CCBs
- **Anticholinergics:** antihistamines, antipsychotics, anti-depressants

Acronym: DIAPPERS for potentially REVERSIBLE causes of urinary incontinence

Delirium

Infection

Atrophic Vaginitis or Urethritis

Pharmaceuticals

Psychological disorder

Endocrine Disorders

Restricted Mobility

Stool impaction



Note

The bladder is like a muscle — it can hold up to 500mls of urine. However, failure to maintain adequate hydration can result in it shrinking and becoming stiff (i.e. can now only hold up to 50mls of urine)

Red Flags

- Haematuria (blood in urine)
- Recurrent UTIs (3+ in the last 6 months)
- Loin pain (lower back)
- Recurrent catheter blockages
- Hydronephrosis or kidney stones on imaging
- Biochemical evidence of renal deterioration

Complications

1. *Social stigma* (restricted activities, depression)
2. *Medical complications* (skin breakdown, increased UTIs)
3. *Institutionalisation* (UI is the second leading cause of nursing home placement)

Diagnosis

- Stress test (diagnostic for **stress incontinence**; specificity >90%)
- Post-void residual
- Blood Tests (calcium, glucose, BUN, Cr)
- Urine Culture (to rule out infections)
- Simple (bedside) Cystometrics
- Bladder diary (record how often you drink and how often you go to toilet)

Non-Pharmacological Treatment

- Reduce/eliminate caffeine and alcohol
- Drink 6-8 glasses of water daily. Avoid excess fluid and drinking at night time
- Quit smoking
- Weight control
- Follow a healthy diet that prevents constipation/faecal impaction
- Reduce physical barriers to toilet (e.g. bedside commode)
- Incontinence pads

Bladder Training

- Pelvic floor exercises (kegel): 3 times a day
- Regular scheduled voiding pattern, with gradual increase in intervals between avoiding. This reverses bad habits and retrains the bladders

Interventional Therapy

- Bulking material injections
- Botox
- Nerve stimulators
- Pessaries: urethral inserts
- Sling surgeries

Pharmacological Treatment

1. *Anticholinergics/Antimuscarinics (oxybutynin, solifenacin, tolterodine)*
 - As it is not specific for M₃ receptors, it results in many anticholinergic side effects
 - Contraindications in narrow angle glaucoma and urinary retention
2. *α-Blockers (tamsulosin, doxazosin, terazosin)*
 - For overflow incontinence in men
3. *Topical Estrogen*
 - Vaginal ring, patch or cream can help tone/rejuvenate tissues in the urethral/vaginal area for women.

Monitoring

- Assess anticholinergic medicines for incontinence after 6 weeks



CHAPTER 11

THE ONCOLOGIC SYSTEM



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Chapter 11

The Oncologic System

General Overview of Cancer

Chapter Resources

Here are a few great resources for Oncology:

1. [NZF Cytotoxic Drugs](#)
2. [NZF Cancer Regimens](#)
3. [BPAC Oncology Category](#)
4. [EVIQ](#)
5. See Pharmacotherapy Principles 6th Edition - Oncologic Disorders

Tumours vs Cancer

A tumour is a mass of cells in which the cell cycle is no longer regulated. When a tumour doesn't spread (although they may still cause tissue damage), they are called *benign*. But when they do, they are known as *malignant* — these are the ones we call *cancer*. The spread of cancer to a secondary site is called *metastasis*.

TYPES OF CANCER		
Name	Description	Prefixes
Carcinomas	Epithelial Tissue (Skin & Internal Organs) <ul style="list-style-type: none">• Lung• Breast (women)• Colon• Bladder• Prostate (men)	<ul style="list-style-type: none">• Adeno- (gland)• Hepato- (liver)• Melano- (pigment cell)
Sarcomas	Non-Epithelial Tissue (Bone & Connective Tissue) <ul style="list-style-type: none">• Fat• Bone• Muscle	<ul style="list-style-type: none">• Lipo- (fat)• Osteo- (bone)• Myelo- (bone marrow)• Myo- (muscle)• Chondro- (cartilage)
Leukemias	Bloodstream <ul style="list-style-type: none">• Blood	<ul style="list-style-type: none">• Erythro- (red blood cell)• Hemangio- (blood vessels)
Lymphomas	Lymph Nodes <ul style="list-style-type: none">• Axillary• Cervical	<ul style="list-style-type: none">• Lympho- (lymphocyte)

Cancer Pathogenesis

For a tumor to develop, it must go through the below three steps successfully. Please note that not all tumors are sufficiently mutated enough to go through each of the below steps — many will simply reverse back to normal without intervention.

STAGES OF CANCER DEVELOPMENT & METASTASIS

Oncogenesis - Proliferation of Tumour Cells

Tumours begin with the formation of DNA mutations in *key gene families*, these disrupt and cause an unregulated cell cycle. This is known as oncogenesis.

1. Tumour Suppressor Genes (*turned off*)

- Growth factors, growth regulations, repair & apoptosis genes, contact inhibition genes

2. Proto-Oncogenes (*turned on*)

- Angiogenic genes e.g. vascular endothelial growth factor (VEGF)
- Allow metastasis and escape from immune surveillance

Successful Proliferation Prevention

The reason why the majority of the time tumours do not happen is often because checkpoints exist in the cell cycle to prevent them:

1. Mitosis & Apoptosis

The normal cell cycle consists of cells being formed by division (mitosis), completing their function and eventually wearing out and dying (apoptosis). Telomeres, protective caps on the ends of chromosome, shorten with each division and act as an internal divisional clock to regulate the cell's lifespan.

Normal DNA replication naturally comes with a certain number of mutations - however they do not lead to cancer as they get repaired, or affect non-coding DNA. If DNA damage is present, the cell should not enter the cell cycle (GA arrest) or mitosis is delayed until the damage is repaired (G2/M arrest). If the damage is not repaired, apoptosis is initiated (genes/proteins involved include p53, Bax and Rb)

2. Cell Turnover

To replace the cell that has undergone apoptosis, another one is produced to maintain a homeostatic balance division. This allows a careful regulation of the cell cycle to prevent mutations from progressing.

When repairs fail (e.g. checkpoint mutation in apoptosis genes) the cell continues to divide and perpetuates the mutation, passing on the change to its daughter cells. When multiple successive mutations build up to a certain threshold, the cell cycle becomes unregulated. Division no longer equals apoptosis and a tumour develops, stabilising the telomere length.

- Tissues with higher cell turnover rates (bone marrow, mucosal surfaces, skin) will have a higher risk of cancer
- The more mutations that are present, the more immunogenic the tumour will be

Proliferation Prevention Failure

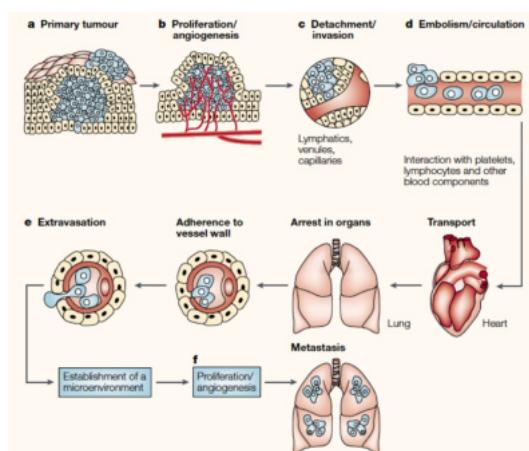
Mutations in tumor suppressor genes or proto-oncogenes have many triggers:

1. *Old Age*: Multiple successive mutations can occur as DNA replication has occurred many times - this eventually meet the threshold for a tumour to develop and thus unregulate the cell cycle.
2. *Hereditary*: It is possible to inherit defective tumour suppressor genes or activated oncogenes, thereby increasing your likelihood to develop cancer.
3. *Environmental Insult*: A buildup of successful mutations can also be obtained from the environment (chemical carcinogens) or physical (radiation)
4. *Infectious Agents*: Human Papillomavirus (HPV) are viruses that cause cutaneous warts, genital warts and cervical cancer! However with the development of a vaccine, this has become less prevalent.

1. Transformation & Proliferation (Drug Target)

STAGES OF CANCER DEVELOPMENT & METASTASIS

	<p>Avoid immune system recognition The immune system has an anti-tumor/anti-cancer response.</p> <p>Successful Immune Response It is a cytotoxic immune response by cellular CD8 T cell that is activated by an APC and responds to any cell with MHC Class I + Foreign Tumor Antigen - the same one used for virus infected cells. There are two things to consider:</p> <ol style="list-style-type: none"> 1. While tumours/cancers are not infections, we hope that enough necrosis/cell stress occurs to activate the APC. 2. While tumors/cancers are self tissues, we hope that the level of mutations are sufficient enough that the immune system labels it as a foreign pathogen. <p>Immune Response Failure There are two reasons why the immune system may fail to eradicate the growth:</p> <p>2. Avoidance</p> <ul style="list-style-type: none"> People Can't Respond <ol style="list-style-type: none"> 1. <i>Age</i>: Immune responsiveness decreases with age — with older people thus having a less effective anti-tumour response 2. <i>Drug/Radiation</i>: Cancer treatment itself destroys the immune system, preventing it from killing the tumours. This is often why immunosuppressed patients (e.g. transplant receivers) are likely to develop cancers Resistant Clones These can essentially render the tumor invisible to the immune system <ol style="list-style-type: none"> 1. <i>Evide the immune system</i>: They do not make any antigens and shut down the MHC-1 pathway 2. <i>Suppress the immune system</i>: via the secretion of certain suppressive molecules <p>Immune Response Pro-Tumor Effect Long term chronic inflammation was found to be associated with oncogenesis. This inflammation can also be associated with factors external to the immune system (e.g. obesity, smoking, GORD, infections)</p>
3. Angiogenesis (Drug Target)	<p>Tumor must vascularise Angiogenesis is the recruitment of blood vessels by tumours to supply oxygen/nutrients necessary for their growth. As the new blood vessels are <i>leaky and inefficient</i>, they are a good target for drug therapy. Lymphangiogenesis was also found to occur prior to the tumour spreading into the lymph nodes.</p>
4. Invasion	<p>Invasion In order for a tumour to be able to invade neighbouring tissues, mutations must occur to allow for the following:</p> <ol style="list-style-type: none"> 1. <i>Decrease in adhesion</i>: via E-cadherin, integrin mutations 2. <i>Ability to move</i> 3. <i>Disrupt/break down extracellular matrix & other physical barriers</i>
5. Penetration	<p>Blood Vessel Penetration, Accumulation of cells in small vessels, & Exit from vessels 1. Movement towards blood vessels in response to oxygen/nutrients 2. Enter leaky new vessels or breach intact vessels 3. Surviving the ride (physical shear stress & platelet adhesion)</p>
6. Spread	<p>Local metastasis via local lymph nodes (new lymphatic vessels), distant metastasis via bloodstream Once the cancer spreads via blood, it starts to spread locally and distally. By this stage, it is difficult to locate the primary source of the tumour and it is difficult to treat it. Some cancers are specific as to where they want to spread, others not. Mechanical lodging plays a large part in where the tumour goes.</p>
7. Growth	<p>Proliferation Following extravasation (exit of the blood vessel), the tumour must now grow and thrive. Many tumours cannot do this as their growth depends on whether they can establish a microenvironment and stimulate angiogenesis.</p>



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Screening, Grading & Staging

SCREENING & DIAGNOSIS	
Stage	Description
Screening	<p>Screening detects the possibility of cancer — not <u>definitive</u> and often uses population based tests.</p> <ul style="list-style-type: none"> • Visual inspection, self-examination (breast self examination, blood in stools, mole checks) • Imaging (mammography, pap smears) • Tests for tumour biomarkers (PSA, CEA, etc...) <p>Sensitivity & Specificity</p> <ul style="list-style-type: none"> • Sensitivity is the ability of screening test to detect disease in a population • Specificity is the ability of screening test to identify the absence of the disease in a population
Diagnosis (definitive)	<ol style="list-style-type: none"> 1. Imaging (X-Ray, CT, RET, MRI) <ul style="list-style-type: none"> • Imaging allows us to find a lump and with time, we have become better at picking up smaller ones. 2. Biopsy (Cancer Grading & Staging) <ul style="list-style-type: none"> • Biopsies allows us to grade and stage the lump found via imaging with microscopical examination. <p><i>Grading (appearance of cancer cells) Depends on Cancer</i></p> <ul style="list-style-type: none"> • 4 or 10 point scale • Low grade = normal tissue structure with well differentiated cells • High grade = undifferentiated disorganized mass <p><i>Staging (size and spread of cancer cells) TNM Staging Method</i></p> <p>T - Tumour</p> <ul style="list-style-type: none"> • TX = Primary tumour cannot be found • T0 = Primary tumour cannot be measured • T1, 2, 3 ... = Size of the tumour <p>N – Node involvement</p> <ul style="list-style-type: none"> • NX = Nodes cant be assessed • N0 = No nodes involved • N1, 2, 3... = Number of nodes involved <p>M – Has the cancer metastasised</p> <ul style="list-style-type: none"> • MX = Cannot be measured • M0 = No metastasis • M1 = Tumour has spread to other parts of the body

Aseptic Dispensing

Introduction

Pharmacists generally work in aseptic conditions with sterile starting materials to prepare aseptic products. Hence we use the term aseptic dispensing.

Sterile vs Aseptic

Sterile means free from all microbiological contaminants i.e. living organisms, particles, and pyrogens.

Whereas *aseptic* means produced from sterile components in a sterile environment – however it does NOT guarantee sterility.

Avoiding Contamination

Aseptic technique is all about avoiding contamination from 2 things: viable matter and non-viable matter.

1. Viable (live):

- Viable material are live things like bacteria, fungi, and viruses.
- Administration of viable material could result in fever, infection, septicaemia, multi-organ failure, death

2. Non-viable:

- These are things like undissolved particulate matter e.g. plastic/rubber material, glass shards, and chemical precipitates. Non-viable material may occlude vessels — if $>12 \mu\text{m}$ they may become trapped in the lungs leading to respiratory failure and death.

Laminar Air Flow (LAF)

LAF is a smooth, steady and constant flow that is used in aseptic dispensing to ensure the product is as clean as possible. The filtration system (HEPA) provides a particle free environment by ensuring a high airflow that is constantly filtered and replenished. Many things can disrupt the flow thus product placement is important! (e.g. large bulky items can thus increase risk of cross contamination)

LAMINAR AIR FLOW - CABINET TYPES		
	HORIZONTAL	VERTICAL
Description	<ul style="list-style-type: none">• Air flow is horizontal towards the operator.• Filter at the back• The product is really well protected. The operator is not	<ul style="list-style-type: none">• Airflow is vertical• There is a glass shield and filter on top• Both product and operator are protected.
Medicines	Medicines that would not harm the operator	Cytotoxics, hormonal medicines, fine powder irritants of allergic potential (e.g: teratogens, antibiotics like penicillins) ect...any medicine that could harm the operator

TYPES OF CHEMOTHERAPIES

Pharmacological Treatment in Oncology

1. Cytotoxic Therapy
2. Endocrine Therapy
3. Targeted Therapies

Goals of Cancer Therapy

- Consider patient's goals
- Prevent mortality/prolong survival
- Prevent complications & minimise ADRs: difficulty breathing, infections susceptibility, metastasis, death
- Improve signs & symptoms: difficulty breathing, pain, cough
- Improve quality of life i.e. 5 dimensions of life:
 1. Physical (pain)
 2. Functional (independence to complete daily tasks)
 3. Psychological (stress, depression, anxiety)
 4. Social (relationships)
 5. Spiritual (beliefs)

Mechanisms of Resistance to Chemotherapeutics

Different tumours have different levels sensitivity to chemotherapy — this sensitivity is related to growth fraction (e.g. lymphomas > sarcomas). This sensitivity changes during treatment which can result in resistance

CELLULAR RESISTANCE		
Regardless of the theory, the rational is to treat as rapidly and early as possible and with a combination!		
	Description	Theory
Primary Resistance	No Response to Administration	Resistance is a property of the tumour from the get-go
Acquired (Secondary) Resistance	<p>Initial regression, but then tumour reappears and patient relapses. Caused by:</p> <p><i>1. Alterations in drug metabolism</i></p> <ul style="list-style-type: none">• Reduced drug uptake (e.g. tumours evolve to do so)• Decreased drug concentration (e.g. less prodrug activation)• Removal of drug (e.g. via efflux pumps) <p><i>2. Modifications to drug target</i></p> <ul style="list-style-type: none">• Alteration of intracellular drug targets (tumour receptor resistant)	<p>Theory 1</p> <p>Tumours are heterogenous families of different little cells. Theory 1 suggests that tumours have a few little resistant clones that remain after therapy - these re-proliferate and repopulate the tumour. Consequently the drug caused their natural selection.</p> <p>Theory 2</p> <p>Therapy is mutagenic and induces resistance in certain cells - which remain after therapy and repopulate the tumour via natural selection.</p> <p>Combined Theory</p> <p>The tumour is resistance due to being repopulated with resistant clones on top of a mutagenic therapy.</p>

Apparent Resistance	<p>This occurs prior to the drug reaching the tumour - this is because the tumour may seem resistant when it actually isn't.</p> <p>A tumour can be sensitive to a drug but not show a clinical response due to 2 things:</p>	<p>1. Incorrect Scheduling</p> <ul style="list-style-type: none"> • Cell cycle specific agents have a maximal effect at a certain time - this may not happen if the interval is too long or the half life is too short. • In those situations, an infusion would be better than a bolus as it allows us to catch a higher proportions of cells in the phase cycle phase. <p>2. Anatomical Isolation</p> <ul style="list-style-type: none"> • The tumour is anatomically isolated, e.g. the core contains cells that are hypoxic and acidic - resulting the drug failing to eradicate it and causing it to regrow.
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Cytotoxic Therapy

Description

Cytotoxic drugs (sometimes known as antineoplastics) describe a group of medicines that contain chemicals which are toxic to cells in order to prevent their replication/growth — making them incredibly useful in cancer.

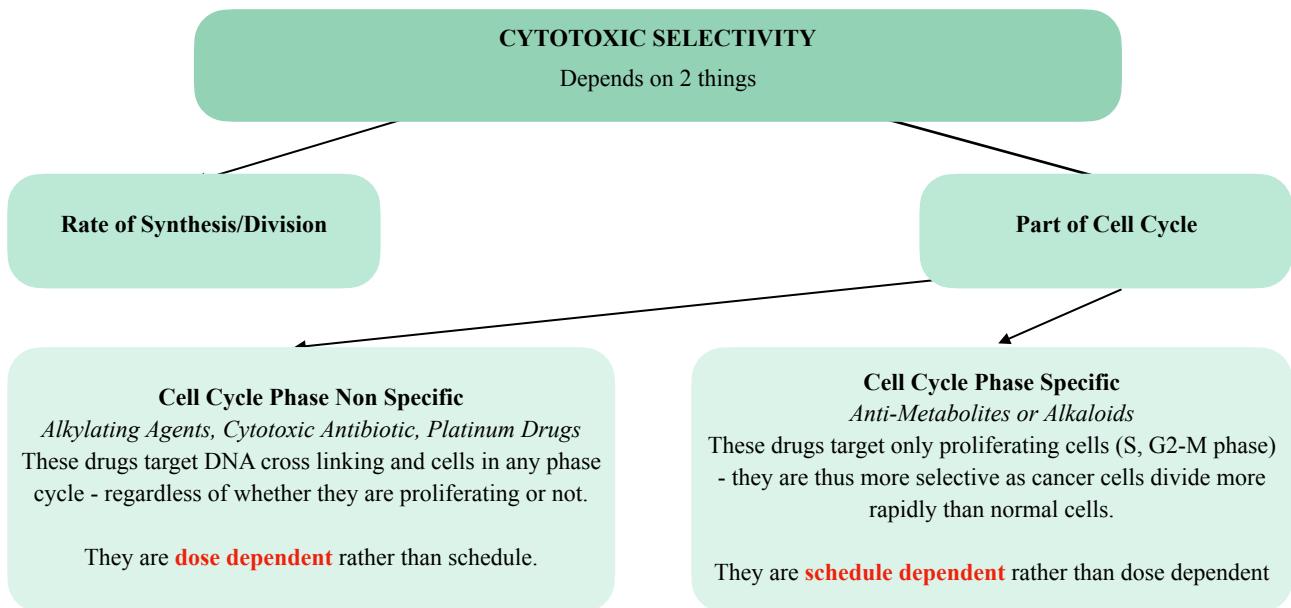


Toxicity

Cytotoxic drugs have a therapeutic index of 1 — which means that the **therapeutic index is equivalent to the toxic dose**. This causes a few issues on healthy cells, particularly rapidly dividing ones.

Mechanism of Action

The selectivity of cytotoxic drugs depends on two things:



The respective selectivity of the cytotoxic will thereby affect the resultant sensitivity to treatment e.g. giving a cytotoxic that works on dividing cells will have a poor effect if cells are in the rest phase.

Kinetics of Cell Killing

Proportional Cell Kill

Growth fraction describes how many cells in a tumour that are dividing. This number is normally 20% — however the greater the growth fraction, the better the chance of cell death.

- For a given dose of a cytotoxic, a fixed proportion of cells are killed.

Intermittent Therapy

- Maximises tumour killing (dose intervals allow recovery of health cells and an eradication level sufficient to prevent recurrence)
- Efficacy increases if treatment is timed to the correct phase of cell division

CYTOTOXIC THERAPY			
	Drug Class	Mechanism of Action	Side Effects
Cell Cycle Non-Phase Specific	Alkylating Agents (Breast, lung cancer)	<p>Cyclophosphamide Alkylating agents bind covalently to DNA, RNA and proteins.</p> <ol style="list-style-type: none"> Target DNA/RNA cross linking by adding an alkyl group to the guanine base. This prevents the cancer cell from multiplying and causes its eventual death. Target proteins to block DNA repair. 	<p>Side Effects</p> <ol style="list-style-type: none"> BMS, Hair loss, GI disturbances Haemorrhagic Cystitis <ul style="list-style-type: none"> Due to toxic metabolite acrolein Risk increases with poor hydration and dose Pre-treatment with Mesna or IV hyperhydration Cardiac Damage <ul style="list-style-type: none"> Cyclophosphamide oxidative stress Heart failure, arrhythmia <p>Metabolism <i>CYP Polymorphism dictate side effects</i></p> <ol style="list-style-type: none"> CYP2C19 = less ovarian side effects CYP2B6 = more renal failure
	Cytotoxic Antibiotics Anthracyclines (Some leukemias, solid tumours)	<p>Daunorubicin, Doxorubicin, Dactinomycin, Epirubicin S Phase</p> <ul style="list-style-type: none"> Mainly target cross linking via DNA intercalation. All isolated from the bacteria streptomyces. Given IV As a rule of thumb should not be given with radiotherapy (risk of hepatic injury) 	<p>Side Effects</p> <ol style="list-style-type: none"> Stomatitis, vomiting, alopecia, skin necrosis (due to extravasation) - note that these are vesicants Cardiotoxicity (with dauno/doxorubicin) Mainly BMS (dactinomycin) Flare reaction
	Cytotoxic Antibiotics Non-anthracyclines (Germ cell tumours, Hodgkin's Lymphoma)	<p>Bleomycin (non-anthracycline antibiotic) S Phase</p> <ul style="list-style-type: none"> DNA intercalation, free radical induced strand breaks. Increased risk of side effects with age and radiotherapy. 	<ol style="list-style-type: none"> Less BMS but more pulmonary/dermatological toxicity (bleomycin) <p><i>Note:</i> cancer, skin and lung cells have low amounts of hydrolase whereas the bone marrow is high in them. It is likely that bleomycin is more toxic in places that have low amounts of that enzyme.</p>
	Platinum Drugs (non-classical alkylating agents) (Solid tumours: testicular, ovarian, bladder, head, neck)	<p>Cisplatin, Carboplatin, Oxaliplatin</p> <ul style="list-style-type: none"> Non-classical alkylating agents that cause intra strand linking. Given IV 	<ol style="list-style-type: none"> N&V, BMS, GI Toxicity Renal Toxicity & Peripheral Neuropathy Ototoxicity
Cell Cycle Phase Specific	Anti-Metabolites (false substrates)	<p>Methotrexate, capecitabine —> 5-FU, Mercaptopurine, cytarabine S Phase</p> <p>Antimetabolites work by mimicking the molecules that a cell needs to grow (e.g. methotrexate is a folate analogue). They are mistakenly taken up by cells and incorporated as 'normal' building blocks, thereby interfering with nucleic acid synthesis due to the following:</p> <ol style="list-style-type: none"> Incorporating into nucleic acids Act as enzyme substances <p>Given IV, Intrathecal</p>	<p>Side Effects</p> <ol style="list-style-type: none"> BMS, Hair loss, GI disturbances Hand-foot syndrome with capecitabine <p>MTX rescue: leucovorin/folinic acid</p>
	Plant Alkaloid Vinka Alkaloid	<p>Vincristine, vinblastine, vinorelbine, vindesine M Phase</p> <p>Inhibit spindle formation for mitosis by binding to tubulin.</p> <p>Given IV.</p>	<p>Side Effects</p> <ol style="list-style-type: none"> BMS, Hair loss, GI disturbances (constipation) Neurotoxicity (vincristine) Neuropathy Paraesthesia
	Plant Alkaloid Taxanes	<p>Docetaxel, Paclitaxel M Phase</p> <p>In contrast of preventing microtubule formation, they stabilise the structure, preventing cell-division in the M phase</p> <p>Given IV.</p>	<ul style="list-style-type: none"> Dose-limiting neutropaenia Arthralgia/myalgia syndrome (mechanism unknown) Paclitaxel: sensory neuropathy (motor at higher dose), hypersensitivity reactions, myalgia Docetaxel: leg oedema (fluid retention – peripheral effect), febrile neutropenia, skin reactions
	Drugs Targeting Eukaryotic Topoisomerase	<p>S/G2/M Phase</p> <p>Topoisomerase I inhibitor: Irinotecan, topotecan</p> <p>Topoisomerase II inhibitor: etoposide, teniposide</p>	<ul style="list-style-type: none"> Diarrhoea, N/V, BMS

CYTOTOXIC SIDE EFFECTS		
Effect	Description	Signs & Symptoms
Bone Marrow Suppression	<p>Cytotoxics can deplete and damage the bone marrow stem cell pool due to their rapid turnover, resulting in falling levels of circulating cells.</p> <p>Lifespan of cells:</p> <ol style="list-style-type: none"> WBCs → 4-5 days Platelets → 9-10 days Erythrocytes → 120 days <p><i>Note:</i> extent, severity and duration of BMS differs with different cytotoxics</p> <ol style="list-style-type: none"> Different effects on precursor stem cells (pluripotent vs unipotent) Kinetics of cell types in peripheral blood (life span and cell turnover) Cycle non-specific drugs will have a greater duration of BMS than phase specific Hydrolase levels with bleomycin 	<p>Following administration (in order of frequency)</p> <ol style="list-style-type: none"> Fall in WCC (in 3-7 days) Leukopenia → Infection Fall in Platelets (in 7-14 days) Thrombocytopenia → Bruising Fall in RBCs (in 6-8 weeks) → Anaemia <p>RBC depletion is rare with a single dose as the bone marrow usually recovers.</p>
Gastrointestinal Toxicity	<p>There are two reasons why this occur</p> <ol style="list-style-type: none"> <i>High turnover rate</i> Mucosal cells in the GI tract have a high turnover rate (4-7d) and have a pathogen rich environment given the extent of local trauma that occurs (e.g. food). <i>Pathogen rich environment</i> The additional burden of BMS can thus subsequently cause progression of significant infections 	<p>3-4 days following cytotoxic administration</p> <ol style="list-style-type: none"> Oesophagitis, diffuse ileitis, colitis, oral mucositis Pain, tingling, dryness, loss of taste, ulceration <p><i>Note:</i> younger patients affected more than older patients due to a greater basal rate turnover.</p>
Dermatological Toxicity	<p>Three types of dermatological toxicity</p> <ol style="list-style-type: none"> <i>Hair Loss</i> This effect is reversible - but occurs as 60-90% of hair follicles are dividing at any one time with a doubling time in 24h. <i>Specific Skin Toxicity</i> The growth of skin cells and capillaries are affected. <i>Extravasation</i> Vesicants can cause severe local reactions 	<ol style="list-style-type: none"> <i>Hair loss:</i> Alopecia <i>Skin:</i> Palmar-plantar syndrome (capecitabine) <i>Vesicants:</i> Inflammation, necrosis and ulceration

Endocrine Therapy

Description

Certain hormonal cancers, such as breast and prostate cancer, can be treated with the following therapies:

ENDOCRINE THERAPY FOR HORMONE SENSITIVE CANCERS				
Drug		Mechanism of Action	Post/Pre Menopause?	Side Effects
Breast Cancer Estrogen	Selective Estrogen Receptor Modulators	Tamoxifen, Clomiphene Citrate, Nafoxidine SERMs - competitively binds to estrogen receptors, effects vary per tissue: <ul style="list-style-type: none"> • <i>Anti-estrogenic effects</i> on the breast tissue and brain • <i>Estrogenic effects</i> on bone, lung liver, uterus 	Pre-Menopausal Women <i>Tamoxifen is however okay in both pre and post menopausal women!</i> Before menopause, your primary source of estrogen is your ovaries, after menopause, it's your peripheral tissues!	As an antagonist in the brain, it causes menopausal symptoms. The tamoxifen flare is a good indication that treatment is working! <ul style="list-style-type: none"> • Hot flushes, nausea, risk of uterine cancer, endometrial cancer, DVTs • <i>Pre menopausal:</i> amenorrhoea • <i>Post menopausal:</i> vaginal bleeding
	Aromatase Inhibitors	Anastrozole, Letrozole (non steroid), Exemestane (steroid) Aromatase inhibitors act predominantly by blocking the conversion of androgens to estrogens in the peripheral tissues - the main source of estrogen following menopause.	Post-Menopausal Women This drug will not work in pre-menopausal women as their main source of estrogen comes from the ovaries.	<ul style="list-style-type: none"> • Stiffness, joint pain • Loss of bone mineral density (osteoporosis, bone fractures)
Prostate Cancer Testosterone	GnRH Analogues	Goserelin, Leuprorelin Activates the negative feedback loop to decrease testosterone production from the testicles (desensitisation and consequently suppressed GnRH secretion)	-	Initial flare (transient rise) will exacerbate symptoms: <ul style="list-style-type: none"> • Sexual dysfunction, hot flushes, growth of breast tissue, osteoporosis
	Anti-Androgens	Flutamide, bicalutamide, cyproterone acetate Selective testosterone antagonist with no effect on pituitary function. Inhibits flare associated with starting GnRH analogues.	-	As selective, has fewer side effects on libido, hot flushes, bone loss but is less effective
	Newer Anti-Androgens	Abiraterone, Apalutamide, Enzalutamide These target 10% of the testosterone produced by the adrenal glands. They are used in advanced cancer to completely shut down testosterone production. They work by selective inhibition of CYP17 (required for androgen synthesis). It is administered with steroids (prednisone) to manage mineralocorticoid excess due CYP17 inhibition causing a perceived cortisol deficit	-	Joint or muscle pain, hypertension, oedema, hot flushes

Targeted Therapies

TARGETED THERAPIES FOR CANCER				
		Mechanism of Action		
Drug		Drug	Target	Side Effects
Small Molecule	NIBS	Gefitinib, Erlotinib, Sorafenib, Sunitinib and Dasatinib Nibs are classes of drugs that are receptor tyrosine kinase inhibitors. Different nibs affect different types of RTKs. • Tinib - small molecular inhibitor • Nib - tyrosine kinase inhibitor The drug will competitively inhibit ATP binding at the catalytic site of the receptor, preventing the receptor from auto-phosphorylating. This prevents cells from proliferating.	<i>Receptor Tyrosine Kinase (RTK)</i> • VEGF, HERs, PDGF Rs These receptors are proto-oncogenes . They mediate cell:cell communication, their activation regulates key cell processes such as growth, motility, differentiation, etc. It is their dysregulation (permanently switched on) that leads to many human diseases including cancer.	Normally well tolerate but can cause: • Frequent: myelosuppression, rash, GI upset, fatigue, arthralgia, myalgia • Rare: cumulative cardiotoxicity, osteonecrosis of the jaw with sunitinib • Interactions: with CYP3A4 substrates (e.g. rifampicin, fluconazole)
	MIBS	Ixazomib, Bortezomib Proteasome Inhibitors		
Monoclonal Antibodies	NABS	Neutralising Monoclonal Antibodies e.g. nab-paclitaxel Nanoparticle albumin-bound drug		
	MABS	Bevacizumab, Trastuzumab, Ado-Trastuzumab, Pertuzumab, Rituximab Man-made proteins that are identical copies of an antibody and target one specific antigen in order to enlist the immune system to fight cancer. -mab preceded by animal source MABS have two targets: 1. <i>Angiogenesis</i> (Bevacizumab) 2. <i>Human Epidermal Growth Factor 2</i> (Trastuzumab and Ado-Trastuzumab)	Bevacizumab on VEGF-A Hypoxic cells at the core of the tumour can induce expression of VEGF which will stimulate angiogenesis, allowing the tumour to grow rapidly and metastasise. Bevacizumab stops this process by grabbing onto VEGF-A in order to prevent it from binding to the VEGF receptor	Specific toxicities depend on MAB mechanism of action • Hypersensitivity • Infusion related SEs Flu-like: fever, chills, nausea and vomiting • Increased risk of Infection • Prescribe with caution: autoimmune disease, HIV • Rare: Tumour Lysis Syndrome
		Bevacizumab Recombinant humanised monoclonal antibody directed at VEGF-A given IV Trastuzumab (Herceptin) This is a humanised mouse monoclonal that turns off HER2 Metastatic breast cancer to switch on a tumour suppressor gene. Ado-Trastuzumab (Kadcyla) Humanised IgG anti-HER2 trastuzumab + cytotoxic DM. MAB conjugated to cytotoxic drugs to target and deliver it directly inside the cancer cell.	Trastuzumab (Herceptin) on HER2 Down regulates tyrosine kinase activation, which activates p27 tumour suppressor gene that is turned off when HER2 active due to AKT phosphorylation.	

HORMONAL CANCERS

Introduction

We will look into two hormonal cancers: breast & prostate cancer.

Breast Cancer

[NZF Breast Cancer Guidelines](#), [Breast Cancer Foundation](#), [EVIQ Breast Cancer](#)

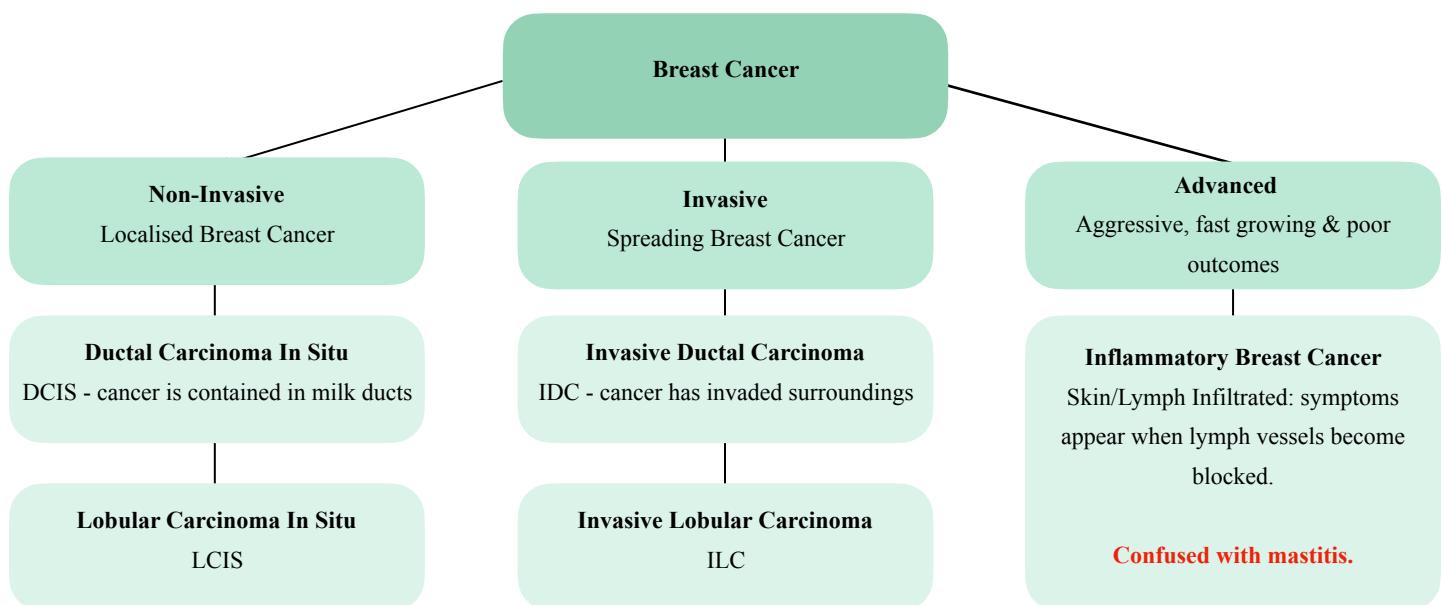
Description

Breast cancer is the third most common cancer diagnosed in NZ and the most common cancer diagnosed in women (usually aged above 50).

Pathophysiology

Cellular proliferation in breast cancer develops due to DNA damage and genetic mutations that can be influenced by exposure to estrogen (premenopausal: ovaries, postmenopausal: peripheral tissue). Breast cancers typically arise in the ducts or lobules of the mammary gland. However, when tumor cells infiltrate surrounding breast tissue, a diagnosis of invasive breast cancer is made.

Estrogen fuels growth and division of cancer cells. Progesterone puts a brake on estrogen fuelled growth.



Risk Factors

	RISK FACTORS FOR BREAST CANCER		PROTECTIVE FACTORS
	Non-Modifiable	Modifiable	Description
Patient	<ul style="list-style-type: none"> • Aged > 50 years • Family History (Breast/Ovarian Cancer in first degree relative) • Male Relative diagnose • Taller height (not understood) • Higher breast tissue density 	<ul style="list-style-type: none"> • Physical Inactivity • Post-menopausal obesity • Shift work: disruption of circadian rhythm 	Exercise
Mutations	Mutations <ul style="list-style-type: none"> • Genetic mutation of BRCA1/2 (pro cancerous genes) 	-	Mutations Those screened for a risk factor gene defect, the following can protect them: <ul style="list-style-type: none"> • Risk-reducing mastectomy, oophorectomy, ovary oblation (in pre-menopausal women)
Estrogen Exposure	Lengthened Estrogen Exposure <ul style="list-style-type: none"> • Female Gender • Menarche (early periods): <12y • Late Menopause: >55y 	Lengthened Estrogen Exposure <ul style="list-style-type: none"> • No pregnancies (pregnancies mature breast cells and encourage normal development, discouraging abnormal growth) • No breastfeeding • First pregnancy from age 30 onwards • HRT, Hormonal contraception 	Decreased Estrogen Exposure <ul style="list-style-type: none"> • Breastfeeding • First pregnancy < 30 years old • SERMs (antagonists on breast tissue) • Aromatase Inhibitors • Hormonal contraception (mimic pregnancy so may be a protective factor)
Substances	Substances Previous radiation therapy	Substances <ul style="list-style-type: none"> • Smoking • Alcohol Intake: any quantity 	Substances Non-smoker, non drinker

Signs & Symptoms

Commonly asymptomatic.

- Painless lumps in breast
- Bloody discharge from the nipple
- Stabbing or aching pain
- Changes in the shape or texture of the nipple or breast (skin dimpling, orange peel skin, nipple inversion)

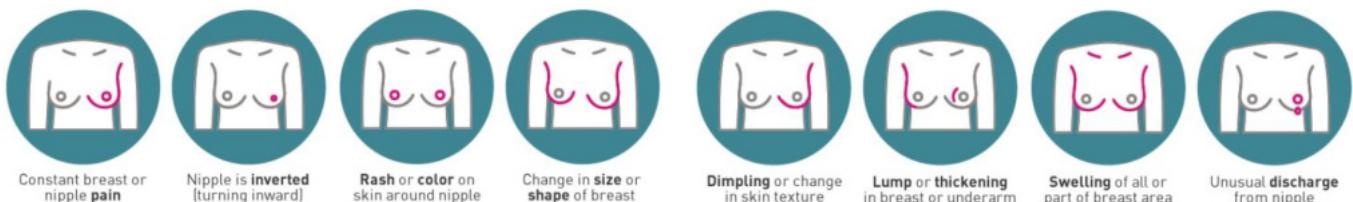
Nodal Involvement

- Axillary Adenopathy: aching, swelling at the armpit

Metastatic Disease

Localised pain depending on the location of metastases (e.g. back, leg abdominal)

- Jaundice (key indication of spread to liver)
- Shortness of breath, cough (spread to lung)



Screening (Asymptomatic Patients)

Breast cancer is highly curable if it is detected early! Screening programmes are not funded for those with breast cancer or men.

1. *Age 20:* monthly self exams | TLC (Touch, Look, Check)
2. *Age 40:* regular mammographies recommended every 2 years
3. *Age 45 - 69:* funded mammographies every 2 years
4. *High Risk Individuals (strong family history or male relative diagnosed):* refer to [GHSNZ](#)

Diagnosis (Symptomatic Patients)

The Triple Test (99.6% specificity)

1. History & Clinical Breast Exam
2. Imaging (mammography/ultrasound)
3. Biopsy (fine needle aspiration, core needle biopsy, open biopsy)

Staging

TNM System (Tumour, Nodes, Metastasis)

STAGING OF BREAST CANCER					
	Stage	Description	Tumour Size	Axillary Lymph Nodes	Metastasis
Early	0	Tumour is confined to breast ducts and lobules + node negative	Tiny cluster of cancer cells in a breast duct (in situ)	-	
	1		≤ 2cm	-	
	2	Tumour is spread to axillary node	< 2cm	Yes	
			2-5cm	Maybe	
			>5cm	No	
Locally Advanced	3	Tumour has spread to superficial structures of the chest wall	Any size	Yes (multiple)	
			> 5cm	Yes	
			Any size (but spread to skin or chest wall)	Maybe	
			Any size	Spread to lymph nodes along breastbone and around collarbone	
Advanced/Metastatic	4	Metastases present at multiple distant sites (bone, liver, lungs, brain) AND lymph node involvement	Any size	Maybe	Yes

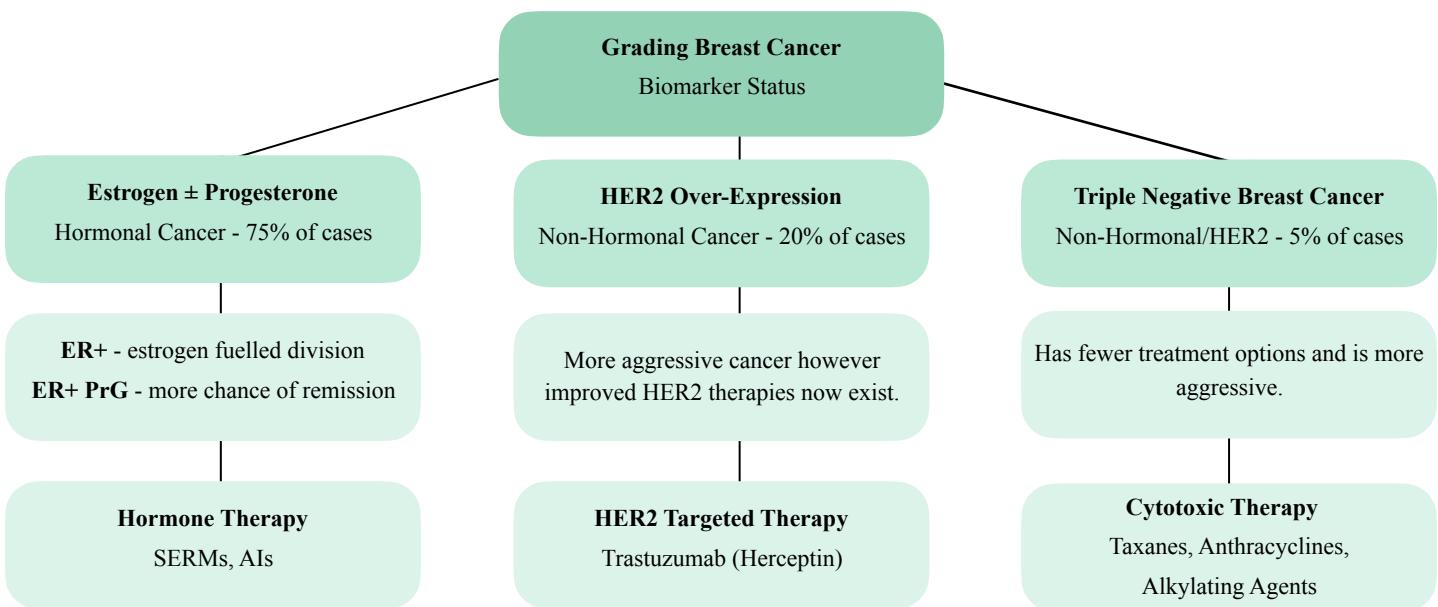
Grading

3 Biomarker Status (ER, PR, HER2)

This is a key part of grading breast cancer as they are prognostic & predictive factors.

Poor Prognostic Factors

- Age younger than 35 years
- Triple-negative disease (ie. the absence of ER, PR, and HER2): relies on aggressive cytotoxic therapy
- Over-expression of HER2 alone



Pharmacological Treatment

[Ministry of Health Breast Cancer Guidelines](#), [NZF Breast Cancer Prescribing Guidelines](#),

The management of patients with breast cancer involves surgery, radiotherapy, drug therapy.

1. *Neoadjuvant therapy* reduces tumour size before surgery and facilitate breast-conserving surgery.
2. *Adjuvant therapy* eradicates residual metastases after surgery.



Choice of Adjuvant Treatment

Choice of adjuvant treatment is determined by factors such as risk of recurrence, presence of steroid hormone receptor, other biomarkers and menopausal status. In some cases, **neoadjuvant therapy** may be preferred over adjuvant therapy, and vice versa.

TREATMENT OF BREAST CANCER	
Stage	Description
Stage 0, 1, or 2 Early Breast Cancer	Goal: Cure Breast Conserving Surgery (Lumpectomy) <ul style="list-style-type: none"> ↳ Adjuvant Radiation Therapy (may be omitted in very elderly) ↳ Adjuvant Chemotherapy (within 2-6 weeks of surgery): cytotoxic and hormonal/HER2 therapy where indicated
Stage 3 Locally Advanced Breast Cancer	Goal: Gain control of disease spread, can be curative <ul style="list-style-type: none"> ↗ Neoadjuvant Chemotherapy (HER/hormonal targeted therapy) • Surgical Resection ↳ Adjuvant Radiation Therapy (may be omitted in very elderly)
Stage 4 Metastatic Breast Cancer	Goal: Palliative care — maintain/improve QoL, prolong time to progression, not curative <ul style="list-style-type: none"> • Chemotherapy (cytotoxic ± hormonal ± HER2) • Radiation therapy (useful for the pain relief of bony metastasis) • No surgery

TREATMENT OF BREAST CANCER	
Drug & Surgical Therapy	Drug
Surgical	<ul style="list-style-type: none"> Lumpectomy Mastectomy
Radiation	
Cytotoxic	Anthracyclines (Doxorubicin, Epirubicin) — <i>most evidence for efficacy</i> Used in combination with other taxanes and cyclophosphamide <ul style="list-style-type: none"> HER2 positive cancers respond better to anthracyclines/taxanes vs other cytotoxics
	Taxanes (Paclitaxel, Docetaxel) Used in combination with other anthracyclines <ul style="list-style-type: none"> HER2 positive cancers respond better to anthracyclines/taxanes vs other cytotoxics
	Alkylating Agents (Cyclophosphamide) Used in combination with other anthracyclines and taxanes
Endocrine/Hormonal	Aromatase Inhibitors (Anastrozole, Letrozole, Exemestane) For <i>post-menopausal</i> women: daily for 5-10 years
	SERMs (Tamoxifen - agonist) For <i>pre-menopausal</i> women (2nd line in post-menopausal women): daily for 5 years <ul style="list-style-type: none"> Tamoxifen flare
Targeted (Monoclonal Antibodies)	Anti-HER2 Therapy (Trastuzumab, Pertuzumab) <ul style="list-style-type: none"> MABs are used as neoadjuvant (stage 3), adjuvant (post surgery), metastatic (stage 4) MABs are given POST anthracyclines with concomitant taxane therapy
Complete Ovarian Suppression	In very aggressive cancers: <ul style="list-style-type: none"> Oophorectomy (removal of ovaries which provide main source of estrogen in pre-menopausal women) GnRH agonist

Prostate Cancer

[NZF Gonadorelin Analogues, Pharmacotherapy Principles 6th Edition - Chapter 92: Prostate Cancer](#)

Description

Prostate cancer is the secondly most commonly diagnosed cancer in men, with a median age at diagnosis of 66 years. It is a very slow growing cancer in which symptoms will develop before spread occurs.

Pathophysiology

The prostate gland is sits inferiorly to the bladder and prostate tissue surrounds the upper urethra near the neck of the bladder. The prostate secretes fluid that nourishes and protects sperm. Its cell growth and differentiation is controlled by androgens (Testosterone, DHT), resulting in the prostate naturally growing larger with age. 75% of prostate cancers occur in the peripheral zone of the prostate gland.

There are 2 primary sources of androgens:

1. Primary production: GnRH → LH, FSH → Testicles → Testosterone → Prostate Growth
2. A small amount of androgen production comes from the adrenal glands

Androgens drive:

- Growth of the prostatic epithelium
- Production of prostatic fluid

Risk Factors

	RISK FACTORS FOR BREAST CANCER		PROTECTIVE FACTORS
	Non-Modifiable	Modifiable	Description
Patient	<ul style="list-style-type: none">• Age >50y• Black African or Caribbean ethnicity• Family history	-	-
Lifestyle	-	<ul style="list-style-type: none">• Obesity• Western diets	<ul style="list-style-type: none">• Regular exercise (maintain normal BMI and waist circumference)• Mediterranean Diet modification: limit red meat, alcohol, saturated fat, calcium
Mutations	<ul style="list-style-type: none">• Prostate-specific genetic mutations• Mutations causing other cancers e.g. BRCA1, BRCA2, ATM, and CHEK2	-	-
Substances	-	<ul style="list-style-type: none">• Smoking (associated with mortality)	-

Signs & Symptoms

Localised disease

- Asymptomatic as malignancy is localised to the peripheral zone, this does not pressure the urethra.

Locally invasive disease

- Ureteral dysfunction, frequency, hesitancy, dribbling, impotence

Advanced disease

- Back pain, spinal cord compression
- Lower extremity oedema, pathologic fractures
- Anaemia, weight loss

Complications

It is common for metastatic spread of prostate cancer to **bone**. A disruption in bone homeostasis commonly causes both osteoblastic and osteoclastic lesions.

- **Signs & Symptoms:** bone pain usually worse at night, fractures, raised calcium & alkaline phosphatase
- **Diagnosis:** Bone metastases are picked up with imaging (bone scan, CT, MRI, X-ray)
- **Treatment:** pain relief, radiation therapy, bisphosphonates (different dose to osteoporosis indication e.g. zolendronic acid 4mg IV 3 weekly)

Screening

Prostate Specific Antigen (PSA) and Digital Rectal Exam (DRE)

There is no nationwide screening programme for prostate cancer for the below reasons.

1. No clear evidence of what age should be screened:
 - Discuss testing in men 50-70 years old or >40 with family history
2. No clear evidence of mortality benefit:
 - diagnosis of malignancy which will not progress in their lifetime may cause harm (psychological, social)
3. Low test sensitivity (false positives)
 - PSA can be increased by prostatitis, UTI, BPH, recent ejaculation, cycling
4. Low test specificity (false negatives)
 - little PSA produced from some cancer cells

Diagnosis

DIAGNOSIS OF PROSTATE CANCER	
Test	Description
1 Prostate Specific Antigen (PSA)	Antigen made by prostate cells whose levels increase with age. Not specific. <ul style="list-style-type: none">• Taken via a blood test in primary care• Levels < 4 are normal• Levels between 4-10 are ambiguous and• Levels > 10 are associated with malignancy Abnormal PSA levels (ug/L) per age group <ul style="list-style-type: none">• Men ≤ 70 years ≥ 4.0• Men 71 - 75 years ≥ 10.0• Men ≥ 76 years ≥ 20.0

2 Digital Rectal Exam (DRE)	Digital palpitation of the peripheral prostate transrectally. Not diagnostic. <ul style="list-style-type: none"> • Performed by a medical professional (often a GP) • Usually done secondary to a raised PSA • 60% sensitivity as relies on human ‘touch’ and has inter-professional variation.
3 Transrectal Ultrasound (TRUS)	Examines the prostate +/- biopsy <ul style="list-style-type: none"> • Done if DRE is positive or PSA is elevated • If TRUS is positive, a biopsy will be undertaken. • Biopsy determines the Gleason Score

Staging

There are two staging methods used:

1. *Gleason Score*
2. *TNM Scoring* e.g. Tumour, Nodes, Metastases



Gleason Score (used in conjunction to the TNM System)

The Gleason Score is a scoring system based off the TRUS Biopsy. It is the sum of 2 samples evaluated for cellular differentiation: 1 (well differentiated) to 5 (very poorly differentiated). Higher scores are associated with a more aggressive disease and poorer outcomes and prognosis

Grading

STAGING OF PROSTATE CANCER		
ISUP grade	Gleason score	Description
1	$3 + 3 = 6$	Cancer cells are likely to grow slowly
2	$3 + 4 = 7$	Most cancer cells look like likely to grow slowly. Some are likely to grow at a moderate rate.
3	$4 + 3 = 7$	Most cancer cells look like likely to grow at a moderate rate. Some are like to grow slowly
4	$4 + 4 = 8$	Cancer cells are likely to grow moderately
5	$4 + 5 = 9$	Most cancer cells likely to grow moderately quickly. Some are likely to grow more quickly
	$5 + 4 = 9$	Most cancer cells are likely to grow quickly
	$5 + 4 = 9$	All cancer cells are likely to grow quickly

Prognosis

- Commonly a slow growing cancer: many men will be diagnosed with a >10 year life expectancy: better candidate for prostatectomy (curative)
- Factors influencing prognosis: extent & histological grade of tumour, patient's age and health, PSA level
- In worse prognoses, prostatectomies will not be conducted due to complications (e.g. permanent damage such as urinary problems in sight of an unchanged survival rate)

Pharmacological Treatment

Due to its relatively slow progression, treatment of prostate cancer depends on the stage, Gleason score, symptoms & life expectancy.

The therapeutic approach is to either:

1. *Lower* androgen levels
2. *Stop* androgen production (from adrenal glands and testes)

We assume in those cases that malignant tissue retains hormone sensitivity.

A note on Androgen Deprivation Therapy (ADT):

It itself isn't curative but it is used in intermediate-high risk disease:

1. Prior to radiation to make it more effective
2. In advanced cancer, if surgery/radiation fails to cure
3. It can be a surgery (e.g. orchectomy) or medicines (e.g. LNRH agonist, anti-androgens)

TREATMENT OF PROSTATE CANCER		
Risk Level	Definition	Recommendation
Curative Low Risk	<ul style="list-style-type: none"> • T1, T2 • GS 2-6 • PSA <10 • Life expectancy > 10 years 	Therapeutic Approach: Stop Androgen Production <ul style="list-style-type: none"> • Observation (DRE and PSA every 6-12 months + biopsy) • Radiation • Radical prostatectomy (removal of prostate gland and tissue)
Not curative High Risk	<ul style="list-style-type: none"> • Poor survival, life expectancy <10 years 	Therapeutic Approach: Lower Androgen Production <ul style="list-style-type: none"> • Observation • Radiation +/- Androgen Deprivation Therapy (ADT) • Orchidectomy (surgical removal of testicles)

TREATMENT OF PROSTATE CANCER		
		Description
Non-Drug Treatment	Radiation	<ul style="list-style-type: none"> • External beam radiotherapy (EBRT) • Brachytherapy
	Surgical	<ul style="list-style-type: none"> • <i>Radical Prostatectomy</i> (curative - used in low risk disease) • <i>Orchidectomy</i> (non-curative - used in high risk disease)
Not curative Drug Treatment (Hormones)	Androgen Deprivation Therapy (ADT)	<p>First Line Androgen Lowering Therapy — lowers androgens <i>GnRH agonist e.g. Goserelin, Leuprorelin acetate</i></p> <ul style="list-style-type: none"> • Inhibits androgen production by testicles to shrink prostate cancer cells or decrease growth • GnRH flare (2-4 weeks) • Cannot be handled by pregnant women <p>Second Line Androgen Synthesis Inhibition — combination stops androgens <i>Anti-androgen e.g. Abiraterone acetate, Apalutamide, Enzalutamide Bicalutamide, Flutamide, Cyproterone acetate — not used alone</i></p> <ul style="list-style-type: none"> • Combined Androgen Blockade (CAB): Anti-androgens must be used in addition to GnRH agonist • Allows blockage of testosterone-producing cells not affected by GnRH (e.g. adrenal cells) • Anti-androgen must be started prior to GnRH to manage GnRH flare • Abiraterone must be administered with steroid to manage mineralocorticoid excess

NON-HORMONAL CANCERS

Introduction

We will look into the following three cancers: lung cancers, skin cancers and colorectal cancers.

Lung Cancers

[Pharmacotherapy Principles 6th Edition - Chapter 90: Lung Cancer, BPAC Lung Cancer Follow Up](#)

Description

Lung cancer is the fifth most common type of cancer in NZ and is most likely in smokers. Two types exist:

1. *Non Small Cell Cancer* (NSCC)
2. *Small Cell Lung Cancer* (SCLC)

TYPES OF LUNG CANCER		
	Non-Small Cell Lung Cancer (NSCLC)	Small Cell Lung Cancer (SCLC)
Prevalence	80-85% of cancers	15-20% of cancers
Origin	Epithelial cells	Nerve producing cells in bronchi
Effect of smoking?	Smokers & non-smokers affected	Rarely in non-smokers
Prognosis	Better survival outcomes. A 5 year survival of: <ul style="list-style-type: none">• Stage I: 77-92%• Stage II: 53-60%• Stage III: 13-36%• Stage IV: 0-10%	<i>Poor prognosis</i> <ul style="list-style-type: none">• Most aggressive type of lung cancer• Rapidly dividing malignancy• Rapidly spreading metastases• High recurrence rate• Most patients present in the extensive stage (late disease)

Risk Factors

	RISK FACTORS FOR BREAST CANCER		PROTECTIVE FACTORS
	Non-Modifiable	Modifiable	
Patient	<ul style="list-style-type: none">• Age• Family history• HIV (immune system dampened)	-	-
Lifestyle	-		<ul style="list-style-type: none">• Healthy Diet
Mutations		-	-
Substances	-	<ul style="list-style-type: none">• History /current use of tobacco cigarettes, pipes, cigars• Exposure to secondhand smoke• Occupational exposures (asbestos, arsenic, radon, chromium, etc.)• Radiation exposure• Air pollution• Beta carotene supplements in heavy smokers	<ul style="list-style-type: none">• Smoking cessation/avoidance

Signs & Symptoms

Commonly Asymptomatic

We often don't find lung cancers until they have metastasised (bone, liver, brain, lymph nodes, adrenal glands)

General symptoms

- Malaise
- Weight loss

Lung Specific

- Haemoptysis
- Cough, Dyspnea, shortness of breath
- Hoarseness (e.g sore throat)
- Recurrent infections (patients on many antibiotics before cancer diagnosis)
- Chest pain

Symptoms related to distant metastasis

- Pain
- Organ-related

Screening

There is no screening method for the general population.

Low-dose Helical CT Scan

- For high risk patients (e.g. smokers)

Diagnosis

1. History & Physical exam
2. Routine Lab Evaluations
3. *Visualisation:* Chest X-Ray, Chest CT, PET-CT Scans (cancer cells take up more glucose)
4. *Tumour sampling:* Bronchoscopy, Biopsy (definitive)

Goal of Therapy

1. *Early Stages - Cure*
2. *Late Stages - Prevent mortality/prolong survival*

Pharmacological Treatment

Staging Lung Cancer NZ, NSCLC Treatment National Cancer Institute

Non Small Cell Lung Cancer (NSCLC)

NSCLC is a type of epithelial lung cancer (e.g. adenocarcinoma, squamous cell carcinoma, and large cell carcinoma). Surgery is the mainstay treatment in early disease (stage 0-3). In late disease the goal shifts from curative to prolonging survival - thus making chemotherapy and radiation more effective there.

TREATMENT GUIDELINES OF NSCLC CANCER		
Stage	Definition	Recommendation
Stage 0	<ul style="list-style-type: none"> The cancer is small in size and has not spread into deeper lung tissues or outside the lungs (also known as carcinoma <i>in situ</i>). 	1. Surgery and/or 2. Endobronchial therapy
Stage 1 (early disease)	<ul style="list-style-type: none"> Cancer <4cm No spread outside the lung or to lymph nodes 	Goal: Cure 1. Surgery or 2. Radiation therapy (if medically inoperable patients) <ul style="list-style-type: none"> <i>If margins are present:</i> surgical resection + (adjuvant chemotherapy and/or radiation)
Stage 2 (loco-regional disease)	<ul style="list-style-type: none"> Different sized cancer May have spread to nearby lymph nodes, other parts of the lung, areas just outside the lung 	Goal: Cure 1. Surgery +/- neoadjuvant/adjuvant chemotherapy or 2. Radiation (if medically inoperable patients) <ul style="list-style-type: none"> Surgery is mainstay <i>If margins are present:</i> surgical resection + (adjuvant chemotherapy and/or radiation) <i>If margins are absent:</i> adjuvant chemotherapy
Stage 3 (locally/regionally advanced disease)	<ul style="list-style-type: none"> Any size Spread to lymph nodes May be growing to other parts of lung, airways, surrounding areas outside the lung 	IIIA 1. Surgery + neoadjuvant/adjuvant chemotherapy (+/- radiation) IIIB/C — non-surgically resectable, hard to cure 1. Chemotherapy and/or 2. Radiotherapy
Stage 4 (Advanced disease)	<ul style="list-style-type: none"> Any size Spread to lymph nodes May have spread to the other lung, to the fluid in the pleura around the lungs or heart, another body part (liver, bones, brain) 	Goal: Prolong survival, relieve symptoms — hard to cure IV, Relapse, recurrent 1. Chemotherapy and/or 2. Radiation

PHARMACOLOGICAL OPTIONS FOR NSCLC CANCER		
Treatment		Description
Non-Drug Treatment	Radiation	
	Surgery	<ul style="list-style-type: none"> Lobectomy (a lobe of the lung is removed) Pneumonectomy (one whole lung is removed) Wedge resection / segmentectomy (only part of the lung is removed)
Chemotherapy Treatment	Neo-adjuvant	<ul style="list-style-type: none"> Platinum based therapy (cisplatin, carboplatin)
	Adjuvant	<ul style="list-style-type: none"> Cisplatin +/- Vinorelbine, etoposide, vinca alkaloids
	Targeted	EGFR inhibitors ('Nibs': erlotinib, gefitinib, afatinib) <ul style="list-style-type: none"> EGFR excess involved in pathology
	Immunotherapy	'Checkpoint Inhibitors' (Durvalumab, Atezolizumab, Nivolumab) <ul style="list-style-type: none"> Checkpoints (proteins) on immune cells need to be turned on or off to start immune response Cancer cells use these checkpoints to avoid being attacked

Small Cell Lung Cancer (SCLC)

This type of lung cancer tends to grow and spread faster than NSCLC. About 70% of people with SCLC will present at the extensive stage. Metastatic sites include bones, liver, brain, lymph nodes, adrenal glands.



Note

Since this cancer grows quickly, it tends to **respond well to chemotherapy and radiation** therapy. However, unfortunately, for most people, the cancer will return at some point.

TREATMENT GUIDELINES OF SCLC CANCER		
Stage	Definition	Recommendation
Limited (equivalent to stage 1-3)	Tumor is in one lung, the mediastinum, and lymph nodes that can be radiated using a single radiation port	Standard chemotherapy treatment with radiation <ul style="list-style-type: none">• Cisplatin (or carboplatin) / Etoposide <p>Radiotherapy, with concurrent chemotherapy, is the treatment of choice for limited stage SCLC.</p>
Extensive (equivalent to stage 4)	Tumor has spread beyond one lung, the mediastinum, and lymph nodes.	Standard chemotherapy treatment <ul style="list-style-type: none">• Cisplatin (or carboplatin) / Etoposide• Cisplatin (or carboplatin) / Irinotecan <p>While radiation cannot be used to treat the extensive stage, it can be used for symptomatic management</p>
Prevention	Recurrence Prevention <i>If occurs in less than 3 months:</i> <ul style="list-style-type: none">• Enrol in clinical trial/supportive care <i>If occurs after 3 months:</i> <ul style="list-style-type: none">• Second line treatment: tocotepan or lorbinecedin or cyclophosphamide/doxorubicin/vincristine	

Skin Cancers

Pharmacotherapy Assessment 6th Edition - Chapter 93: Melanoma

Description

The skin is the body's largest organ and holds many functions. However due to an impaired ozone layer, New Zealand holds the highest rates of skin cancer.

Risk & Protective Factors

	RISK FACTORS FOR BREAST CANCER		PROTECTIVE FACTORS
	Non-Modifiable	Modifiable	Description
Patient	<ul style="list-style-type: none">• Genetics• Light skin colour, hair colour, eye colour, freckles• Certain types of moles		
Lifestyle		<p><i>UV Radiation is the main cause</i></p> <ul style="list-style-type: none">• Frequent or long-term sun exposure• Artificial UV light (sun-beds)• History of childhood sunburns	<ul style="list-style-type: none">• Avoid artificial suns: tanning, sun lamps• Limit sun exposure: avoid midday sun, apply sunscreen (at least SPF30), UVA/UVB blocking sunglasses <p><i>Please note:</i></p> <ol style="list-style-type: none">1. Clouds don't protect you2. Sand, water, snow and ice magnify exposure3. Increased altitude = increased exposure
Substances		<ul style="list-style-type: none">• Certain chemicals (rare)	



Sun Protection Factor (SPF)

High SPF = longer period of protection. Sunscreen wears off so much be reapplied every few hours especially when sweating, swimming, or towelling off.

Screening

Early detection is key!

- Self examination
- Apps
- Mole maps
- Healthcare visits
- Node sampling

Staging

ABCDEs of Melanoma Screening

- Asymmetry
- Border
- Colour (multiple)
- Diameter ($> 6\text{mm}$)
- Elevation

Prognostic Features

1. Breslow (Depth)

- Good prognosis: $< 1\text{mm}$
- Intermediate prognosis: $1 - 4\text{mm} \rightarrow$ recommend sentinel lymph node biopsy
- Bad Prognosis: $> 4\text{mm}$

2. *Clarks Level*: Staging score (spread)
3. *Sentinel Lymph Node Biopsy*: Allows us to determine if the melanoma has spread to the lymph system by sampling and screening the node we assume it would've travelled to first. A lymphadenectomy is recommended for positive nodes.

Pharmacological Treatment

TYPES OF SKIN CANCER				
	Types	Description	Signs & Symptoms	Treatment
Pre-Cancer	Actinic Solar Keratosis (ASK)	Pre-Cancer Skin cancer begins as actinic solar keratosis — a form of precancerous benign skin that has the potential to turn into cancer and spread if untreated.	Thick, scaly patches of sun-damaged skin	1. Cryosurgery 1. Topical treatment (fluorouracil, imiquimod)
Non Melanoma	Basal Cell Carcinoma (BCC)	Seldom life threatening, easily detected and treated. Basal cells form the deepest layer of the epidermis and function as precursors to those above them. These are the least dangerous of skin cancers as they grow slowly and rarely spread beyond their original location.	Open sores, reddish patches, shiny bump, pink growth, scar-like area, lump that bleeds and crusts.	1. Surgical excision 2. Cryosurgery 3. Topical treatments (fluorouracil, imiquimod) 4. Radiation
	Squamous Cell Carcinoma (SCC)	Not dangerous if if treated and detected early. Squamous cells are the most abundant cells in the skin and are located primarily in the epidermis. Their abnormal growth is considered more aggressive and concerning than BCC as these can spread.	Wart-like growth, scaly red patches, open sores that persist, often appear as elevated growths with a central depression.	
Melanoma	Melanoma Skin Cancer	Deadliest form of skin cancer. Cancer that arises in a pigment producing cell (caused by UV exposure) - it is most common in 25-44 years old	Mainly 'new spots' that appear — doesn't have to be a sun site. Can be an existing spot.	1. Surgical excision (Moh's surgery)* 2. Immunotherapy e.g. Pembrolizumab (Keytruda) 3. Radiotherapy



*Moh's Surgery

Moh's surgery cuts out the melanoma with a depth depending on Breslow's depth. It yields higher clearance rates than standard excision and smaller wounds, therefore better cosmetic results. The surgery is widely accepted as treatment of first choice for neck/face melanoma and high risk basal cell carcinoma and SCC.

Colorectal Cancer

[Colorectal Cancer Treatment National Cancer Institute](#)

Description

Colorectal cancer (CRC), also known as bowel cancer, colon cancer, or rectal cancer, is the development of cancer anywhere in the large intestine or the rectum. It is the second highest cause of cancer death, secondary to lung cancer.

Pathophysiology

This type of cancer usually starts as a polyp (a benign growth) that has the potential to turn into a malignant tumour. It is usually then, 95% of the time, an adenocarcinoma.

Risk Factors

	RISK FACTORS		PROTECTIVE FACTORS Description
	Non-Modifiable	Modifiable	
Patient	<ul style="list-style-type: none">Male genderAge >50Personal or family history of colorectal cancer or polypsLynch SyndromeIBD, Diabetes		
Lifestyle		<ul style="list-style-type: none">Physical inactivityDiet low in fiber and high in red, processed meat or animal fatLow fiber dietsObesity	<ul style="list-style-type: none">Physical ActivityMediterranean diet and high fiber dietsLimit red meatSelenium, folic acid, calcium
Substances		<ul style="list-style-type: none">High alcohol intakeSmoking (protective in UC)	<ul style="list-style-type: none">Stop smoking, drinking

Signs & Symptoms

Often symptomatic in early disease

- Change in bowel habits, abdominal pain, blood in stools, tenesmus (feeling of incomplete bowel emptying), anorexia, weight loss, N/V, weakness

Bowel Screening

The National Bowel Screening Programme is free for *asymptomatic* people aged 60 - 74.

- Patients are offered a two-yearly screening with home test kit for faecal samples, which screens for presence of blood in stools (*not* diagnostic)
- Positive tests are referred for colonoscopy

Diagnosis

- Colonoscopy + biopsy* of detected polyps
- Imaging:* Chest x-ray, CT scan, PET scan (if metastasised to lung, liver or peritoneal cavity)

TNM Staging & Prognosis

As colon cancer can cause malabsorption, issues with drug therapy absorption can occur. Consequently, surgery is the mainstay treatment in curable disease. Depending on the stage of disease and whether the tumour originated in the colon or rectum, further chemotherapy +/- radiation may be needed to cure these patients. In the metastatic setting, pharmacologic intervention is the main treatment option.

Rectal cancer has poorer outcomes

- Difficult to resect, propensity for recurrence
- Surgeons aim to preserve rectal function, colostomies are sometimes required

Pharmacological Treatment

Staging & Prognosis of Colorectal Cancer		
TNM Stage	Definition	Recommendation
Stage 0 or 1 Localised	• Cancer is confined to the lining of the colon	Goal: Cure 1. Surgery
Stage 2 Localised	• Cancer may penetrate the wall of the colon into the abdominal cavity • Does not invade any local lymph nodes	Goal: Cure COLON CANCER 1. Surgery RECTAL CANCER 1. Radiation +/- neoadjuvant chemotherapy 2. Surgery (but difficult)
Stage 3 Localised (Nodes)	• Cancer invades one or more lymph nodes but has not spread to distant organs	Goal: Cure COLON CANCER 1. Surgery <i>and</i> 2. Adjuvant Chemotherapy RECTAL CANCER 1. Radiation +/- neoadjuvant chemotherapy 2. Surgery (but difficult)
Stage 4 Metastatic	• Cancer has spread to distant locations in the body (liver, lungs etc.)	Goal: Unlikely curable — palliative, prevent recurrence 1. Surgery of metastasised cells 2. Chemotherapy: Cytotoxic +/- Targeted 3. Immunotherapy

TREATMENT OF COLORECTAL CANCER		
Description		
Non-Drug Treatment	Radiation	Routine in rectal cancer
	Surgical	
Chemotherapy	Cytotoxic	First Line: FOLFOX; Leucovorin (folinic acid) + 5-fluorouracil (5-FU) + oxaliplatin Second Line: Mayo Clinic regimen; 5-FU + Leucovorin Other: <ul style="list-style-type: none"> • Capecitabine alone • CAPOX/XELOX: Capecitabine + oxaliplatin • FOLFOXIRI: Leucovorin + 5-FU + irinotecan • FUOX: 5-FU + oxaliplatin
	Targeted	First Line: Bevacizumab (VEGF) Other: Cetuximab, panitumumab, ramucirumab, afibbercept
	Immunotherapy	First Line: Pembrolizumab Other: nivolumab, ipilimumab

Table 91–4**Treatment Regimens for Adjuvant Colon Cancer**

Stage II^a	Stage III
High Risk <ul style="list-style-type: none"> • Capecitabine or 5-FU plus leucovorin • FOLFOX • CapeOx • FLOX 	Good Performance Status <ul style="list-style-type: none"> • FOLFOX • CapeOX • FLOX • Capecitabine or 5-FU plus leucovorin
Low Risk^b <ul style="list-style-type: none"> • Observation or clinical trial • Capecitabine or 5-FU plus leucovorin 	Poor Performance Status <ul style="list-style-type: none"> • Capecitabine

^a Individualized assessment of patient risk is necessary to determine if treatment is required. Clinical trials or observation may be an appropriate option.

Treatment Options for Metastatic Colon Cancer^a

First-Line Therapy	Second-Line Therapy
Good Performance Status <ul style="list-style-type: none"> • FOLFOX or FOLFIRI with bevacizumab • FOLFOX or FOLFIRI with cetuximab or panitumumab^c • FOLFOXIRI with or without bevacizumab • 5-FU + leucovorin or capecitabine with or without bevacizumab 	If First-Line Irinotecan <ul style="list-style-type: none"> • FOLFOX with or without bevacizumab^b • Irinotecan with or without cetuximab^{c,d} • Capecitabine or 5-FU plus leucovorin
Poor Performance Status <ul style="list-style-type: none"> • Capecitabine or 5-FU plus leucovorin with or without bevacizumab 	If First-Line Oxaliplatin <ul style="list-style-type: none"> • FOLFIRI with or without bevacizumab • FOLFIRI with ziv-aflibercept • Irinotecan with ziv-aflibercept • FOLFIRI or irinotecan with or without cetuximab or panitumumab^{c,d}

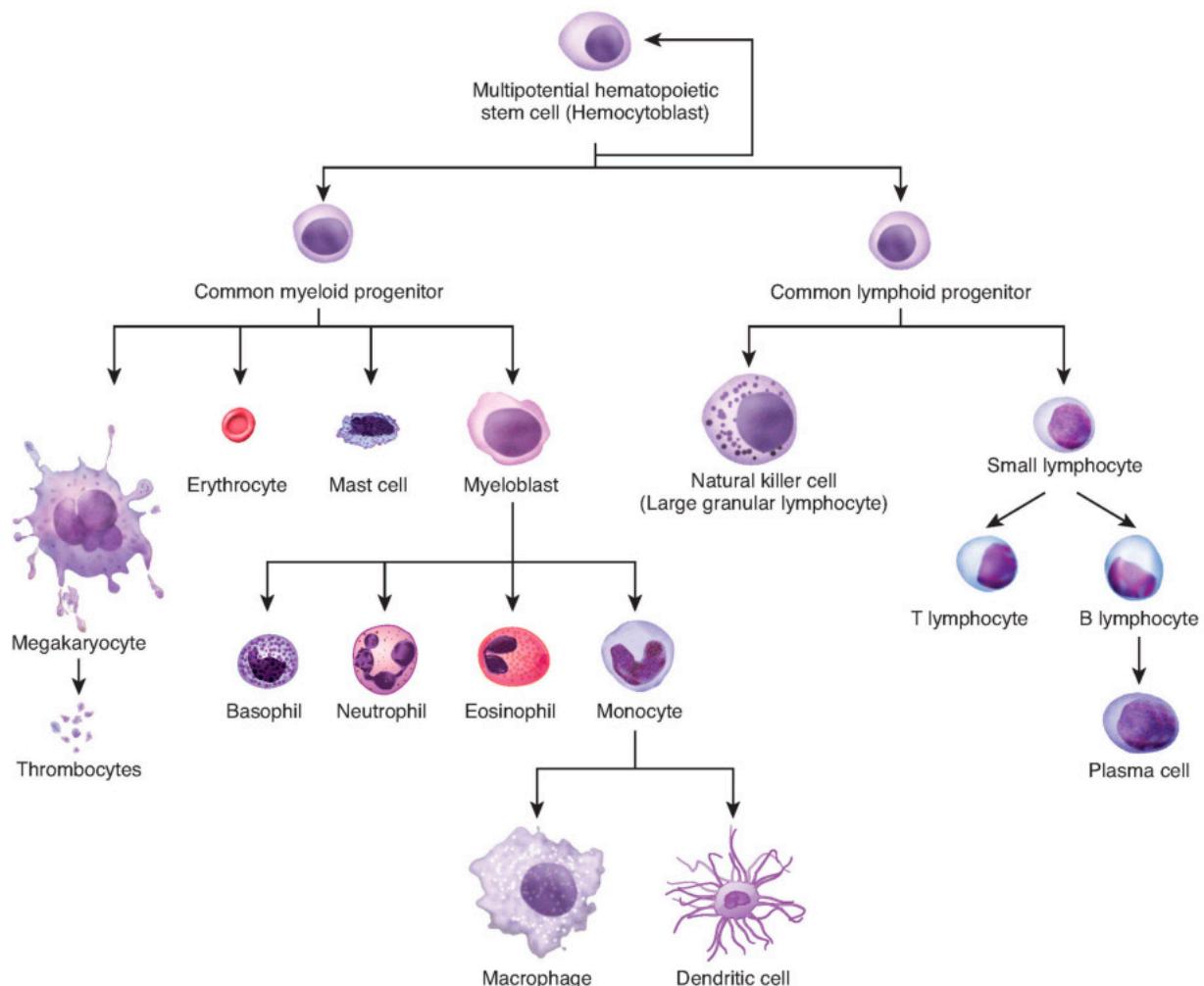
^a CapeOX may replace FOLFOX in selected patients.

HAEMATOLOGICAL (NON-SOLID) CANCERS

Description

Haematological cancers affect roughly 21,000 New Zealanders every year and include leukemias, lymphomas and multiple myelomas. Please find a comparison below

HAEMATOLOGICAL CANCERS			
Types	Leukemias	Lymphomas	Myelomas
Description	Bone Marrow Leukemias are a umbrella term for 'cancers of the bone marrow'	Lymph System Lymphomas are a umbrella term for 'cancers of the lymphatic system'	Plasma Cells A cancer of plasma cells (type of WCC which produces antibodies)
Mainly Affects:	Mainly affect blood and bone marrow	Mainly affect lymph nodes	
Symptoms	<ul style="list-style-type: none"> • Non specific symptoms • Circulate • No screening • No staging 	<ul style="list-style-type: none"> • Specific Symptoms • Do not circulate • No Screening • Staging TNM 	



Leukaemias

[Pharmacotherapy Assessment 6th Edition - Chapter 96: Acute Leukaemias](#)

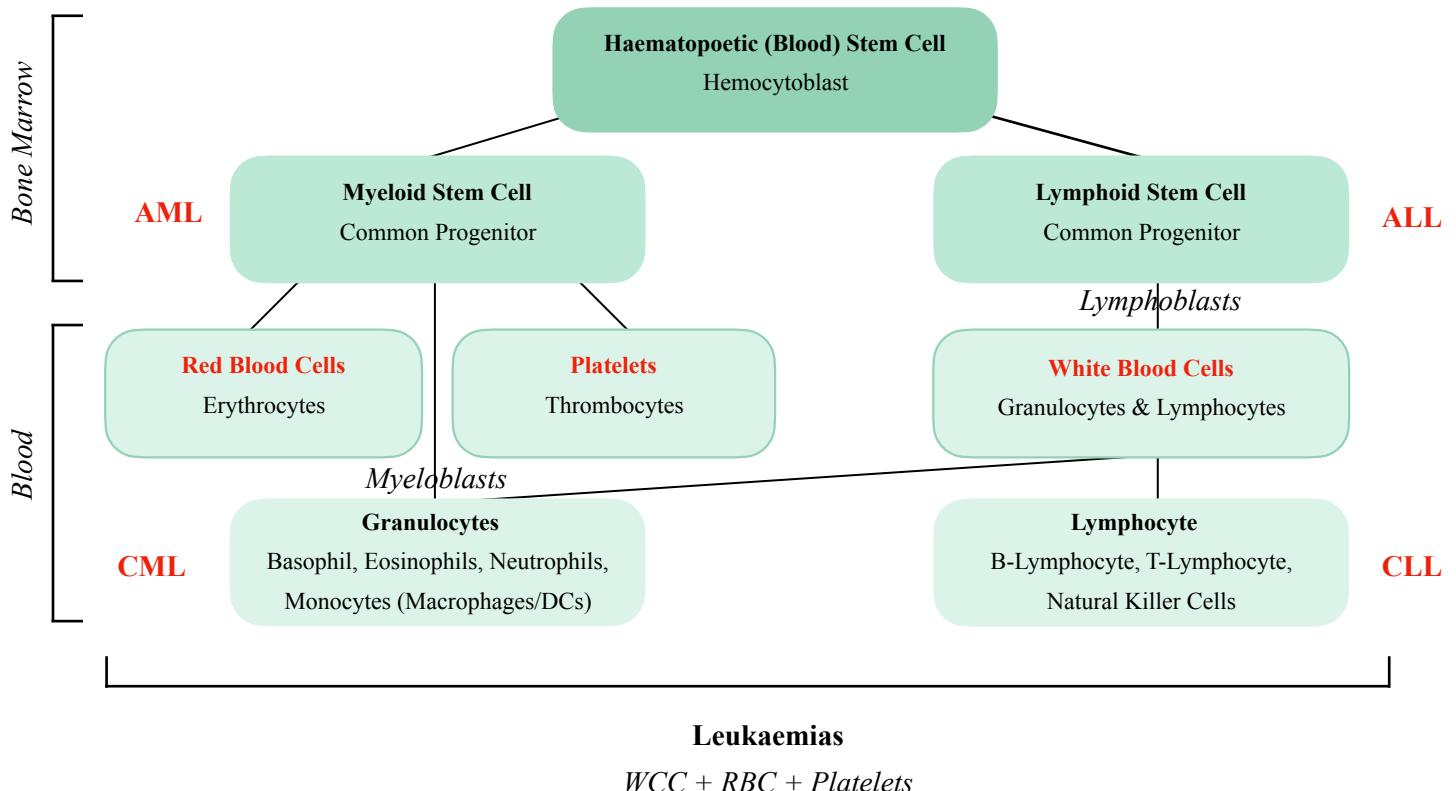
Description

Leukaemias are an umbrella term for ‘cancers of the bone marrow’

Pathophysiology

The Bone Marrow

The bone marrow is a blood forming tissue that produces the myeloid and lymphoid lineage from the blood stem cells. Under normal conditions, it contains a small number of healthy immature blood cells (blast cells) which mature and develop into red blood cells, white blood cells and platelets, which are eventually released into the blood stream.



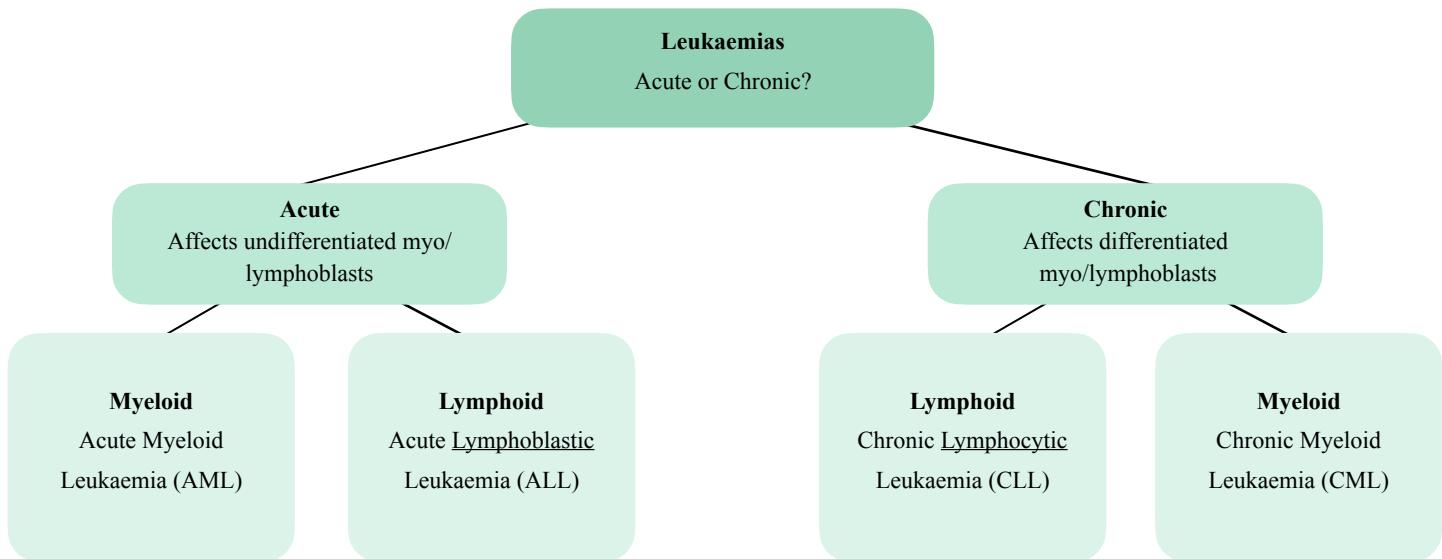
Leukemias

Leukemias describes the defective cellular differentiation of blood stem cells into mature cells. Instead of developing properly, an excessive production of immature haematopoietic cells occurs which eventually crowds out the bone marrow and interferes with normal cellular production. This causes a deficiency in RBCs, WBCs and platelets resulting respectfully in anaemia, neutropenia and thrombocytopenia. Consequently, the body is unable to fight infections.

Classification

Leukaemia cancers can be classified into four main types: acute or chronic, myeloid or lymphoid.

1. Acute Myeloid Leukaemia (AML)
2. Acute Lymphoblastic Leukaemia (ALL)
3. Chronic Myeloid Leukaemia (CML)
4. Chronic Lymphocytic Leukaemia (CLL)



TYPES OF LEUKAEMIA		
	Acute	Chronic
General Description	Acute Leukaemia (AML + ALL) <ul style="list-style-type: none"> • <i>Rapid</i> onset • Proliferation of <i>immature blast</i> cells (loss of function) • Most common overall in <i>childhood</i> (not AML) 	Chronic Leukaemia (CML + CLL) <ul style="list-style-type: none"> • <i>Slower</i> multiplication of defective cells • Proliferation of <i>mature cells</i> (function partially reserved) • More common overall in <i>adults</i>
Myeloid	Acute Myeloid Leukaemia (AML) <ul style="list-style-type: none"> • Not common overall - most common acute leukaemia in adults (40-60 years old) 	Chronic Myeloid Leukaemia (CML) <ul style="list-style-type: none"> • Most common leukaemia (40-60 years old) • 95% associated with Philadelphia chromosome
Lymphoid	Acute Lymphoblastic Leukaemia (ALL) <ul style="list-style-type: none"> • Most common childhood cancer (male predominance) • Good prognosis in childhood, poorer in adults. 	Chronic Lymphocytic Leukaemia (CLL) <ul style="list-style-type: none"> • Associated usually with B cell malignancy (> 60 years old)

Risk Factors

	RISK FACTORS	
	Non-Modifiable	Modifiable
Patient	<ul style="list-style-type: none"> • Genetic conditions e.g. Down syndrome • Family history • Fraternal twins 	
Mutations	<ul style="list-style-type: none"> • CML: Philadelphia chromosome 	
Lifestyle		<ul style="list-style-type: none"> • Viral infections?
Medicines		<ul style="list-style-type: none"> • Alkylating agents • Topoisomerase inhibitors
Substances		<ul style="list-style-type: none"> • Smoking • Pre-natal X-rays • Postnatal radiation exposure • Prior cytotoxic chemotherapy • Exposure to benzene and industrial solvents

Signs & Symptoms

While a crossover of symptoms occur between leukaemia types, CLL is usually asymptomatic and ALL is usually associated with bone pain (due to an overcrowding of the bone marrow)

1. *Anaemia* (\downarrow RBC/haematocrit): fatigue, SOB, dizziness, pale
2. *Thrombocytopenia* (\downarrow platelets): bruising, prolonged wound healing, bleeding gums/nose, heavy periods
3. *Infections* (\downarrow WCC): +/- fever, pneumonia, UTI, cellulitis, colds/flu, shingles
4. *Other*: weight loss, night sweats, swollen/painful lymph nodes, abdominal discomfort, bone pain in ALL



*Note

Lymphoid leukaemia may only affect WBC development but immature WBCs crowding out the functionality of myeloid cells cause a crossover of symptoms.

Screening

No screening indicated at present due to low individual incidence and early diagnosis may not change treatment (e.g. chronic leukaemias)

Diagnosis

1. Physical exam
2. Complete blood cell count
3. Bone marrow biopsy

Staging

No formal staging process. General classifications:

4. *Untreated*: need to diagnose
5. *Remission*: symptom free, $<5\%$ blast cells, WBC/RBC and platelets within normal range
6. *Recurrent*: return of disease in patient who had achieved remission

Prognosis

- ALL: childhood (98% remission, 90% cure); adults (80-90% remission)
- AML: 60-70% remission
- CML: 71% 5-year survival
- CLL: 87% 5-year survival

Pharmacological Treatment

TREATMENT OF ACUTE LEUKAEMIA CANCER		
	ALL	AML
Prognostic Features	<ul style="list-style-type: none"> Age, WBC count, cytogenetic abnormality, DNA content (ploidy), CNS leukaemia, minimal residual disease (MRD) following induction 	<ul style="list-style-type: none"> Age, performance status, cytogenetics
Goal	Complete remission, chemotherapy induces myelosuppression	
Chemotherapy	<p><i>Remission induction (4-6 weeks)</i></p> <ol style="list-style-type: none"> Glucocorticoid (oral prednisone/dexamethasone) <i>and</i> IV Vincristine <i>and</i> IV L-asparaginase <i>and</i> CNS Prophylaxis: Intrathecal chemotherapy (methotrexate) If high risk: Anthracycline (IV daunorubicin) <p><i>Consolidation + Intensification/Reinduction (8 weeks):</i> reduce residual cells to prevent relapse</p> <ul style="list-style-type: none"> Same treatment as remission induction + additional chemotherapeutic agents <p><i>Maintenance (2-3 years)</i></p> <ol style="list-style-type: none"> Oral methotrexate 6-mercaptopurine Intermittent pulses: vincristine, glucocorticoid 	<p><i>Remission induction: 10 days</i></p> <ol style="list-style-type: none"> Antimetabolite: Cytarabine (7 days) <i>and</i> Anthracycline: Daunorubicin (3 days) CNS prophylaxis if required: intrathecal cytarabine +/- methotrexate, systemic high dose cytarabine For high risk: Anthracycline (IV daunorubicin) <p><i>Consolidation (2-4 cycles):</i> reduce residual cells to prevent relapse</p> <ol style="list-style-type: none"> High dose cytarabine <p>OR</p> <p><i>Stem Cell Transplant</i></p>
Relapse treatment	<ul style="list-style-type: none"> Chemotherapy or Stem Cell transplant 	<ul style="list-style-type: none"> Chemotherapy or Stem Cell transplant

A note on Chronic Leukaemia

As cells usually remain functional (low risk for developing infections) and is often incurable, therapy consists of watchful waiting, *and/or*

- CML: tyrosine kinase inhibitor therapy (imatinib, bosutinib, dasatinib, nilotinib)
- CLL: bendamustine, cyclophosphamide, fludarabine, rituximab

Complications of Treatment

- Tumour Lysis Syndrome (TLS):* oncologic emergency characterised by metabolic abnormalities resulting from the death of blast cells and the extensive release of purines, pyrimidines, and intracellular potassium and phosphorus. Deposition of uric acid (from the breakdown of purine) and calcium phosphate crystals in the renal tubules can lead to acute renal failure.
- Infection:* severe myelosuppression from the cancer or chemotherapeutic treatment increases risk of sepsis

Lymphomas

Description

Lymphomas are an umbrella term for ‘cancers of the lymphatic system’. Similar to leukaemias, they are also characterised by a haematopoiesis disorder. The main difference is that while they are both forms of blood cancers and overlap much, leukaemias will affect the blood and bone marrow while lymphomas mainly affect the lymph nodes.

Malignant lymphocytes (B/T/NKC) accumulate in lymph tissue to create the malignancy and can infiltrate non-lymphoid tissue—these however, typically do not circulate. Lymphomas thus also differ from leukaemias in the sense they will not be detected in the circulation.

There are over 40 different kinds of lymphoma, which are classified into 2 broad groups:

1. Hodgkin lymphomas (HL)
2. Non-Hodgkin lymphomas (NHL) | More Common

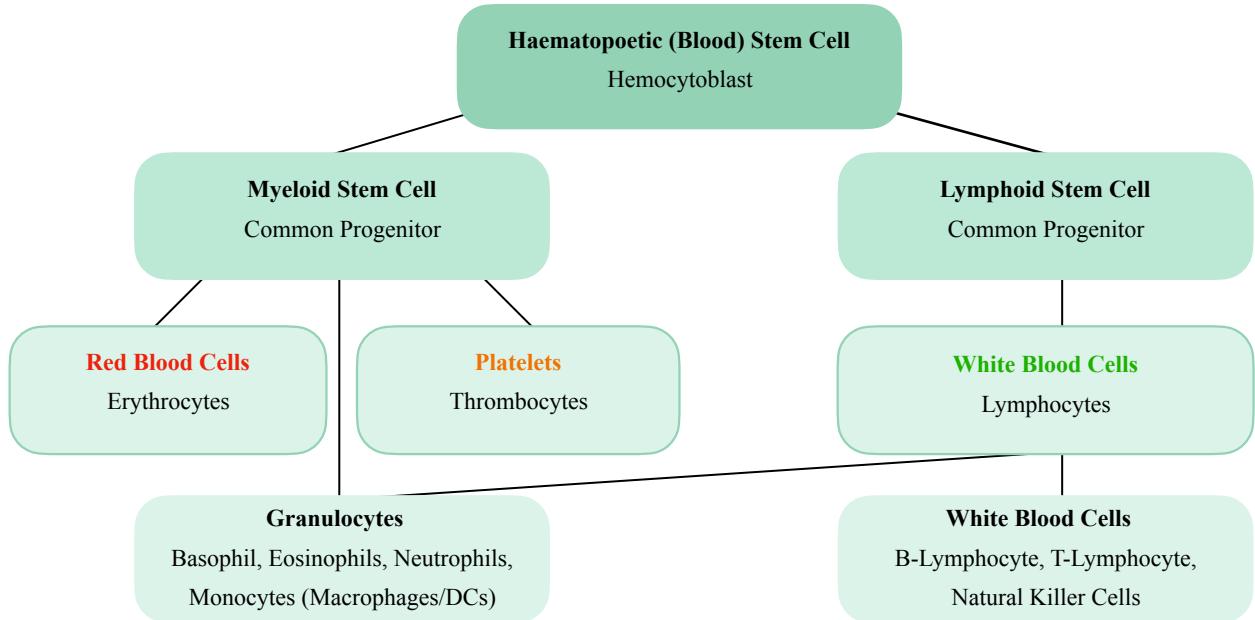
LYMPHOMAS		
	Non-Hodgkin	Hodgkin
Prevalence	<ul style="list-style-type: none">• Occurs usually in older people (>50 years old)• 2nd most common childhood cancer	Occurs usually in younger adults
	~85% of lymphomas in total (more common)	~15% of lymphomas in total (more rare)
Characteristics	<ul style="list-style-type: none">• 35 subtypes exist• More indolent and aggressive	<ul style="list-style-type: none">• 5 subtypes exist• More curable
	<ul style="list-style-type: none">• B Cell Lymphomas (more prevalent)• T Cell Lymphomas	Classic type is most common (nodular lymphocyte-predominate HL) • Reed-Sternberg cell in all 5 HLs
Treatment	CHOP Regimen	ABVD Chemo+Radiation

Pathophysiology

Bone Marrow

Pluripotent stem cells in the bone marrow are able to differentiate to both lymphoid and myeloid progenitor cells. Lymphoid progenitor cells undergo normal gene rearrangement to yield either B cell or T cell lineage precursor cells. Normal maturation for naive B cells includes expression of cell surface antibody or the cells undergo apoptosis. When naive B cells recognise antigen with their cell surface antibody, they accumulate in the lymph nodes, spleen, or other lymphoid tissue.

The pathophysiology of HL is defined by the presence of the Reed-Sternberg (RS) cells in a grouping of lymph nodes, in which the RS cells are thought to be of B cell origin. Their presence is associated with infection with the Epstein-Barr virus.



Leukaemias

WCC + RBC + Platelets

Lymphomas

White Blood Cells

Risk Factors

	RISK FACTORS		
	Both	Non-Hodgkin	Hodgkin
Patient	<ul style="list-style-type: none"> Male Immunosuppression: autoimmune, HIV/AIDS, post-transplant 	Increasing Age (>50)	<ul style="list-style-type: none"> Age: 15-30, 55-70 Family history
Mutations	Abnormalities in regulatory genes		
Medicines	Immunosuppressive: post-transplant médication		
Substances	Exposure to radiation, fertiliser and pesticides		
Viruses	Epstein-Barr virus	H.Pylori	<ul style="list-style-type: none"> Other viruses: cytomegalovirus, HSV, HIV, adenoviruses

Signs & Symptoms

Unlike leukaemias, symptoms of lymphomas are much more specific (viral-like symptoms)

- Swollen lymph nodes (neck, under arms, supraclavicular, groin), enlarged spleen
- SOB, dry cough, chest pressure
- GI complications
- Back, chest, abdominal pain
- Fever, night sweats, weight loss, pruritus

Screening

For the same reasons as leukaemias, no screening is indicated

Diagnosis

- Physical* examination (careful attention to lymph nodes) & history
- Imaging*: CT, PET scans
- Biopsy*: bone marrow, lymph nodes
- Prognostic tools*: CBC, LDH (lactate dehydrogenase in NHL), blood smear

Staging

TNM Staging

Unlike leukaemias, a staging process exists.

Prognosis

HL: 89% 5-year survival

NHL: 74% 5-year survival

Pharmacological Treatment

The principle goal is to cure with radiation and/or chemotherapy

STAGING & TREATMENT OF HODGKINS LYMPHOMA CANCER (R-CHOP 21)		
TNM Stage	Definition	Recommendation
Stage 0 or 1 Localised	<i>Lymphoma is limited to:</i> <ul style="list-style-type: none"> • One node or a group of adjacent nodes • Single extra nodal lesion without nodal development 	<ol style="list-style-type: none"> 1. Radiation 2. Chemotherapy: <ol style="list-style-type: none"> a) ABVD (usually 2 cycles) <ul style="list-style-type: none"> • Adriamycin (doxorubicin) • Bleomycin • Vinblastine • Dacarbazine b) BEACOPP <ul style="list-style-type: none"> • Bleomycin • Etoposide • Adriamycin (doxorubicin) • Cyclophosphamide • Procarbazine • Prednisone
Stage 2 Localised	<i>Lymphoma is limited to:</i> <ul style="list-style-type: none"> • Two or more nodal groups on the same side of the diaphragm • Limited contagious extra nodal involvement 	
Stage 3 Localised/Advanced	<i>Lymphoma is found on:</i> <ul style="list-style-type: none"> • Nodes on both sides of diaphragm or nodes above the diaphragm with spleen involvement 	<ol style="list-style-type: none"> 1. Chemotherapy: <ol style="list-style-type: none"> a) ABVD <ul style="list-style-type: none"> • Adriamycin (doxorubicin) • Bleomycin • Vinblastine • Dacarbazine b) (R)-CHOP <ul style="list-style-type: none"> • Rituximab — if C20 positive • Cyclophosphamide • Doxorubicin • Vincristine • Prednisone
Stage 4 Advanced/Metastatic	<i>Lymphoma has spread.</i> <ul style="list-style-type: none"> • Additional noncontagious extra lymphatic involvement 	

A note on Non-Hodgkin's Lymphoma (NHL)

1. Watchful waiting is a standard approach (median survival time is 6-10 years)
2. Radiation (however limited role relative to HL)
3. CHOP chemotherapy or R-CHOP immunochemotherapy may be considered

ONCOLOGIC SUPPORTIVE CARE FOR ADRs OF CHEMOTHERAPY

Description

Toxicities are commonly observed with chemotherapy as the agents target rapidly dividing normal and cancer cells — thus treatment complications may be life threatening. For this reason, supportive care is a crucial component of oncology.

Supportive care is treatment that we give to a patient to:

- To prevent, control or relieve complications & side effects
- To improve patient's comfort and quality of life

RISK MEDICATIONS SUMMARY								
	Doxorubicin (Anthracycline)	Cisplatin (Platinum)	5-FU (Antimetabolite)	Capecitabine (Antimetabolite)	High Dose Cytarabine (Antimetabolite)	Vinka Alkaloids	Taxanes	Misc
Mucositis								Alkylating agents, topoisomerase II inhibitors
Diarrhoea			+	+				Irinotecan, EGFR Inhibitors
Constipation						+		Antiemetics, Opioids
N&V	+	+	+	+			+	
Hypersensitivity							+	Monoclonal Antibodies
Photosensitivity			+			+		MTX
Alopecia							+	
Hand Foot Syndrome	+		+	+	+			
Nail Syndrome								Docetaxel
Extravasation	+	+				+	+	Anthracycline
Tumour Lysis Syndrome								Leukaemia, lymphoma, solid tumours
Ocular Toxicity					+			
Otological toxicity		+						
Nephrotoxicity		+						



Supportive Care vs Palliative Care

Supportive care differs from palliative care 'end of life' approach and is appropriate for patients of any age and at any stage in a serious illness and can be provided together with curative treatment.

Gastrointestinal Complications

Introduction

Chemotherapy is associated with various gastrointestinal complications - please revisit *Chapter 4 — Gastrointestinal Conditions* for information on these conditions as this section will only focus on supportive care.

Oral Mucositis

Description

Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract (especially the mouth and throat). It usually occurs as an adverse effect of chemotherapy and radiotherapy treatment for cancer, typically manifesting 5-14 days post therapy and lasts typically 2-3 weeks.

Risk Factors

- High-dose chemo with alkylating agents or topoisomerase II inhibitors
- Methotrexate

Prevention

- Cryotherapy (ice chips swishing for 30 min before bolus CT)
- Oral glutamine for head & neck cancer if radiation Tx + CT

Pharmacological Treatment

- Oral Care
- Routine mouth care by an oncologic dentist



Other Ways to Help Oral Mucositis

1. Folinic acid to counteract methotrexate
2. Diarrhoea may be associated with mucositis: loperamide or octreotide

Diarrhoea

Description

Diarrhoea in cancer is caused directly by toxicity to epithelial cells leading to inflammation and prostaglandin release.

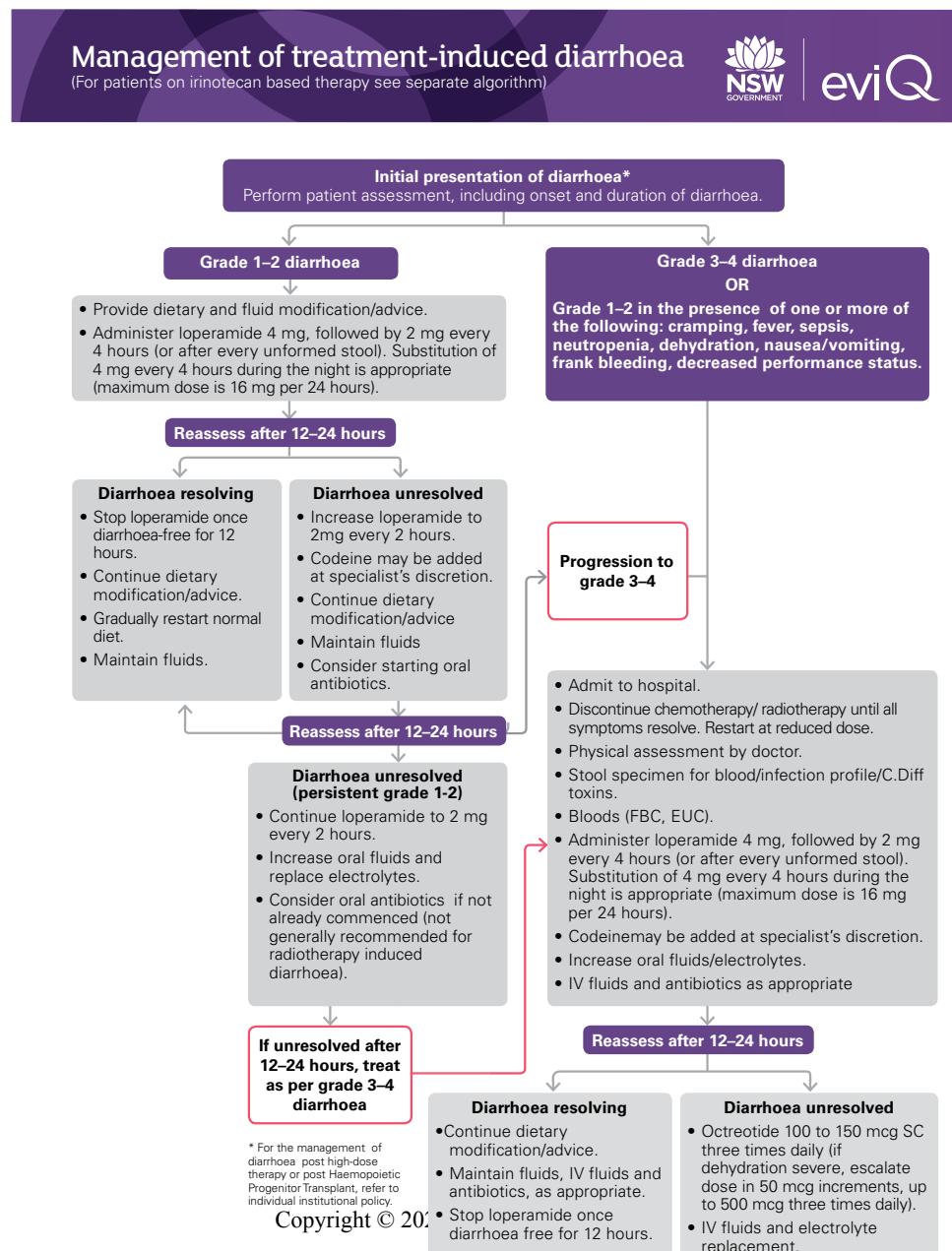
Causes

- Most commonly experienced with: 5-FU, Irinotecan, Capecitabine, EGFR Inhibitors

Pharmacological Treatment

EVIQ Management of Acute Chemotherapy-Related Diarrhoea

- Loperamide* 4mg orally, then 2mg every 2 hours until diarrhoea free
- Octreotide*: if not responding to loperamide
- Corticosteroids*: in severe cases
- Antidiarrhoeals*: do **not** use in patients with suspected C. Diff



Constipation

Description

Chemotherapy or opioid medication can cause this.

Causes

- Vinca alkaloids
- Opioids
- Anti-emetics (ondansetron)

Non-Pharmacological Treatment

- Manual or surgical evacuation, hydration, diet

Chemo-Induced N&V (CINV)

Oncology Antiemetic Policy — Canterbury

Description

80% of cancer patients will experience chemotherapy-induced nausea and vomiting (CINV) — there are 4 types that exist:

1. *Acute*: up to 24h after CT; peak 5-6 hours
2. *Delayed*: starts 24h - 7 days after CT
3. *Anticipatory*: begins as next dose/cycle becomes closer
4. *Breakthrough*: happens despite treatment/prevention
5. *Refractory*: treatment/prevention does not work

Risk Factors

- Types of CT, dose, schedule, and administrations of other drugs
- Previous use of CT
- Female, Age <50 years old
- Non-drinker or light drinker
- Experiences motion sickness or pregnancy morning sickness
- Being prone to vomiting

Causes

Classification of treatment emetogenic risk:

1. Minimal (< 10%): Capecitabine
2. Low (10 - 30%): 5-FU, taxanes
3. Moderate (30 - 90%): Doxorubicin — *Emetic risk duration of 2 days - provide prophylaxis*
4. High (> 90%): Cisplatin — *Emetic risk duration of 3 days - provide prophylaxis*



What If The Patient is On Multiple Chemo Drugs?

Antiemetic treatment for combination chemotherapy is determined according to the chemotherapeutic drug with the **greatest emetogenicity risk**

Complications

- Serious metabolic imbalance, dehydration, anorexia
- Deterioration in mental and physical status
- Treatment withdrawal

Principles of Treatment

- Anti-emetic use in CINV aims to minimise its likelihood during the period of emetic risk
- Emetic prophylaxis should be provided throughout the entire period of risk e.g. **2 days** for moderately emetogenic CT and **3 days** for highly emetogenic CT

- Optimal emetic control in the acute phase (first 24h) is **essential** in preventing N/V in the delayed phase

Pharmacological Treatment

ANTI-EMETICS		
Class	Drugs	Indication
Serotonin (5-HT3) antagonists	Ondansetron, Granisetron, Dolasetron, Palonosetron	Indicated in acute nausea and vomiting: before chemo and for a few days post-chemo
NK-1 receptor antagonists	Aprepitant, Rolapitant, Fosaprepitant	Indicated in delayed nausea and vomiting • Often used in combination with other anti-emetics
Benzodiazepines	Lorazepam, Alprazolam	Indicated in anticipatory NV by reducing anxiety and helping the person feel more relaxed • Often used in combination with other anti-emetics.
(Antipsychotic)	Olanzapine	Indicated in breakthrough and delayed nausea and vomiting.
Steroids	Dexamethasone	Indicated for prophylaxis of nausea and vomiting • Often used in combination with other anti-emetics.
Dopamine antagonists	Prochlorperazine, Metoclopramide	Indicated when NV is not well controlled by other drugs
Cannabinoids (contain the active ingredient in marijuana)	Dronabinol, Nabilone	Indicated when the usual anti-emetic drugs don't work

Emetogenic risk	Acute NV prevention - prior to chemo	Delayed NV prevention			
		Day 1	Day 2	Day 3	Day 4
High	<u>Option 1:</u> NK1 + 5-HT3 + Steroid		NK1 + Steroid	NK1 + Steroid	Steroid
	<u>Option 2:</u> NK1/5-HT3 + Steroid		Steroid	Steroid	Steroid
	<u>Option 3:</u> Olanzapine + 5-HT3 + Steroid		Olanzapine	Olanzapine	Olanzapine
Moderate	<u>Option 1:</u> 5HT3 (Palonosetron Preferred) + Steroid ± NK1		5HT3 Monotherapy, Days 2-3		-
	<u>Option 2:</u> NK1/5-HT3 + Steroid		Steroid Monotherapy, Days 2-3		-
	<u>Option 3:</u> Olanzapine +5-HT3 + Steroid		NK1 + Steroid		-
Low	Steroid OR Dopamine anta OR 5-HT3			None	

Antiemetic Regimens for Chemotherapy - [Canterbury Guidelines](#)

Emetogenicity Chart for Cytotoxic Agents	RISK	INTRAVENOUS AGENTS		ORAL AGENTS
	High (>90%)	Cisplatin ≥ 50mg/m ² Streptozotocin Cyclophosphamide > 1500 mg/m ² Dacarbazine Carmustine Dactinomycin		
	Moderate (30-90%)	Cisplatin < 50mg/m ² Oxaliplatin Cytarabine > 1 gm/m ² Carboplatin Ifosfamide Cyclophosphamide < 1500 mg/m ²	Doxorubicin Daunorubicin Epirubicin Idarubicin Irinotecan	
	Low (10-30%)	Paclitaxel Docetaxel Mitoxantrone Topotecan Etoposide Pemetrexed Methotrexate Liposomal Doxorubicin	Mitomycin Gemcitabine Cytarabine ≤ 100 mg/m ² 5-Fluorouracil Bortezomib Cetuximab Trastuzumab	Procarbazine Cyclophosphamide Etoposide Temozolomide Vinorelbine
	Minimal (<10%)	Bleomycin Busulfan Fludarabine Vineblastine Vincristine Vinorelbine Bevacizumab		Chlorambucil Hydroxyurea Methotrexate Imatinib Gefitinib Capecitabine
Combination regimens have greater emetogenic potential than any single agent. Identify the most emetogenic agent in the combination then assess the relative contribution of other agents: Minimally emetogenic agents do not add to the emetogenicity of a regimen, while adding one or more mild-moderate agents increases the combinations emetogenicity by 1 level.				

The below is a guideline only, and individual regimens will have the suggested accompanying anti-emetic regimen printed on the chemo prescription chart.

Recommended Antiemetic Regimens for Chemotherapy

Emesis Risk	Drug	Acute: Pre chemo	Delayed: Post chemo
High	Dexamethasone*	16-20mg IV/PO	8mg od-bd d2,3 8mg mane d4 (+/- d5)
	Ondansetron	8mg IV or 16mg PO	Nil
	Domperidone		20mg prn (qid)
Moderate	Dexamethasone	8mg IV/PO	4-8mg daily d2,3, +/- 4mg d4.
	Ondansetron	8mg IV or 16mg PO	Nil
	Domperidone		prn
Low	Dexamethasone	4mg PO or 20mg PO	
	Domperidone	Nil routine	prn
Minimal	Domperidone		prn

*Note: If Aprepitant is given reduce dexamethasone doses by 50% when given on the same day as Aprepitant

If on 16mg of dexamethasone decrease to 12mg rather than by 50% if on Aprepitant when given on the same day.

Dermatological Toxicities

Introduction

Dermatologically-involved tissues tend to be rapidly dividing sites - making them unfortunate targets to chemotherapy.

Photosensitivity

Description

Photosensitivity is an enhanced skin sensitivity or an unusual reaction when your skin is exposed to ultraviolet radiation (sunlight).

Causes

- 5-FU, MTX, Vinblastine

Signs & Symptoms

- Redness, Inflammation
- Blistering, Weeping, Peeling

Pharmacological Treatment

1. Corticosteroids
2. Analgesics

Prevention

- Wear sunscreen
- Cover up
- Avoid sunbeds

Alopecia

Description

Chemotherapy-induced hair loss is the result of hair being a rapidly-dividing site, therefore an unfortunate target. Usually occurs 1 - 2 weeks post-chemotherapy and is **reversible** (1 - 2 months after cessation of therapy). However, high-dose chemotherapy used in the setting of hematopoietic cell transplantation can lead to rapid and complete alopecia.

Causes

- *Taxanes*: total body alopecia (axillary, pubic hair, eyebrows, eye lashes)

Non-Pharmacological Treatment

- Counselling and psychological support are the best as alopecia will be transient

Prevention

- Scalp tourniquet, scalp hypothermia (cryotherapy), medical therapy

Nail Disorders (Beau's Lines)

Description

Beau's lines are horizontal ridges or dents in one or more of your fingernails or toenails. They're a sign that an illness, injury or skin condition interrupting your nail growth.

Causes

- Docetaxel

Non-Pharmacological Treatment

Resolves once nail regrowth occurs and/or upon treatment cessation

Hand-Foot Syndrome (Palmer-Plantar /Acral Erythema)

EVIQ Hand-Foot Syndrome

Description

Hand-foot syndrome (also called palmar-plantar erythrodysesthesia) is a side effect of certain chemotherapy drugs. It tends to appear within the first 2 to 3 months of treatment and is a skin reaction that occurs when a small amount of the medication leaks out of the capillaries and usually onto the palms of the hands and soles of the feet.

Causes

- 5-FU, Capecitabine, doxorubicin, High dose cytarabine

Signs & Symptoms

- Swelling and blistering on the palms of the hands and soles of the feet.
- Numbness tingling, burning, or itching sensation
- Redness (resembling a sunburn), swelling, discomfort, tenderness, rash

Non-Pharmacological Treatment

1. Symptomatic treatment

- Cold compress
- Soak hands and feet in a basin of cold water for 15 minutes 3 to 4 times per day
- Avoid exposure of hands and feet to heat - bathe/shower in lukewarm water (limit use of hot water)
- Avoid sun exposure and use a sunscreen SPF 30+ or greater
- Do not walk barefoot - avoid activities that cause excessive friction and rubbing of the skin surfaces
- Use barrier gloves when dealing with chemicals such as detergents and cleaning products
- Wear cotton gloves - especially if standing for long periods
- Avoid tight-fitting shoes
- Avoid situations that raise body temperature e.g. steam, sauna, hot baths, heating pads, vigorous exercise

Pharmacological Treatment:

1. Drug cessation

2. Symptomatic treatment

- Lanolin lotions
- 10% urea emollient
- Analgesia
- Topical corticosteroid

Instructions

Gently apply an emollient to hands and feet daily. Preparations containing urea moisturise dry skin by reducing water loss from the epidermis (upper layer of skin) resulting in softer and more supple skin. Urea is naturally present in healthy skin. It is one of three natural moisturising factors in the outer horny layer of our skin. The other two natural moisturising factors are lactic acid and amino acids. There are markedly reduced amounts of urea in dry skin conditions. Urea draws and retains water within skin cells, softens the horny layer, and has anaesthetic effects.



Refer If:

Reinforce when to seek immediate medical attention: temperature greater than or equal to 38° and/or discharge or odour from any open areas. And when unable to perform activities of daily living (ADLs), or when pain is not controlled, or peeling or blistering.

Miscellaneous

Pain Management

Visit *Chapter 20 - Fever, Pain & Infection* for information on this condition

Description

Pain is one of the most troublesome symptom of cancer and chemotherapy.

Signs & Symptoms

- Symptoms associated with different types of pain

Less obvious (if patient is unable to communicate)

- Tachycardia
- Diaphoresis
- Grimacing on movement
- Guarding (involuntary muscle response to protect yourself)
- Anxiety

Pharmacological Treatment

For all patients on **opioids**, also prescribe:

- **Regular** combination laxative (Laxsol)
- **PRN** antiemetic (metoclopramide)

Hypersensitivity Reactions

Description

Hypersensitivity reactions to chemotherapy agents are defined as unexpected reactions with signs and symptoms not consistent with known toxicity of these drugs. These reactions range from mild to life-threatening and are difficult to predict.

Signs & Symptoms

- Fever, chills, nausea/vomiting, angioedema
- Pruritic rash, flushing
- Acute dyspnoea
- Bradycardia, hypotension

Note: Severe reactions only occur as a <5% chance

Causes

1. Taxanes: reaction onset within 2-3 days of exposure (fast) due to excipients
2. Monoclonal antibodies (Mabs)

Pharmacological Treatment

1. Pre-medication
 - d) Taxanes: H₁ and H₂ antagonists, steroids
 - e) Mabs: Paracetamol, antihistamines, steroids.
 - If severe, stop or interrupt infusion and give fluids and adrenaline
 - Can re-challenge/desensitise in mild grades: slow infusion, provide supportive care

Options for Managing

- Prescribe medications to help with symptoms
- Change treatment dose
- Hold treatment until the symptoms are better
- Permanently stop the drug if symptoms are severe and could be life-threatening

Extravasion

Description

Extravasion describes the leakage of intravenously (IV) infused, and potentially damaging, medications into the extravascular tissue around the site of infusion. It is not a side effect but rather a given risk with the administration of any IV medicines.

Risk Factors

Often occurs when the needle is not placed properly.

Signs & Symptoms

Pain, swelling, stinging, burning and damage at the injection site.

Complications: Tissue sloughing, pain, loss of mobility in the extremity, infection

Causes

Vesicants are the name for agents (particularly chemotherapeutics) that may cause severe tissue damage and necrosis if they escape from the vasculature.

1. Anthracyclines (most severe)
2. Vinca alkaloids
3. Taxanes
4. Platinum Drugs
5. Cisplatin

Prevention

Good administration technique

Pharmacological Treatment — SLAP

1. Stop infusion
2. Leave venous access
3. Aspirate
4. Plan

Anthracyclines: cold compresses

- **Antidotes:** I/V Dexrazoxane or dimethyl sulfoxide topical solution

Vinca alkaloids: warm compresses

- **Hyaluronidase** for vinca alkaloids and *taxanes*

Tumour Lysis Syndrome (TLS)

Description

Tumour Lysis Syndrome is a condition that occurs when a large number of cancer cells die within a short period, releasing their contents into the blood. This is most common in the first cycle of treatment. It can result in metabolic abnormalities and is often an oncologic emergency that can cause death.

Signs & Symptoms

- *Metabolic abnormalities:* Hyperuricaemia, hyperkalaemia, hyperphosphataemia, secondary hypocalcaemia, uraemia
- *Other:* N/V/D, anorexia, lethargy, oedema, fluid overload, congestive heart failure, haematuria, cardiac dysrhythmia, seizures, muscle cramps, tetany (muscle spasms), syncope

Risk Factors

Patient

- Increased WCC (greater than $25 \times 10^9/L$)
- Increased LDH (greater than $2 \times ULN$)
- Renal insufficiency/failure
- Dehydration, decreased urinary flow
- Pre-existing uraemia, hyperuricaemia, or hyperphosphataemia

Tumour-Related Factors

- High tumour cell proliferation rate
- Bulky disease (greater than 10 cm)
- Chemo-sensitive malignancies
- Higher risk malignancies: non-Hodgkin's lymphoma, Burkitt's lymphoma, ALL, AML, solid tumours

Therapy

- Highly potent therapy, novel, or targeted therapy

Pharmacological Treatment

Prophylaxis in intermediate/high risk to manage hyperkalaemia, hyperphosphataemia, and hypocalcaemia

1. First Line: Vigorous IV hydration
2. Decrease uric acid: Allopurinol or Rasburicase

Management

If prophylaxis fails: manage hyperkalaemia, hyperphosphataemia, hypocalcaemia, and other clinical manifestations

Ocular Toxicities

Description

Ocular toxicity induced by cancer chemotherapy includes a broad spectrum of damages. Understanding the ocular side effects will assist the ophthalmologist and oncologist to recognise them early and intervene before blindness occurs.

Causes

Cytarabine-HiDAC

Signs & Symptoms

Excessive tearing, pain, photophobia, presence of foreign body

Prevention

1. Artificial tears (lubricating eye drops)
2. Topical corticosteroids

Pharmacological Treatment

1. Saline
2. Topical corticosteroids

Otological Toxicities

Description

Chemotherapy has potential to damage auditory function, particularly the inner ear.

Causes

Cisplatin

Prevention

- Replace cisplatin with carboplatin

Monitoring

As this effect is cumulative and irreversible, it is important to monitor auditory function

Nephrotoxicity

Description

Chemotherapy has the potential to cause kidney damage — this is a dose limiting risk however.

Causes

Cisplatin (dose limiting toxicity)

Risk Factors

- Higher doses, previous exposure
- Pre-existing kidney damage
- Use of other nephrotoxic agents

Signs & Symptoms

- Increased serum creatinine
- Decreased urine output
- Electrolyte imbalances: hypokalaemia, hypomagnesemia, hyponatraemia

Prevention

- Lower doses
- Replace cisplatin with carboplatin
- Aggressive hydration, Magnesium

Pharmacological Treatment

- Replenish electrolytes
- Discontinue cisplatin

Monitor

- Fluid balance/overload
- Weight

Febrile Neutropenia

NZF: https://nzf.org.nz/nzf_4905

Description

Febrile neutropenia refers to the occurrence of a fever during a period of significant neutropenia (significant reduction in neutrophils).



Fever vs Febrile Neutropenia

A fever may be caused by an infectious agent while neutropenia is the most common complication of cancer treatment in oncologic patients 10-14 days post-chemotherapy, or less commonly post-radiation treatment.

Neutropenia is of worry and is an oncologic emergency as it is associated with a profound impairment in the inflammatory response: leading to a lack or minimisation of the usual signs and symptoms of infection in the background of the patient being at an increased risk of contracting one.

Signs & Symptoms

Due to an inability to mount an inflammatory response, many patients with febrile neutropenia do not demonstrate localising signs or symptoms other than fever. Immunity can be so suppressed that patients have very few infectious symptoms or even be afebrile.

Possible Symptoms

- Tachycardia, tachypnoea, hypotension, cough, dyspnoea, hypoxia
- Rigours, diaphoresis, altered mental status
- Decreased capillary refill/cyanosis/mottling
- Decreased urine output
- Signs & symptoms specific to an infectious source

Complications: Mortality, sepsis

Diagnosis

Febrile neutropenia is clinically defined as:

1. Fever: $\geq 38^{\circ}\text{C}$ on two consecutive occasions ≥ 1 hour apart, *or* $\geq 38.5^{\circ}\text{C}$ on one occasion, **AND**
2. Neutropenia: neutrophil count of $< 0.5 \times 10^9/\text{L}$, *or* recent intensive chemotherapy where neutropenia is expected

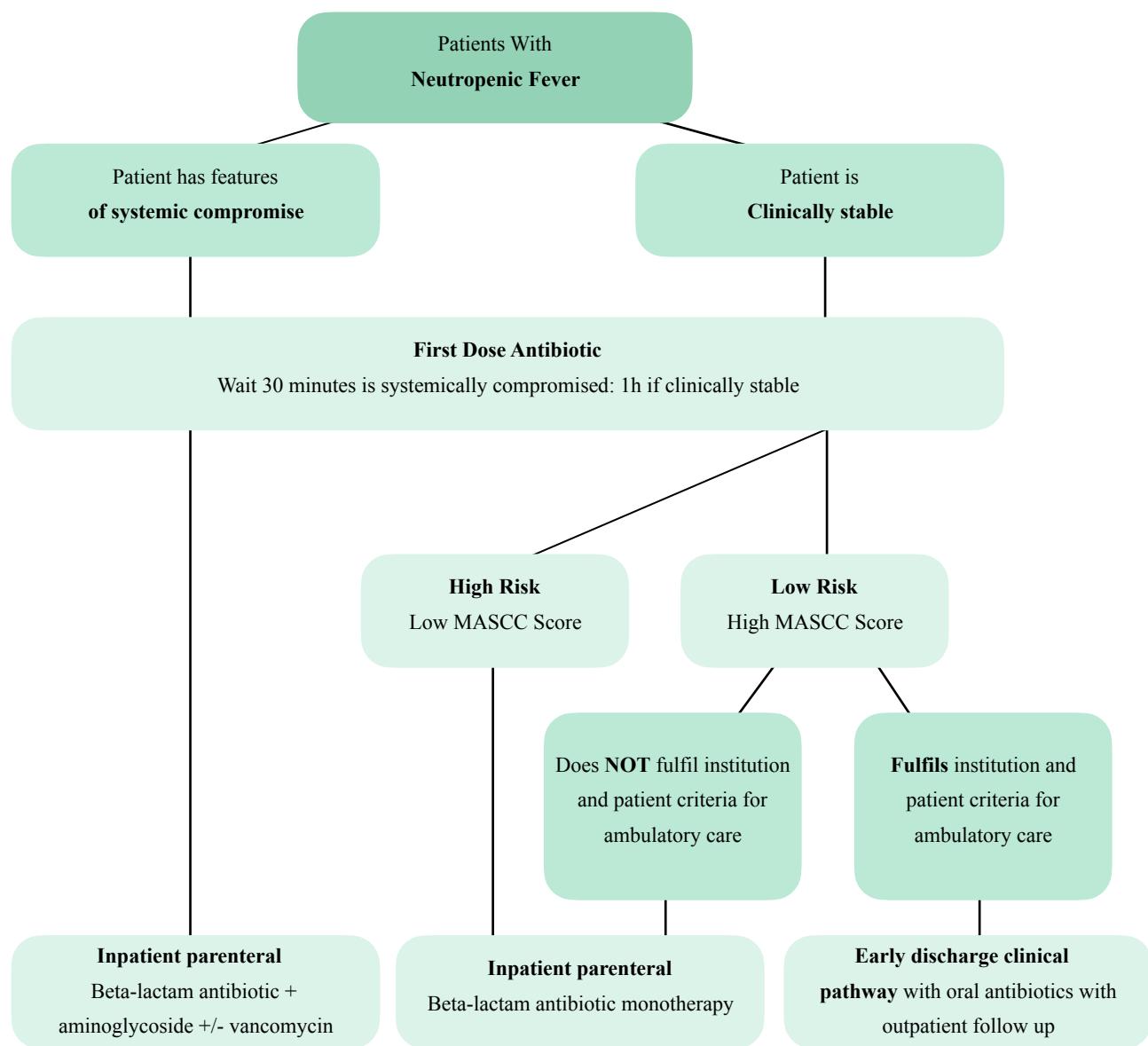
Pharmacological Treatment

Treatment

A [MASCC score](#) will determine whether empiric broad spectrum antibiotics should be considered to protect and prevent the patient from developing an infection due to their essentially non-existent immune response

1. β -lactams: piperacillin + tazobactam
2. +/- Gentamicin (dose using IBW)
3. +/- Vancomycin

MASCC Score	
Characteristic	Score ($>21 = \text{Low risk}$, $<21 = \text{High risk}$)
Burden of Illness	No or mild symptoms = 5 Moderate symptoms = 3 Severe symptoms = 0
No hypotension	5
No COPD	4
Solid tumour or haematological malignancy with no previous fungal infection	4
No dehydration requiring IV fluids	3
Outpatient at presentation	3
Age <60 years	2



Prevention

High risk patients or patients who have experienced previous febrile neutropenia may require prophylaxis in subsequent cycles. Note that prophylaxis is often used in lymphomas due to WBC suppression associated with cytotoxic therapy.

1. *Pegfilgrastim* (SC injection on day 3 or 4 of cycle): stimulates production of neutrophils from precursor cells, therefore reducing risk of infection
 - *ADR*: GI disturbances, anorexia, headache, asthenia, fever, musculoskeletal pain, bone pain, rash, alopecia, injection-site reactions, thrombocytopenia, leucocytosis

Anaemias

Visit *Chapter 19 - The Haematological System* for information on Anaemias

Description

The cancer itself, chemotherapy and subsequent effects of chemotherapy can cause anaemia.

The Cancer

2. Some tumours are more likely to cause anaemia (e.g. leukaemia, lymphoma): cancer competes with bone marrow function and interferes with normal RBC production
3. Some tumours have a higher risk of bleed: cancers of the GI system (colon, stomach cancers) OR fast growing tumours may cause frequent bleeding
4. Triggered immune response with release of various cytokines that interfere with bone marrow function and shorten RBC survival
5. Cancer cells release cytokines that can lead to iron sequestration, reducing RBC production

Cancer Treatment

- Chemotherapy agents target rapidly dividing cells

Other

- Missing certain vitamins or minerals in the diet due to not eating enough
- Low iron levels in blood

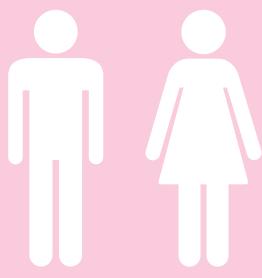
Risk Factors

Cancer-specific Risk Factors

- **Platinum-based** chemotherapy: major risk factor for anaemia
- Certain types of tumours (e.g. ovary)
- Risk of tumour bleeding
- Cancers that involve the **marrow space** (leukemia, lymphoma)
- Pre-existing low haemoglobin level before cancer diagnosis

Complications

- Can affect QoL
- Shortens survival
- Can make heart work harder (to meet oxygen demands)
- Can make it hard to breathe normally
- Severe anaemia may mean you have to **delay or reduce** the dose of your cancer treatment
- It can cause some cancer treatments to not work as well as they should



CHAPTER 12

MENS & WOMENS HEALTH



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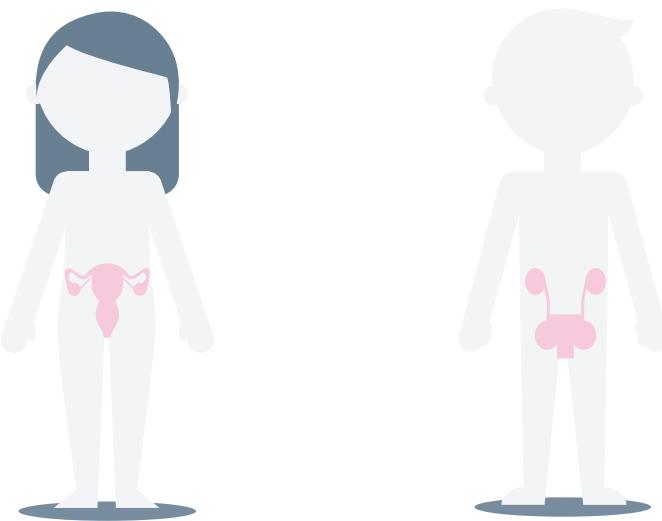
Chapter 12

Men & Women's Health

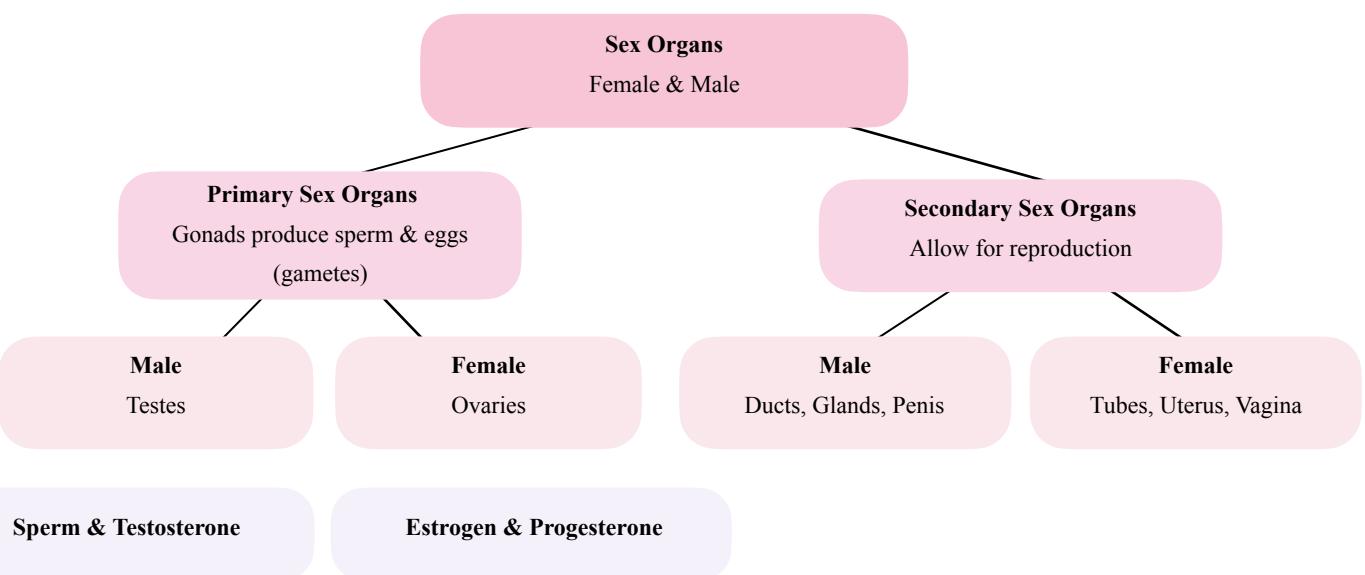
Female & Male Sex Organs

Introduction

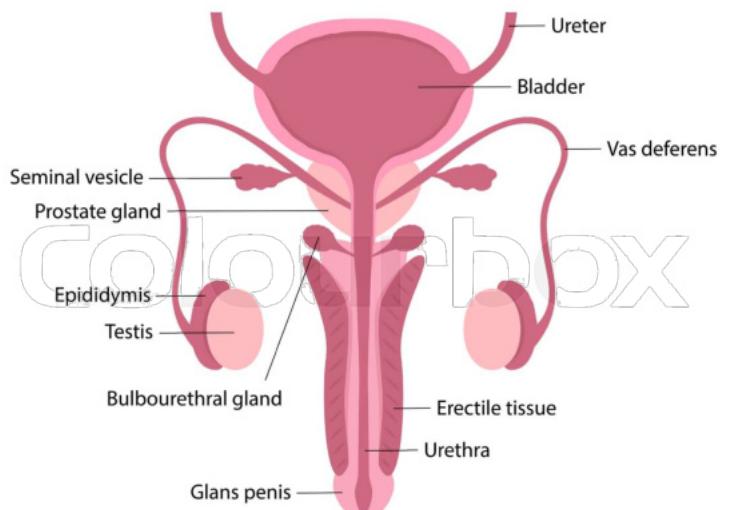
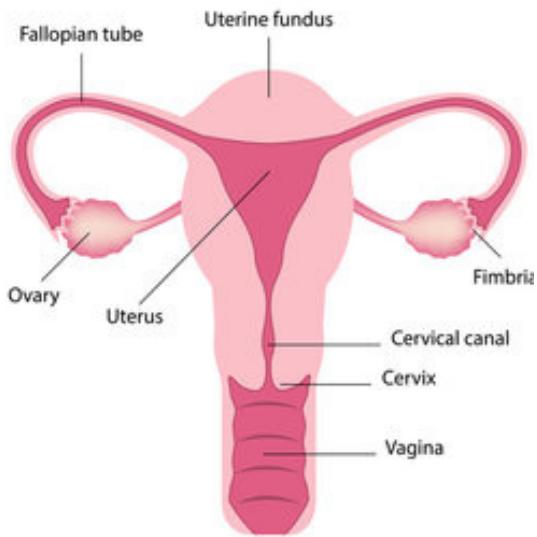
Welcome to the largest chapter in this handbook! Let's start with some anatomy.



There are two types of sex organs:



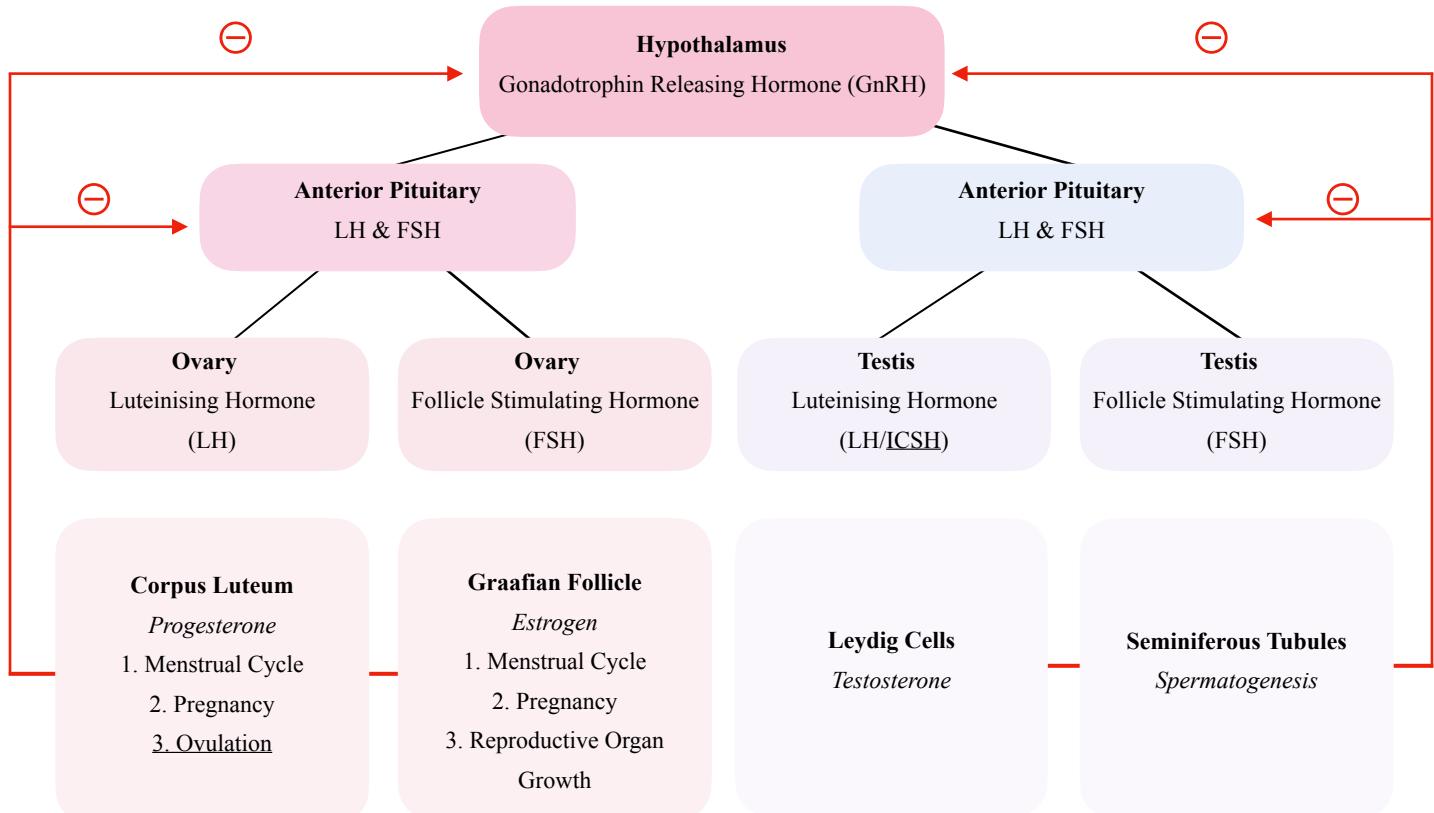
Structure	Description	Function
Oogenesis (Oocytes)	Ovaries The ovaries are female primary sex organs/gonads. They take turns in releasing eggs every month — however if one ovary is absent or dysfunctional, the other will release eggs every month.	They have 2 important functions: 1. Gamete (oocyte) production 2. Hormone production (Estrogen, Progesterone, Inhibin, and small amounts of androgen (Testosterone))
	Oocyte Oocyte are mature eggs (female gametes). Females achieve peak oocyte level at birth and gradually lose them over time.	During ovulation, the oocyte is released from the ovaries to the fallopian tubes. If fertilisation occurs in the fallopian tube, the oocyte will travel to the uterus and implant on the endometrium to develop into a pregnancy. If unfertilised, the oocyte disintegrates and is shed as part of the uterine lining during your period.
	Uterus & Uterine Tubes (Oviduct) These are the female secondary sex organs. This is where the fertilised oocyte travels to for implantation.	The uterus aims to harbour the embryo, provide nutrients, and produces vaginal and uterine secretions. It also passes the male sperm to the fallopian tube and expels the fetus at the end of its development.
	Endometrium This is the mucus lining of the uterus — it is the thickest when the egg is released from the ovary.	Allows attachment of the fertilised egg. 1. It develops if a fertilised egg implants. 2. In any other situation, the outer layer of cells in the lining are shed and passed out of the body during menstruation
	Vagina This is a female secondary sex organ. <ul style="list-style-type: none">It is made of stratified squamous epithelium (stretchy).Protected from infections due to a natural microflora (bacteria ferment glycogen to lactic acid — low vaginal pH of 4)	Provides a site of insertion for the penis. <ul style="list-style-type: none">Expands in length and width during arousalVaginal lubrication is provided by Bartholin's glands near the vaginal opening and cervix.
	Mammary Glands (not part of RT) These are female secondary sex characteristics and are not associated with the female RT. <ul style="list-style-type: none">Mammary alveoli join to form lobules, each which have a lactiferous duct that drain into nipple openings.	Provide milk to the baby. <ul style="list-style-type: none">Secretory alveoli develop mainly in pregnancy with rising levels of prolactin, estrogen, and progesterone.This causes further branching, increased adipose tissue and a richer blood supply.
Gametogenesis (Sperm)	Testes The testes are the male primary sex organs, they are contained in a sac called the scrotum which hangs around the upper thighs.	The testes function to produce two things: 1. Sperm Cells (Gametogenesis) 2. Testosterone (Interstitial Leydig Cells)
	Scrotum The scrotum is made of loose skin, fascia and smooth muscles divided into 2 pouches by a septum.	Its purpose is to protect the testes and maintain their temperature at 2°C lower than body temperature.
	Sperm Cells Sperm cells develop from germ cells in the seminiferous tubules of the testes. Sertoli cells found in those tubules control this sperm production by both supporting and inhibiting this process (inhibin) depending on which one is needed.	It is designed to move and fertilise an egg. <ul style="list-style-type: none"><i>Mitochondria:</i> sperm energy source that powers tail motility<i>Acrosome (head tip):</i> contains enzymes that dissolve the path to penetrate the egg, Fate: only viable in the uterus for up to 5 days (vs egg; 12-24 hours)
	Epididymus This a coiled tube at the back of the testicle that connects the testes to the penis. The produced sperm is carried out of the seminiferous tubules and stored in the epididymus.	It is the storage site of sperm cells (50-120 million sperm/ml). Sperm remain for 40-60 days and are absorbed if not ejaculated within this time. About 90% of the fluid secreted by testes is absorbed by this structure.
	Seminal Fluid (Semen) During ejaculation, the semen is the fluid expelled during orgasm. It is a mixture of secretions from the: <ul style="list-style-type: none">Epididymus (sperm)Seminal VesiclesProstateBulbourethral Glands	It is the fluid that nourishes and transports the sperm, and is made of the following 5 main constituents: <ul style="list-style-type: none"><i>Fructose:</i> source of energy for the sperm<i>Sperm:</i> causes fertilisation of the egg<i>Clotting Factors:</i> semen clot to stay in the female reproductive tract, then the clot is dissolved by anticoagulant factors 15-30 min later<i>Prostaglandins:</i> stimulate peristaltic uterine contractions to draw the semen up<i>Spermine:</i> neutralising base that reduces the acidity of the female vagina to improve sperm survival
	Penis The penis is made of two erection cylinders (corpora cavernosum) which wrap around the urethra.	These fill up with blood during an erection



Female & Male Sex Hormones

Endocrine Pathways

There are 2 endocrine pathways that act on the primary sex organs:



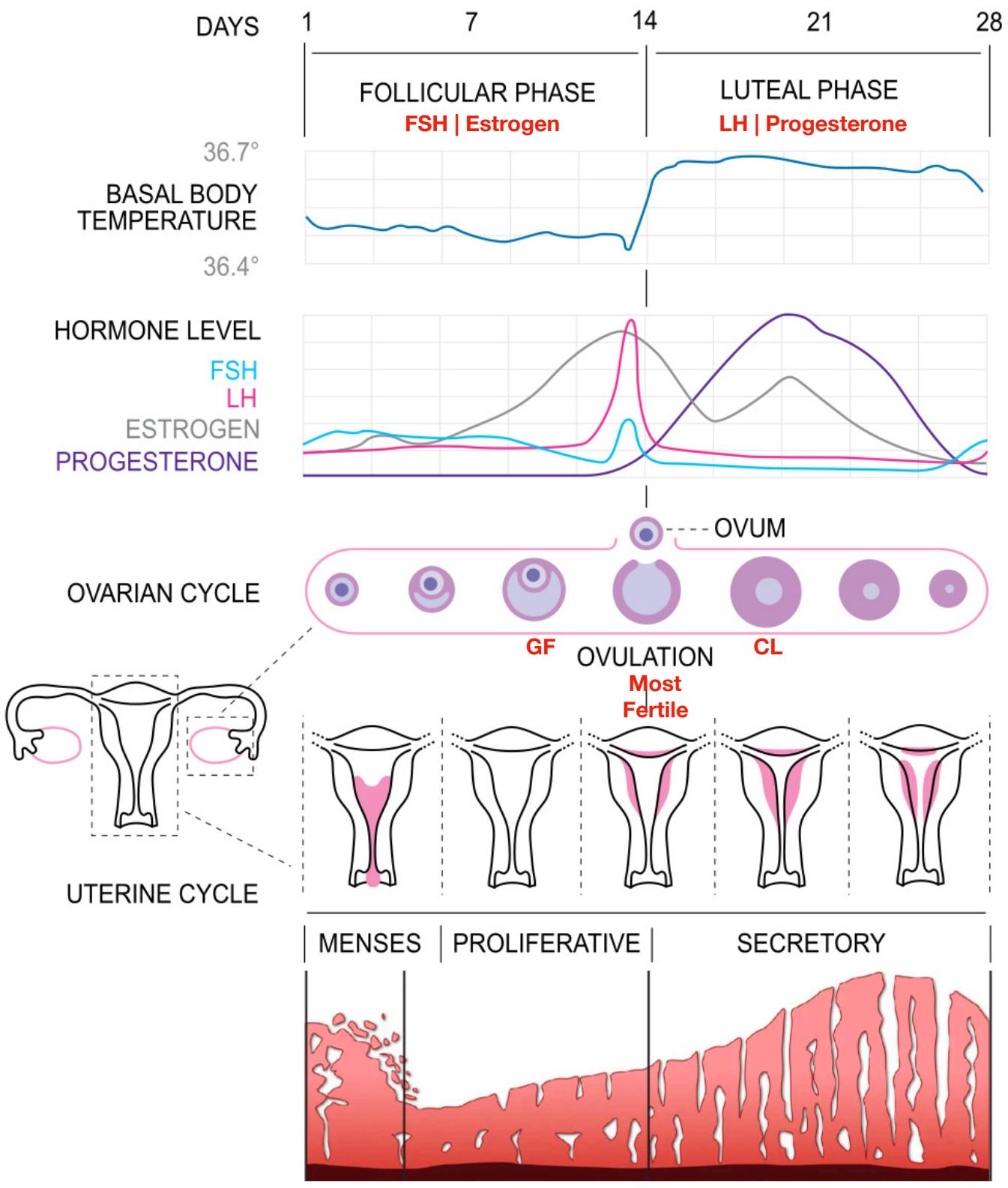
Hormone	Endocrinology	Clinical Use
GnRH	<p>Hypothalamus (GnRH) → Anterior Pituitary (FSH/LH) Released in a pulse-like manner to stimulate FSH & LH release.</p>	<p>Continuous GnRH Agonist/Antagonist</p> <ul style="list-style-type: none"> Reduces FSH/LH release (initial flare with negative feedback) Treats various sex-hormone dependent conditions e.g. goserelin/leuprorelin for breast/prostate cancer, endometriosis <p>Pulsatile GnRH Agonist</p> <ul style="list-style-type: none"> Stimulate FSH & LH release E.g. fertility treatment
Estrogen	<p>Anterior Pituitary (FSH) → Ovaries (E)</p> <p><i>Puberty</i></p> <ul style="list-style-type: none"> Reproductive organ growth (breast ducts, uterus) Fat deposition (hip, breasts) Bone arrest (height) <p><i>Menstrual Cycle</i></p> <ul style="list-style-type: none"> Salt/H₂O Retention (bloating) Lipoprotein profiles (weight gain) ↓ Bone resorption (menopausal osteoporosis) ↑ Coagulability (blood clot) <p><i>Pregnancy</i></p> <ul style="list-style-type: none"> Breast duct system growth (feeding / milk) ↑ Uterine blood flow (placenta) <p><i>CNS</i></p> <ul style="list-style-type: none"> Neuroprotection, Cognition, Emotional instability Brain development (male vs female brain) 	<p>Pharmacological effect of estrogen is dependent on age</p> <ul style="list-style-type: none"> Contraception (prevent pregnancy) Menstrual disorders Menopausal symptoms & Osteoporosis (HRT) Increases risk of certain cancers (Tamoxifen, Anastrazole: ↓ estrogen levels)
Progesterone	<p>Anterior Pituitary (LH) → Ovaries/Placenta (P) Mainly synthesised in the corpus luteum and acts to help women get pregnant.</p> <p><i>Uterus:</i> Prepares endometrium <i>Cervix:</i> Changes secretions to be hostile to sperm <i>Vagina:</i> Changes mucosa</p> <p><i>Breast:</i> Prepares lactation, progesterone increases in ducts</p> <p><i>CNS:</i> Sedative effect in pregnancy, neuroprotection</p> <p><i>Metabolism:</i> Impaired glucose intolerance (diabetes) and increases LDL/decreases HDL (hyperlipidaemia) with prolonged use</p> <p>Testis, Adrenal Cortex & CNS Synthesised in small amounts</p>	<p>Progesterone</p> <ul style="list-style-type: none"> Contraception HRT (only for intact uterus) Threatened/Habitual Miscarriage (agonist helps body continue pregnancy) Endometriosis <p>Mifepristone (Progesterone Antagonist) — BPAC Abortions</p> <ol style="list-style-type: none"> <i>Medical abortion (medical alternative to surgical termination)</i> Mifepristone (Progesterone Antagonist): Uterus lining breaks down in absence of progesterone and pregnancy cannot continue. Effective up to 63 days gestation (9 weeks or 2 months) Misoprostol (Prostaglandin): Used 24-48 h after mifepristone to cause cervical dilation & uterine contraction which allows the passage of the fetus. Please note Misoprostol's ability to dilate and soften the cervix means it is also used in IUD insertions and its ability as a prostaglandin means it can also provide protection from stomach ulcers. <i>Surgical Pregnancy Termination</i> Mifepristone: Dilates/opens the cervix to allow a surgical abortion procedure to be done. <i>Labour Induction for In Utero Fetal Death</i> Mifepristone: Progesterone surpasses contractility. Its antagonism initiates labour by stimulating uterine contractions in order to expel the dead fetus. In a normal pregnancy with a live fetus, labour is initiated by natural drastic drops in the levels of estrogen/progesterone.
Hormone	Endocrinology	Clinical Use

Testosterone	<p>Anterior Pituitary (LH/ICSH) → Testes (T) LH stimulates androgen secretion from Leydig Cells. Testosterone is converted to di-hydrotestosterone (DHT) in a dynamic exchange (98% bound, 2% free). DHT is the most potent androgen, having an effect on the development of secondary sex organs.</p> <p>Secretion is highest in the morning, lowest in the afternoon. Released in a pulse-like manner in 1-3 hours intervals (overall similar amounts in 24 hour period).</p> <p>Adrenal Cortex (Male & Females) & Ovary (Females) Synthesised in small amounts</p> <ul style="list-style-type: none"> • <i>Skin:</i> Facial/body hair growth, Baldness • <i>Male Sex Organs:</i> Sperm, Prostate growth, ED • <i>Muscle:</i> Mass & Strength • <i>Brain:</i> Sex drive, Aggression • <i>Bone marrow:</i> RBC production • <i>Bone:</i> Bone density maintenance 	<ol style="list-style-type: none"> 1. Replacement Therapy (TRT) <i>E.g. Testosterone Deficiency (Male Hypogonadism)</i> <ul style="list-style-type: none"> • Caused by pituitary or testicular disease • 2.5mg/day patches or IM pellet injections • ADR: Suppression of GnRH, liver injury (reversible) 2. Transgender Masculinisation Therapy <ul style="list-style-type: none"> • Testosterone blocks pituitary-gonadal axis and induces masculinisation by stimulating receptors in target organs • Results in development of male secondary sex characteristics and suppression of female characteristics. 3. Anti-Androgen Therapy (e.g. Cyproterone) <i>E.g. Contraception (POP), PCOS, Acne, Prostate/Breast Cancer (Goserelin), Male Hyper-Sexuality Disorder</i> <ul style="list-style-type: none"> • Cyproterone: weak pro-gestational activity and suppresses gonadotropin synthesis.
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Female & Male Sexual Response

Ovulation & Ejaculation

Phase		Description
Follicular Phase	Menstrual Phase (Days 1 - 4) <i>Variable</i>	<ul style="list-style-type: none"> • Variable cycle length. Shedding of the thickened endometrium i.e. period.
	Proliferative Endometrium (Days 4 - 13)	<p>Follicle Development (FSH → Estrogen)</p> <ul style="list-style-type: none"> • Oocytes (female egg/gamete) are contained in ovarian follicles. FSH will stimulate follicle development until they become Graafian Follicles (GF), which are ovarian follicles in the later stages of development. • Estrogen is produced by the GF and causes proliferation & regeneration of the endometrium (5-6 days to mid-cycle).
Luteal Phase	Secretory Endometrium (Days 14 - 28)	<p>Ovulation (LH → Progesterone)</p> <ul style="list-style-type: none"> • Consistent length cycle • High estrogen levels mid-cycle cause the release of the LH hormone which induces ovulation (the egg is released from the ovary into the fallopian tube via suction guidance at its opening). • It will travel there for a couple of days and wait to be fertilised on its journey to the uterus where it will implant in the endometrium. If unfertilised, the egg disintegrates and is shed as part of the uterine lining during menstruation. • Back in the ovary, where the follicle was, the GF develops into the corpus luteum (CL) — a remnant of the follicle which secretes the hormone progesterone <p>Two Effects of Progesterone:</p> <ul style="list-style-type: none"> • Endometrium: prepares it for implantation by maintaining the thickness. • Hypothalamus & pituitary: inhibit LH. <p>From here the production of progesterone is impacted by 2 outcomes.</p> <ol style="list-style-type: none"> 1. <i>If fertilisation occurs:</i> ↑ progesterone production as the corpus luteum continues to function. Eventually the placenta develops to continue the progesterone production. Both estrogen and progesterone are maintained high throughout to support the pregnancy. 2. <i>If fertilisation does not occur:</i> Levels of both estrogen and progesterone fall. The corpus luteum degenerates into corpus albican. The endometrium withers away, and the shedding of the uterine lining forms the menstrual flow (period starts). This brings us back to the follicular phase where we begin again.
Male Sexual Response	Erection	Allows penetration. Enabled by the deep artery.
	Ejaculation	<p>Expels the semen</p> <ol style="list-style-type: none"> 1. Ejaculation is initiated by sympathetic nerve impulses 2. Ducts/accessory glands contract and empty their contents into the urethra to form the seminal fluid 3. Urethral sphincters constrict and prostate gland swells to prevent urine mixing with semen 4. Bulbospongiosus muscles contract rapidly and rhythmically to propel semen out of the urethra
	Refractory Period	This is a period following ejaculation lasting anywhere from 10 minutes to a few hours where another erection and orgasm is unable to be attained.



CONTRACEPTION

Introduction to Contraceptions & Types

Description

Family Planning Contraception

Contraception, also known as birth control, is an artificial method of preventing pregnancy. It can be used until patients reach **menopause** (12 months after the last period) or **age 55 years**. The benefits of contraception often outweigh health risks, for example, spacing children decreases infant morbidity and mortality and the risk of spontaneous abortions.

Uses & Health Benefits

However, contraceptives have many uses! — Do not always assume they are being used to prevent pregnancy!

Primary Use
Prevent Pregnancy

Secondary Use
Heavy or Irregular Menstruation
Endometriosis, PCOS, Acne,
Dysfunctional Uterine Bleeding

Health Benefits / Advantages Associated with Contraceptives	
Health Benefit	Description
Ovarian/Endometrial/ Colorectal Cancer	Reduced risk with OC (especially COC, implant, IUD) even in women with BRCA1 & BRCA2 mutations.
Withdrawal Bleeding and Dysmenorrhea	COC reduces bleeding and regulates cycle.
Menstrual blood loss in menorrhagia	Reduced with COCs, implant, or levonorgestrel IUD — useful for anaemic patients
Acne	Treated with COC (with progesterone of lower androgenic properties)
Peri-menopause	Lighter, predictable bleeding; vasomotor symptom relief; positive effect on bone mineral density
PID and Benign Breast Disease	Reduced incidence
Ectopic Pregnancy	Reduces risk of ectopic pregnancy however paradoxically, if you get pregnant while on contraception, your risk of that pregnancy being ectopic is more likely.

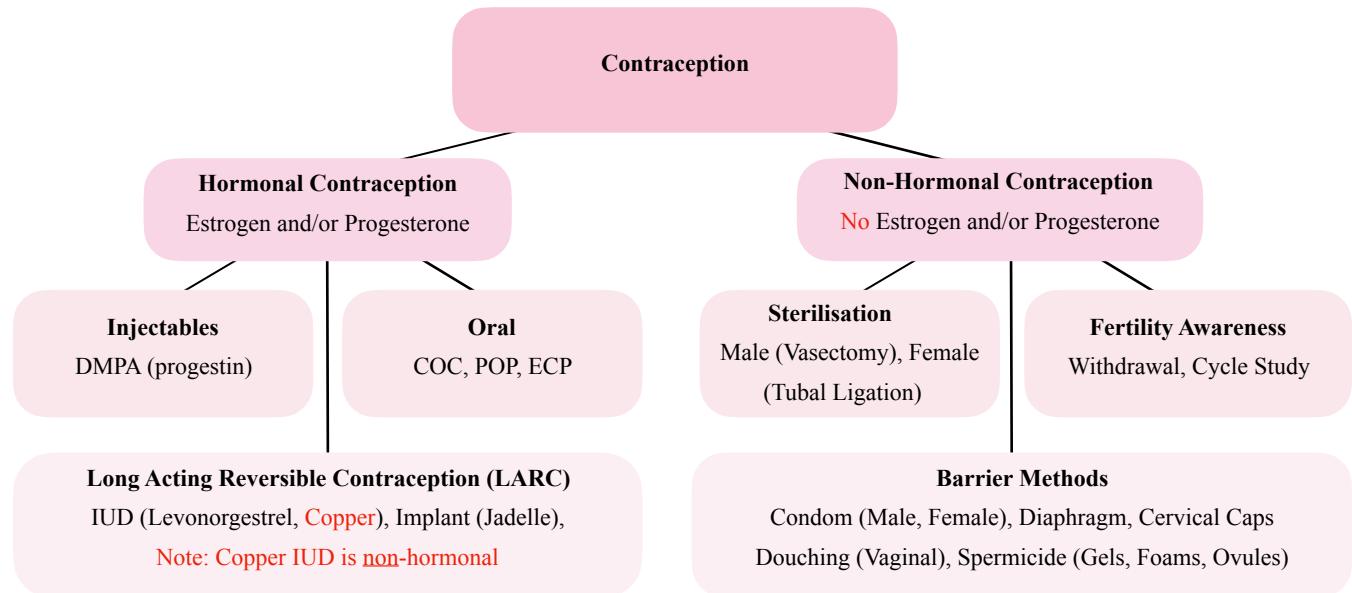
Mechanism of Action

Different methods of contraception have different mechanisms of action. However the general aim is to oppose steps in the conception process:

1. Ovulation Hormones
2. Fusion of sperm and ovum
3. Zygote implantation

As we go through each contraceptive method, we will cover their respective mechanism of action.

Types of Contraception



1. *Other hormonal methods:* Vaginal rings, Contraceptive patches (UK)
2. *Combination hormonal:* COC, vaginal rings
3. *Progestin only:* POP, Jadelle implant, Levonorgestrel IUD (Jaydess, Mirena)

Efficacy

Top-Tier (most effective)

1. IUD
2. Implant
3. Sterilisation

Second-Tier (very effective)

1. OC
2. Injection
3. Patches
4. Vaginal Ring

Third-Tier (effective)

1. Barriers
2. Natural family planning



Efficacy Matters!

Studies show that methods of contraception that rely on regular adherence in order to work are not very effective - educating patients on other birth control options that are available to them can help prevent unwanted pregnancies! Especially if they are on teratogenic medications that have strict contraceptive requirements e.g. Isotretinoin

Contraception - Your Choice

Contact Family Planning for detailed information on any of these methods



Method	What is it? How does it work?	Chance of getting pregnant	Health concerns	Advantages	Disadvantages
LONG ACTING REVERSIBLE CONTRACEPTION					
IMPLANT An implant consists of two small, thin rods made of a flexible plastic-like material. They are inserted under the skin of the upper arm.	<ul style="list-style-type: none"> progestogen is released from rods put under the skin of the arm by thickening mucus in cervix. May stop ovaries from releasing an egg each month 	less than 1 in 100	no serious risk	<ul style="list-style-type: none"> lasts 5 years fit and forget useful for those who can't take the combined pill or who might forget pills or appointments 	<ul style="list-style-type: none"> irregular bleeding which often gets better with time and can be controlled with medication
INTRA UTERINE DEVICE - IUD An intrauterine device (IUD) is a small, T-shaped device made of plastic and copper. It is inserted into the uterus to prevent pregnancy.	<ul style="list-style-type: none"> put inside the uterus 2 types - Copper IUD or progestogen-releasing IUD (Mirena or Jaydess) stops sperm reaching an egg 	less than 1 in 100	very small chance of pelvic infection when IUD put in	<ul style="list-style-type: none"> can stay in place for 3 years or more fit and forget doesn't interfere with sexual intercourse progestogen-releasing IUDs – lighter periods or no period at all, suitable for those with heavy periods 	<ul style="list-style-type: none"> needs to be inserted by an experienced doctor or nurse Copper IUDs may cause heavier periods or cramping Progestogen-releasing IUDs may cause irregular bleeding in the first few months
HORMONAL CONTRACEPTION					
DEPO PROVERA Depo Provera is a long-acting injection of progestogen. It is given every 12 weeks.	<ul style="list-style-type: none"> an injection of progestogen stops ovaries from releasing an egg each month 	typically 3 in 100 but less than 1 in 100 if next injection given on time	no serious concerns	<ul style="list-style-type: none"> one injection lasts 12 weeks doesn't interfere with sexual intercourse usually no periods useful for people who can't take combined pill 	<ul style="list-style-type: none"> irregular bleeding, no periods or occasional heavy bleeding periods and fertility take an average of 6 months to return after stopping the injection weight may change
COMBINED ORAL CONTRACEPTIVE PILL A combined oral contraceptive pill (COC) contains both oestrogen and progestogen. It is taken daily to prevent ovulation and change the way the body reacts to sperm.	<ul style="list-style-type: none"> pill made of 2 hormones, oestrogen and progestogen stops ovaries releasing an egg each month 	typically 8 in 100 but less than 1 in 100 if used perfectly	very small chance of blood clots, heart attacks and strokes. More likely in people over 35 who smoke, are overweight or have a family history of these conditions	<ul style="list-style-type: none"> simple and easy to take doesn't interfere with sexual intercourse periods usually regular, shorter, lighter and less painful less chance of cancer of lining of the uterus or ovaries can be taken up to menopause if a healthy non-smoker 	<ul style="list-style-type: none"> should not be used by people over 35 who smoke must remember to take it daily may have irregular bleeding
PROGESTOGEN ONLY PILL A progestogen-only pill (POP) contains only progestogen. It is taken daily to prevent ovulation and change the way the body reacts to sperm.	<ul style="list-style-type: none"> pill made of 1 hormone – progestogen by thickening mucus in cervix and may stop ovaries from releasing an egg each month 	typically 8 in 100 but less than 1 in 100 if used perfectly	no serious risk	<ul style="list-style-type: none"> doesn't interfere with sexual intercourse can be used at any age can be used when breast-feeding useful for those who can't take combined pill 	<ul style="list-style-type: none"> may have irregular bleeding
BARRIERS					
EXTERNAL CONDOM An external condom is a thin latex barrier that fits over the erect penis to catch sperm during ejaculation.	<ul style="list-style-type: none"> a thin rubber barrier fits over erect penis and catches sperm on ejaculation best used with water-based lubricant 	typically 15 in 100 but 2 in 100 if used perfectly every time	none known	<ul style="list-style-type: none"> easy to use and carry used only when needed helps protect against STIs available from Family Planning clinics and other health care providers can buy from pubs, clubs, pharmacies and many shops cheaper on prescription 	<ul style="list-style-type: none"> some people are allergic to rubber must be put on when penis is erect and before sexual intercourse some people say it reduces sexual feeling can slip off or break
INTERNAL CONDOM An internal condom is a thin polyurethane barrier that goes into the vagina to catch sperm during ejaculation.	<ul style="list-style-type: none"> a thin polyurethane barrier goes into the vagina and catches sperm on ejaculation 	typically 21 per 100 but 5 per 100 if used perfectly	none known	<ul style="list-style-type: none"> helps protect against STIs gives user choice and control easy to use 	<ul style="list-style-type: none"> relatively expensive can only buy them online need to insert every time
FERTILITY AWARENESS					
FERTILITY AWARENESS Fertility awareness involves tracking body temperature and cervical mucus to predict when ovulation occurs. This allows for sexual intercourse outside the fertile window.	<ul style="list-style-type: none"> body temperature, cervical mucus and periods checked. These body signs show when you are more likely to get pregnant 	typically 25 per 100 but can be 3 per 100 if used perfectly	none	<ul style="list-style-type: none"> after learning method, no further costs or visits to health professionals required helps you understand how your body works 	<ul style="list-style-type: none"> expert instruction needed to learn method no sexual intercourse during fertile time must chart temperature and cervical mucus daily body signs can be difficult to recognise and may vary
EMERGENCY CONTRACEPTION					
EMERGENCY CONTRACEPTION Emergency Contraception (ECP) is a combination of progestogen and copper IUD. It is used after unprotected sex to delay ovulation or stop sperm reaching an egg.	<ul style="list-style-type: none"> Emergency Contraceptive Pill (ECP) or copper IUD used after unprotected sexual intercourse delays ovulation or stops sperm reaching an egg 	<ul style="list-style-type: none"> ECP – 2 per 100 for those of average weight, may be higher if heavier IUD – less than 1 per 100 	<ul style="list-style-type: none"> ECP – none known IUD – risk of pelvic infection if user has STI 	<ul style="list-style-type: none"> reduces chance of pregnancy after unprotected sexual intercourse ECP – can be used up to 72 hours after unprotected sexual intercourse can get ECP for future use can be used if other method fails, eg. broken condom or missed pill can buy from pharmacies 	<ul style="list-style-type: none"> ECP should be taken within 72 hours of unprotected sexual intercourse double dose needed for those who are heavier. Failure rate may be higher IUD needs to be fitted by an experienced doctor or nurse and can be uncomfortable
PERMANENT CONTRACEPTION					
VASECTOMY & TUBAL LIGATION Vasectomy is a surgical procedure where the tubes carrying sperm from the testicles are cut. Tubal ligation is a surgical procedure where the fallopian tubes are sealed or tied off to prevent eggs from reaching the uterus.	<ul style="list-style-type: none"> permanent contraception an operation vasectomy – tubes cut to stop the sperm getting to the penis tubal ligation – clips put on tubes to stop the egg getting to the uterus 	less than 1 per 100	<ul style="list-style-type: none"> vasectomy – rare possibility of long-term scrotal pain tubal ligation – very slight risk from reaction to anaesthetic or damage to internal organs 	<ul style="list-style-type: none"> one operation only permanent 	<ul style="list-style-type: none"> not easily reversible requires an operation may have short term side effects, eg. pain, bruising

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Contraception in Women with Medical Conditions

Risk/Benefit Analysis

WHO lists conditions where pregnancy may exacerbate the risk to a woman's health. The following guidelines allow us to determine the safest contraceptive methods, given a woman's underlying conditions.

Table 1: Recommendations regarding the likely benefits and risks of different contraceptive options. Adapted from the World Health Organization, Centers for Disease Control and Prevention and Faculty of Sexual and Reproductive Healthcare.^{4,14,15}

Patient characteristics	Oral contraceptives		Depot medroxyprogesterone acetate injections (DMPA)	Levonorgestrel implant	IUDs	
	Combined oral contraceptives (COCs)	Progestogen-only oral contraceptives (POPs)			Levonorgestrel	Copper
Younger (e.g. < 18 years) or nulliparous			a			
Aged ≥ 50 years or over ⁶	b		b			
Taking hepatic-enzyme inducing medicines, e.g. some anticonvulsants						
At increased risk of venous thromboembolism (VTE)	c					
With, or at increased risk of, cerebro- or cardiovascular diseases						
Hypertension			d			
Smoking in patients aged over 35 years	e					
Valvular heart disease or atrial fibrillation						
Stroke or ischaemic heart disease						
Vascular disease						
With multiple cardiovascular risk factors						
With diabetes and complications, or diabetes for > 20 years						
Migraine with aura						
Post-partum						
Immediately						
< 4 weeks	g				f	f
4 - 6 weeks	g					
> 6 weeks						
Following termination of pregnancy or spontaneous abortion			i	i	h	h
Current or previous breast cancer			i	i	i	i

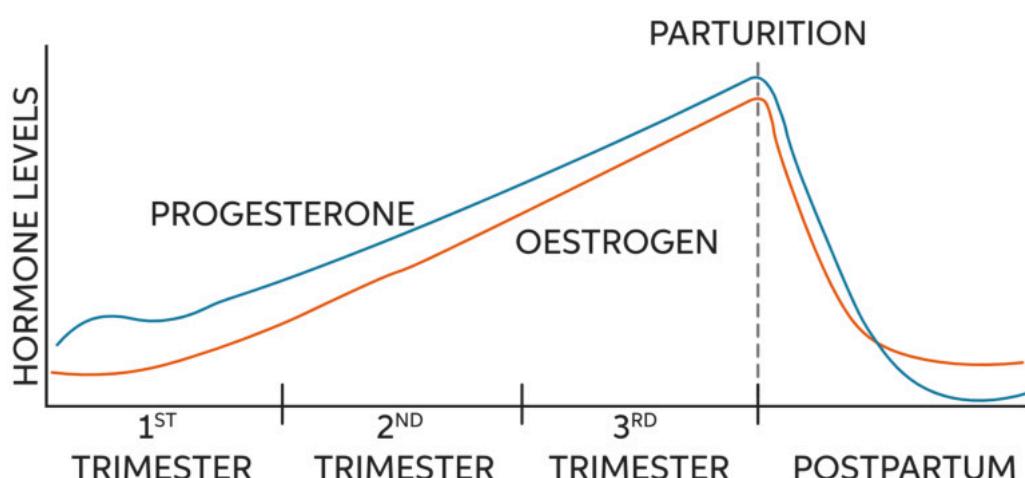
Benefits are likely to outweigh risks Risks may outweigh benefits for some patients, see footnotes for details Not recommended, risks are likely to outweigh benefits



Estrogen Containing Contraceptives and Pregnancy: A Big No No

During menstruation, estrogen and progesterone are at the lowest. During and following ovulation they reach new highs. This high consistently grows and is maintained during pregnancy and levels drop then subsequently drop following postpartum.

Low levels of estrogen during menstruation serve to aid in decreased coagulability, high levels during pregnancy aid in the growth of the breast tissue and following postpartum, low levels help in the production of breast milk. This is why oral contraceptives containing estrogen are contraindicated during breastfeeding.



HORMONAL CONTRACEPTION IN WOMEN WITH MEDICAL CONDITIONS		
Condition	Contraindication	Recommendation
Migraines	<p>Migraines with aura + estrogen-containing contraceptives increase risk of stroke</p> <ul style="list-style-type: none"> Estrogen is associated with increased LDL and clotting risk. <p><i>A note on migraine without aura</i></p> <ul style="list-style-type: none"> If migraines occur without aura and are related to estrogen fluctuations in menses: use continuous COC or extended cycle treatment (may also control hormonal fluctuations & migraines) If migraines start to occur (even without aura) after usage of COC, cease! <p><i>Overall risk</i></p> <ul style="list-style-type: none"> Caution: use of hormonal contraception in those with migraines without aura Not recommended: use of hormonal contraception in women > 35 years + smoking Contraindication: hormonal contraception use in those with migraines with aura 	<ol style="list-style-type: none"> 1. Progestin Only 2. IUD 3. Barrier Methods
Obesity	<p>Obesity + Age + COC are independent risk factors for VTE</p> <p>Additionally, COCs and transdermal patches may be less effective in obese women</p>	<ol style="list-style-type: none"> 1. Progestin Only 2. Injection, Implant, IUD (if obese + >35) 3. Barrier Methods 4. Vasectomy
Drug Interactions	<p><i>Anti-Epileptics (e.g. Carbamazepine, phenobarbital, phenytoin, primidone, topiramate)</i></p> <ul style="list-style-type: none"> Hepatic enzyme inducers which decrease contraceptive blood levels of estrogen and progestin and thereby reduces contraceptive effectiveness of: COC, patch, POP, implant. Anti-epileptics may also cause birth defects OCs have been shown to increase drug levels of lamotrigine; with problems occurring during pill-free phases or when starting/stopping OCs <p><i>Antibiotics</i></p> <ul style="list-style-type: none"> Most antibiotics do not interact with oral contraceptives as long as they are taking their contraceptive consistently and correctly. Rifampin, rifabutin and tetracycline are the exception. Also monitor for diarrhoea and vomiting. <p><i>Herbal Medications (e.g. St John's Wort)</i></p> <ul style="list-style-type: none"> Can affect OC metabolism <p><i>Anti-Virals (e.g. HIV Drugs)</i></p> <ul style="list-style-type: none"> Various antiviral agents (for treatment of HIV) can have different hepatic enzyme effects (being substrates, inducers, or inhibitors), therefore contraceptive methods that bypass the potential for drug interactions are recommended, ie., IUDs <p><i>Anti-Coagulants (e.g. Warfarin)</i></p> <ul style="list-style-type: none"> COC's increase risk of blood clots — anticoagulant dosing may need to be adjusted. 	<ol style="list-style-type: none"> 1. DMPA 2. IUD (copper or levonorgestrel) 3. Take higher dose of OC 4. Have a 4 day pill break instead of 7 (to ensure hormone concentrations in blood)

Oral Contraception

Overview of Oral Contraceptives

Introduction to Oral Contraceptives

Oral contraceptives (COC, POP, ECP) are the most commonly used method of birth control. They are available in various doses and cycle combinations of female hormones estrogen and progestin, which are produced naturally in the ovaries.

Selecting a Pill — [BPAC Oral Contraceptives Selection Guide](#)

The choice of oral contraceptive is influenced by the patients' specific needs (contraceptive or non-contraceptive benefits), preferences, and presenting co-morbidities (see risk-benefit analysis table)

Things to consider:

1. Can the woman take estrogen?
2. What is the lowest dose she can be given?
3. Any clinical concerns? (e.g. hirsutism/acne: desogestrel, drospirenone, or cyproterone)

Early Danger Signs of OCs — ACHEs

SIGN	DIFFERENTIAL DIAGNOSIS
Abdominal pain (severe)	Gallbladder disease, pancreatitis, hepatic adenoma, thrombosis, ectopic pregnancy
Chest pain (severe), SOB	Pulmonary embolus, MI
Headaches (severe)	Stroke, HTN, migraine
Eye problems (blurred vision, flashing lights, blindness)	Stroke, HTN, vascular insufficiency
Severe leg pain (calf or thigh)	DVT

Supplying Oral Contraceptives

1. PHARMACIST'S SUPPLY OF "SELECTED ORAL CONTRACEPTIVES"

Accredited pharmacists can sell up to 6 months (**unfunded**) OC supply to a patient given that: (see [PSNZ Requirements for SOC's](#))

1. They have been prescribed the same OC within the last **3 years** from the date of an original prescription (by an NZ or overseas prescriber)
2. Have not developed risk factors
3. It is for **contraception** indication only
- 4. They are aged 16 - 39 (COC) or 16 - 52 (POP)**

Pharmacists *cannot swap* between OCs unless:

1. Formulation is not available in NZ for overseas women
2. Previous OC user is wanting postpartum contraception and is breastfeeding (supply a **short course of POP** i.e. one original pack of up to 3 months supply, to give time for patient to seek medical practitioner)

COC	POP
<i>Ava, Microgynon, Levlen</i> 1. Ethinylestradiol (\leq 35mcg) + Levonorgestrel	
<i>Brevinor, Norimin</i> 2. Ethinylestradiol (\leq 35mcg) + Norethisterone	1. Levonorgestrel (<i>Microlut</i>) 2. Norethisterone (<i>Noriday</i>) 3. Desogestrel (<i>Cerazette</i>)
<i>Ginet</i> 3. Ethinylestradiol (35mcg) + Cyproterone acetate	

2. EMERGENCY SUPPLY OF ORAL CONTRACEPTIVES

Pharmacists (accreditation not needed) can supply oral contraceptives given that:

1. Previously prescribed by NZ prescriber in last 3 months
- 2. 72h supply or minimum pack size (1 month/28 tabs)**
3. Pharmacist satisfied that person requires emergency supply
4. Record sale electronically and advise prescriber ASAP

See Medicines Regulation S.44(m): Emergency Supply

3. EMERGENCY CONTRACEPTIVE (ECP)

There are two types of emergency contraception that exist in NZ

1. ECP (Postinor-1) to a patient up to 72 hours after unprotected sex. See [Best Practice PSNZ Guidelines](#) for its supply
 - Accredited pharmacists can supply this (must be directly to the woman)
 - Check BMI and weight: 1 tablet if < 70 kg or < 26 kg/m² (**maximum 2 tablets funded**)
 - Go through ECP checklist e.g. check drug interactions, counsel on side effects e.g. lighter next period, unusual bleeding, abdominal pain
 - Record of the supply of the ECP as a dispensed medicine
2. Refer for Copper IUD
 - Note: Hormonal IUD (Mirena) is **not suitable as emergency contraception**

ORAL HORMONAL CONTRACEPTION SUMMARY			
	COC	POP	ECP
Description	Available in various dose combinations of estrogen and progestin	Contains only progestin	Contains only progestin (levonorgestrel)
Pharmacist Supply	<ul style="list-style-type: none"> Requires accreditation, unfunded Pharmacist's supply: 6 months Emergency Supply: 1 pack (28 tabs) 	<ul style="list-style-type: none"> Requires accreditation, unfunded Pharmacist's supply: 6 months Emergency Supply: 1 pack (28 tabs) 	Requires accreditation but funded <ul style="list-style-type: none"> Max 2 tablets funded
Disadvantage	<ul style="list-style-type: none"> Daily dosage, expensive, many side effects Reversible and can be used throughout the woman's reproductive lifespan. 	<ul style="list-style-type: none"> Daily dosage, expensive, many side effects, stricter adherence needs, less effective Reversible and can be used throughout the woman's reproductive lifespan. 	<ul style="list-style-type: none"> Time limit within which it must be taken after unprotected sex/contraceptive failure: <ul style="list-style-type: none"> Postinor: up to 72 h Copper-IUD: 5 days Postinor delays ovulation (increased pregnancy risk) Copper IUD must be fitted by an expert and causes heavier/painful periods
Effectiveness	More effective <ul style="list-style-type: none"> 99.9% theoretically 97-98% with perfect taking 91% or less in reality 	Less effective due to fewer mechanisms <ul style="list-style-type: none"> 99% theoretically 96-97.5% with perfect taking (Jadelle) Not for the forgetful! 	<ul style="list-style-type: none"> Most effective if taken within first 24 h for Postinor
Mechanism of Action	<ol style="list-style-type: none"> Suppresses ovulation Makes mucus hostile to sperm Keeps endometrium thin 	<ol style="list-style-type: none"> Some form of ovulation suppression Makes mucus hostile to sperm Keeps endometrium thin 	<ol style="list-style-type: none"> Postinor delays ovulation Copper IUD interferes with sperm motility
Regimen	<ol style="list-style-type: none"> Traditional (sugar pills) Continuous (no sugar pills) methods 	No sugar pills	<ol style="list-style-type: none"> Postinor-1 (Levonorgestrel) Copper IUD
Indication	First choice oral contraceptive due to less stricter adherence requirements, efficacy and additional non-contraceptive benefits	Given to women with contraindications to estrogen (e.g. POP can be given anytime during breastfeeding but COC cannot)	Given to women who have had unprotected sex/contraceptive failure. Copper IUD also provides future contraception and is not affected by weight.
Contra-indications/ Cautions	COCs should not be used in patients with: <ol style="list-style-type: none"> Risk factors for VTEs, CVD Older women > 50 Women > 35 + smoking > 15 cigarettes Breastfeeding women (estrogen decreases prolactin) Breast Cancer (as hormonal cancer) 	POPs should not be used in patients with: <ol style="list-style-type: none"> Unexplained vaginal bleeding Severe liver disease (e.g. decompensated cirrhosis) Breast cancer 	ECP should not be used if: <ol style="list-style-type: none"> Possibility of an existing pregnancy Family history of CVD, Endometrial cancer Live Tumor
Side Effects	Breast tenderness, breakthrough bleeding, nausea, mood changes, etc...	Unpredictable bleeding patterns due to variable suppressions of ovulation	Menstrual irregularities after taking
Missed Pills	Pills are considered missed if they are past the 12 hour window and didn't have 7 days of consecutive pill taking leading up to it. <i>Window</i> <ul style="list-style-type: none"> 12 hour 7 day rule <ul style="list-style-type: none"> 7 consecutive hormone pills protects you for next 7 days 	Pills are considered missed if they are past the 3 hour window (12 for cezarette) and didn't have 2 days of consecutive pill taking leading up to it (7 for cezarette) <i>Window</i> <ul style="list-style-type: none"> 3 hours (12h for cezarette) 2 day rule (7 days for cezarette) <ul style="list-style-type: none"> 2 consecutive hormone pills protects you for the next 24 hours. 	-
	ECP <ul style="list-style-type: none"> ECP should be considered if unprotected sex occurred in the absence of the 7 day rule. 	ECP <ul style="list-style-type: none"> ECP should be considered if unprotected sex occurred in the absence of the 2 day rule. 	<ul style="list-style-type: none"> Must be taken within 72 hours (Postinor) or 5 days (Copper IUD) of unprotected sex
	<ol style="list-style-type: none"> If vomiting occurs within 2 hours of taking pill, another pill should be taken ASAP Diarrhoea alone without vomiting has to be severe enough to reduce the absorption of the pill. 	If vomiting or diarrhoea is persistent, i.e. lasting more than 24 hours, an additional contraceptive method should be used during the illness and until: <ul style="list-style-type: none"> 7 consecutive hormone pills have been taken if using COCs (protected for next 7 days) 2 consecutive hormone pills have been taken if using POPs (lasts 24 hours) Seven consecutive hormone pills have been taken if using Cerazette 	
Vomiting & Diarrhoea			

Combined Oral Contraception (COC)

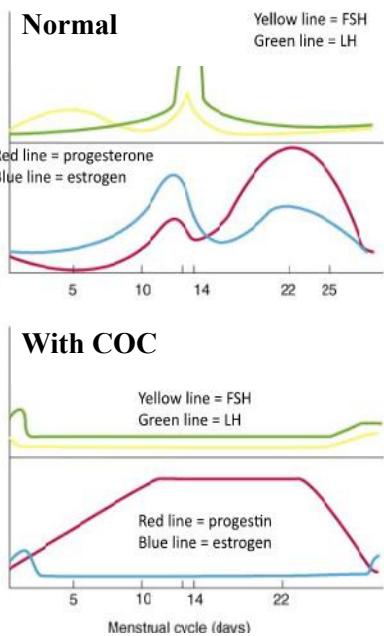
Description

The COC contains artificial versions of both hormones. It is the first line oral contraceptive choice as it requires less strict adherence to regular dosing times than POPs, and provides additional non-contraceptive benefits. However, the estrogen component stimulates hepatic production of clotting factors. Thus, where estrogen is contraindicated, progesterone containing methods should be considered.

Mechanism of Action

Deception is the mechanism of hormonal contraceptives —here there is a full suppression of ovulation.

1. Continuous high levels of estrogen & progesterone are associated with pregnancy
2. As the hypothalamus reads oral hormonal contraceptives as pregnancy, it suppresses ovulation to prevent another one.



Estrogen

Inhibits the secretion of FSH via **negative feedback** on the anterior pituitary to block *the development of the ovarian follicle*.

Progesterone

Inhibits the secretion of LH and *thus prevents ovulation*.
Makes the cervical mucus *less suitable for the passage of sperm*

Estrogen & Progesterone

Act together to alter the endometrium (keeps it thin) *to discourage implantation*.

Side Effects

Adverse Effects Associated With Type of Hormonal Activity		
Estrogenic	Progestational	Androgenic
<ul style="list-style-type: none">• N&V, Bloating, Breast Fullness• Breakthrough Bleeding• Decreased libido• Irritability, Headache, HTN• Cervical ectropion• Thrombophlebitis	<ul style="list-style-type: none">• Headache• Breast Pain/Tenderness• HTN	<ul style="list-style-type: none">• Acne/Oily Skin• Weight Gain• Hirsutism• Fatigue• Depression

Solutions to Side Effects

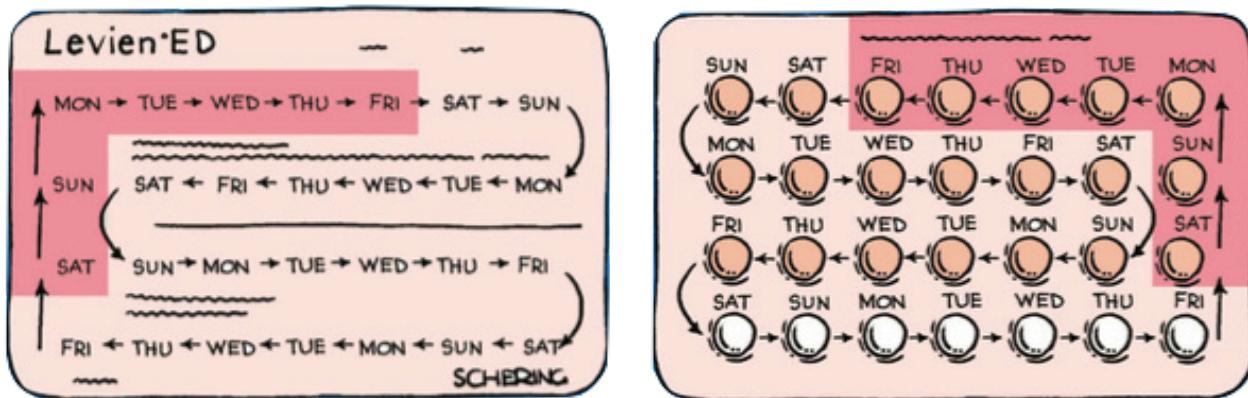
Managing Adverse Effects Associated with COCs	
Adverse Effect	Suggested Action
Acne <i>Note: POPs & IUDs worsen acne</i>	1. ↑ Estrogen and/or 2. ↓ Progestogen or 3. Select a less androgenic or anti-androgenic progestogen (e.g. desogestrel, drospirenone, or cyproterone)
Bloating/Fluid Retention	1. ↓ Estrogen and/or 2. Change to a progestogen with a mild diuretic effect (e.g. drospirenone)
Breakthrough Bleeding	1. ↑ Estrogen and/or 2. Change progestogen type (e.g. levonorgestrel or desogestrel) 3. Smoking Cessation
Breast Tenderness	1. ↓ Estrogen and/or 2. ↓ Progestogen and/or 3. Change progestogen (e.g. levonorgestrel)
Headache	1. ↓ Estrogen and/or 2. Change progestogen (e.g. levonorgestrel) 3. If headaches occur in hormone free interval, consider an extended/continuous regimen
Abdominal Cramping or Heavy Bleeding during Hormone Free Interval	1. Extended or Continuous regimen
Nausea	1. ↓ Estrogen and/or 2. Take the pill at night 3. Change to POP
Weight Gain	No longer a concern

Contraindications & Cautions

Cautions & Contraindications to COCs (Health Risks)	
Avoid use of COC in women > 35 years old + smoke > 15 cigarettes — this is a risk factors for the below:	
Health Risk	Description
Myocardial Infarction	<ul style="list-style-type: none"> Risk of MI/ischaemic stroke with COC is very low Risk increases with CVD risk factors (age, smoking, diabetes, HTN, migraines, obesity, family history <50y)
Ischaemic Stroke	<ul style="list-style-type: none"> COCs not recommended in aged ≥ 50 years (or > 40) due to the risks (e.g. CV events) $>$ benefits. If it must be given, older patients (>40 years) should be given a lower estrogen dose.
Venous Thromboembolism (VTE)	<ul style="list-style-type: none"> Risk of VTE without COC: 2 in 10,000 Risk of VTE with COC: 12 in 10,000 <ul style="list-style-type: none"> COC use is contraindicated/cautioned if risk factors for VTE (e.g. surgery, prolonged immobility, < 3 weeks postpartum, women > 35 + smoking > 15 cigarettes, history of VTEs) Risk of VTE during pregnancy/postpartum: >20 in 10,000 (highest risk) <ul style="list-style-type: none"> COCs can be started from 6 weeks (breastfeeding) or 3 weeks (not breastfeeding) postpartum POPs can be initiated at any time during breastfeeding
Breast Cancer	<ul style="list-style-type: none"> COCs are associated with a increased or reduced risk of cancers <ul style="list-style-type: none"> Increased risk of: breast and cervical cancers — do not give hormonal contraception (including POP) Decreased risk of: endometrial, ovarian and colorectal cancers
Mood Changes	<ul style="list-style-type: none"> This is possible with long term use of COC. Caution of increasing risk for depression & anxiety.

Regimens

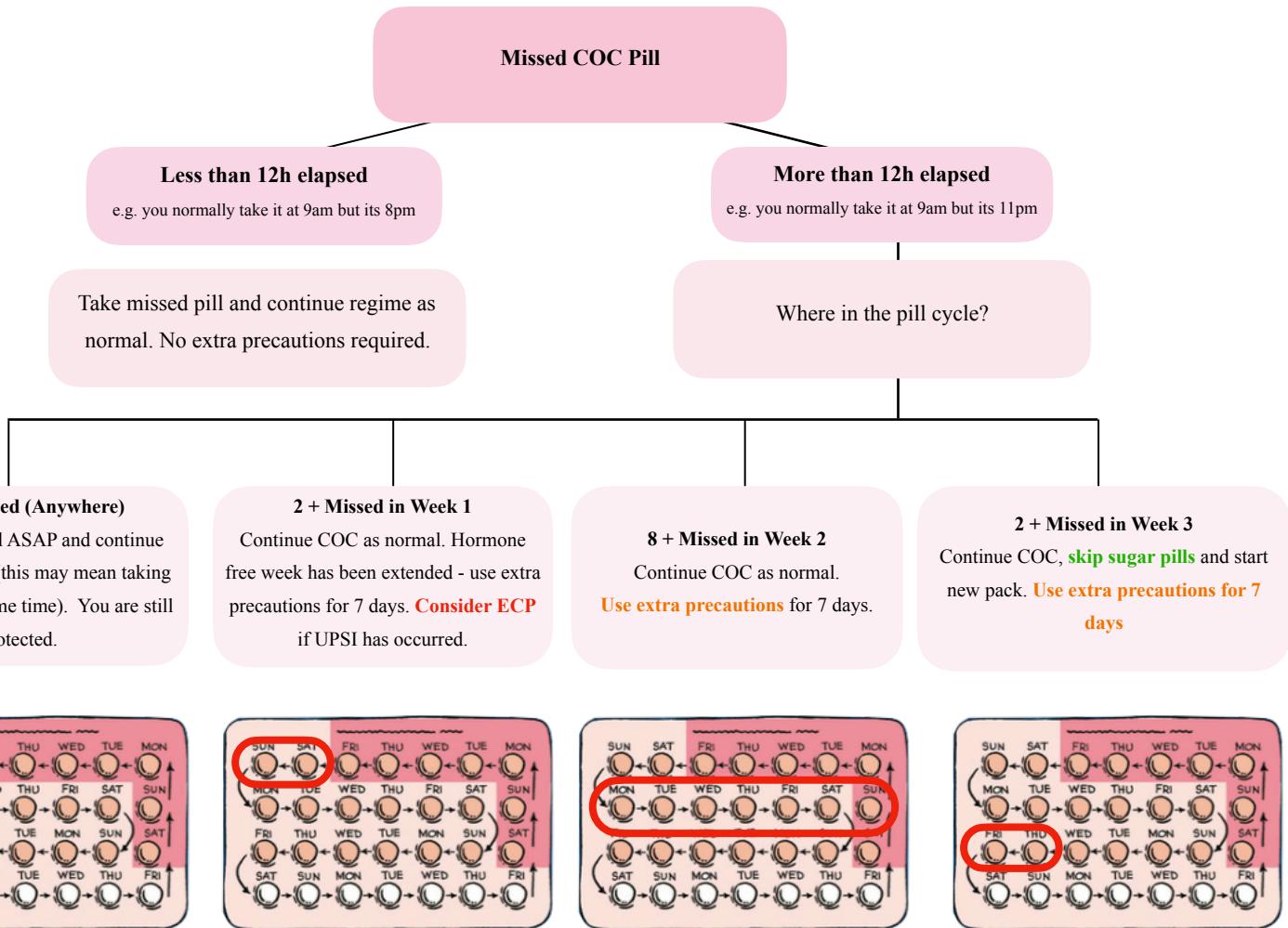
COC pills are organised in the following way — they consist of 21 active hormonal (coloured) pills and 7 hormone free/sugar pills (white). These can be started anytime and the user will have protection after taking one pill OD at the same time everyday for 7 days a row (starting on the day corresponding to the packet). However, starting **within 5 days** from the start of your period provides immediate protection.



TYPES OF COC REGIMENS			
Regimen	Duration of Hormone Pills (Days)	Duration of Hormone Free Pills (Days)	Reason
Standard	21	7	The purpose of hormone free intervals is to allow a withdrawal bleed at the end of the month (28 days) in order to confirm you are not pregnant.
Shortened	21	4	This method is useful if patient is on certain hepatic enzyme inducers that have an interaction with the pill. A shorter pill break or higher OC dose can counter-interact such interactions.
Extended	63 or 84 every 3 or 4 packets of pills	4-7 every 3 or 4 packets of pills	Patient may choose to have a period every other month.
Continuous	30	None	<p>This is the ideal method as withdrawal bleeds are not medically necessary. A continuous regimen decreases chance of contraceptive failure (missed pills) and avoids ADRs associated with the hormone free interval (e.g. pain, bloating, headaches, etc...) due to eliminated hormonal fluctuations.</p> <ul style="list-style-type: none"> If pack contains sugar pills, stop at day 21 and start a new pack. Note: increased risk of breakthrough bleeding but this decreases with time.

Missed COC Pills

One of the disadvantages of using oral contraceptives is that their efficacy relies on good and prompt adherence. It is thus important to have a good understanding of what happens when pills are missed and when is a person not protected. A COC pill is considered missed if it was taken past the **12 hour window**. Missed doses may cause spotting, bleeding, vomiting, diarrhoea (due to fluctuating hormone levels)



Note: please ignore the weekdays listed in the pack photos and assume that 1 row = 1 week.



MISSING COC PILLS GUIDELINES

The 7 day rule states 7 days of coverage minimum are required for you to be protected (for the next 7 days)

This means if you have taken 7 days of consecutive active pill taking, you may miss up to 8 pills before extra precautions are required for 7 days.

Hour	Week	Missed Doses	Traditional (21 Active + 7 Sugar)	Continuous (No Sugar Pills)
< 12 hours	Any	1	If it's been less than 12 hours since your missed dose: Missing one dose anywhere in the pack within 12 hours of your normal taking time is alright. Continue the pack as normal, you are still protected — this may mean taking two hormone pills at the same time (to continue the seven day rule) Side effect: If you miss 1 or more pills, you may get spotting or bleeding	
			If it's been more than 12 hours since your missed dose: <i>If you've missed 1 pill anywhere in the cycle</i> <ul style="list-style-type: none"> It's okay just continue and take it as soon as possible. You are still protected. Side effect: If you miss 1 or more pills, you may get spotting or bleeding	In this method, you are only contraceptively compromised if you miss more than 8 pills in a row.
	Week 1	2	If it's been more than 12 hours since your missed dose: <i>If you miss 2+ pills in Week 1</i> The hormone free week is extended and/or the seven day rule has not yet been met — there is a risk of ovulation after about 8 or 9 days <ul style="list-style-type: none"> Take dose as soon as you remember and continue pack as normal Use a back up birth control method (e.g. condom) for 7 days until you are protected again. Consider the ECP if you have had unprotected sex in the 7 days leading to the missed pills (hormone free interval or week 1) Side effect: If you miss 2 or more pills, you may get diarrhoea or vomiting	If person misses pill, seven active hormone pills must be taken correctly after the missed pills to restore contraceptive protection.
			If it's been more than 12 hours since your missed dose: <i>If you miss 8+ pills in Week 2</i> Missing pills in Week 2 requires no additional precautions as long as the person was correctly taking active pills for 7 days — until the number of missed pills exceeds 8. <ul style="list-style-type: none"> Continue COC till end of pack as normal Use precautions for 7 days (consider ECP if UPSI occurs while you are catching up on the 7 day rule in Week 3) Side effect: If you miss 8 or more pills, you may get diarrhoea or vomiting	If person misses pill but before that they took correctly/consistently an active pill for at least 7 days in a row prior to missing — its okay for them to miss up to 8 pills before additional contraceptive precautions (e.g. condoms or abstinence) are required for the next 7 consecutive days of active pill taking. However if person missed pill but before that didn't take correctly/consistently an active pill for at least 7 days in a row prior to missing, they must now use extra precautions for 7 days. ECP should be considered if unprotected sex was had during this time.
	Week 3	2	If it's been more than 12 hours since your missed dose: <i>If you miss 2+ pills in Week 3</i> <ul style="list-style-type: none"> Continue COC Skip sugar pills and go straight to next pack without a break Use precautions for 7 days. (consider ECP if UPSI occurs while you are catching up on the 7 day rule in Week 3 and Week 1 of the next pack) Side effect: If you miss 2 or more pills, you may get diarrhoea or vomiting	



Note

Missed pills here indicate pills that have been blatantly missed i.e have yet to be resolved. For example 1 missed pill anywhere in the pack can be resolved simply by taking it ASAP (which means potentially 2 doses at the same time)

Products Available

These are the formulations available in NZ. All COCs contain the same estrogen (ethinylestradiol) in varying doses, along with different progestogens. The progestogens vary in their androgenic properties;

- Norethisterone & levonorgestrel are more androgenic than desogestrel
- Drosiprenone & cyproterone are anti-androgenic (effective for acne)

Selection of COCs — Trial & Error

- A reasonable choice for a first-time COC-user is a formulation containing ≤ 35 micrograms ethinylestradiol + either **levonorgestrel** or **norethisterone**.
- If a patient experiences adverse effects with one COC, another formulation may be trialed.

COMBINED ORAL CONTRACEPTIVE FORMULATIONS AVAILABLE IN NZ		
Estrogen (Ethinylestradiol) Dose	Progesterone (Progestogen/Progestin) Dose	Brand Name
20 micrograms	Levonorgestrel 100 micrograms	Microgynon 20 ● Loette Femme-Tab ED ●
	Desogestrel 150 micrograms	Mercilon 28 ○
	Drosiprenone 3mg	Yaz
30 micrograms	Levonorgestrel 150 micrograms	Levlen ED ● Ava 30 Microgynon 30 ○ † Microgynon 30 (ED) Monofeme Femme-Tab ED ●
	Desogestrel 150 micrograms	Marvelon ○
	Drosiprenone 3mg	Yasmin
35 micrograms	Norethisterone 500 micrograms	Brevinor ● † Norimin ●
	Norethisterone 1 mg	Brevinor-1 21 day ○ † Brevinor-1 28 day ED ●
	Cyproterone 2mg	Estelle-35 † Estelle-35 (ED) Ginet 35 ● Diane-35 (ED)
50 micrograms	Levonorgestrel 120 micrograms	Microgynon 50 (ED) ●

● Partially Subsidised ○ Fully Subsidised † - Formulation without placebo pills
 (ED) = Everyday formulation, includes placebo pills. Not all ED formulations have ED in their brand names.

COC		
Ethinylestradiol + Levonorgestrel	Ethinylestradiol + Norethisterone	Ethinylestradiol + Cyproterone acetate
<p>Levlen</p> 	<p>Brevinor</p> 	
<p>Microgynon</p> 	<p>NORIMIN® 28 Day</p> 	<p>Ginet</p> 

Progesterone Only Pill (POP)

Description

Progestogen-only formulations are a suitable alternative for those who wish to use an oral contraceptive but prefer not to use a COC or contraindications to estrogen use e.g. breastfeeding/postpartum, any risk of CVD and so forth.

Mechanism of Action

Progesterone only pills work by primarily increasing the viscosity of cervical mucus so that sperm can't travel through it. Following unprotected sex, sperm die within hours if they cannot get out of the acid vagina via fertile mucus.

As the POP pill has fewer mechanisms than the COC, it is less effective but it is safer than the COC in older women, smokers, breastfeeding, CV risk factors, diabetes, lipid disorders, estrogen-related SE (e.g. blood clots), migraine headaches, postpartum. However, **compliance** is an ultimate factor which determines the suitability of the pill. The POP's effect only lasts for 24 hours so the pill must be taken within 3 hours of the usual time each day. However, as Cerazette has additional effects of stopping egg development each month and changing uterus lining to decrease fertilisation rates, it has a 12 hour window.

While they may also prevent ovulation (50% of cycles), it is not comparable to the suppression by COCs - we thus assume that the ovulation is the same as with a normal cycle, i.e. 28 day cycle, ovulating on day 14. The effect on periods can vary. Some women taking the POP continue to have regular normal periods. However, some have irregular periods, some have very infrequent periods and some have no periods at all. Some women also have occasional 'spotting' between periods.

Progesterone

Inhibits the secretion of LH and *thus prevents ovulation (assume normal ovulation as this effect varies)*

Makes the cervical mucus *less suitable for the passage of sperm*

Side Effects

- Menstrual irregularities (due to variable suppression of ovulation), N/V, headache, dizziness, breast discomfort, depression, skin disorders, disturbance of appetite, changes in libido.
- Androgenic: acne/oily skin, weight gain, hirsutism, fatigue, depression

Contraindications

- Unexplained Vaginal Bleeding
- Severe Liver Disease
- Current Breast Cancer

Missed Pills

2 Day Rule

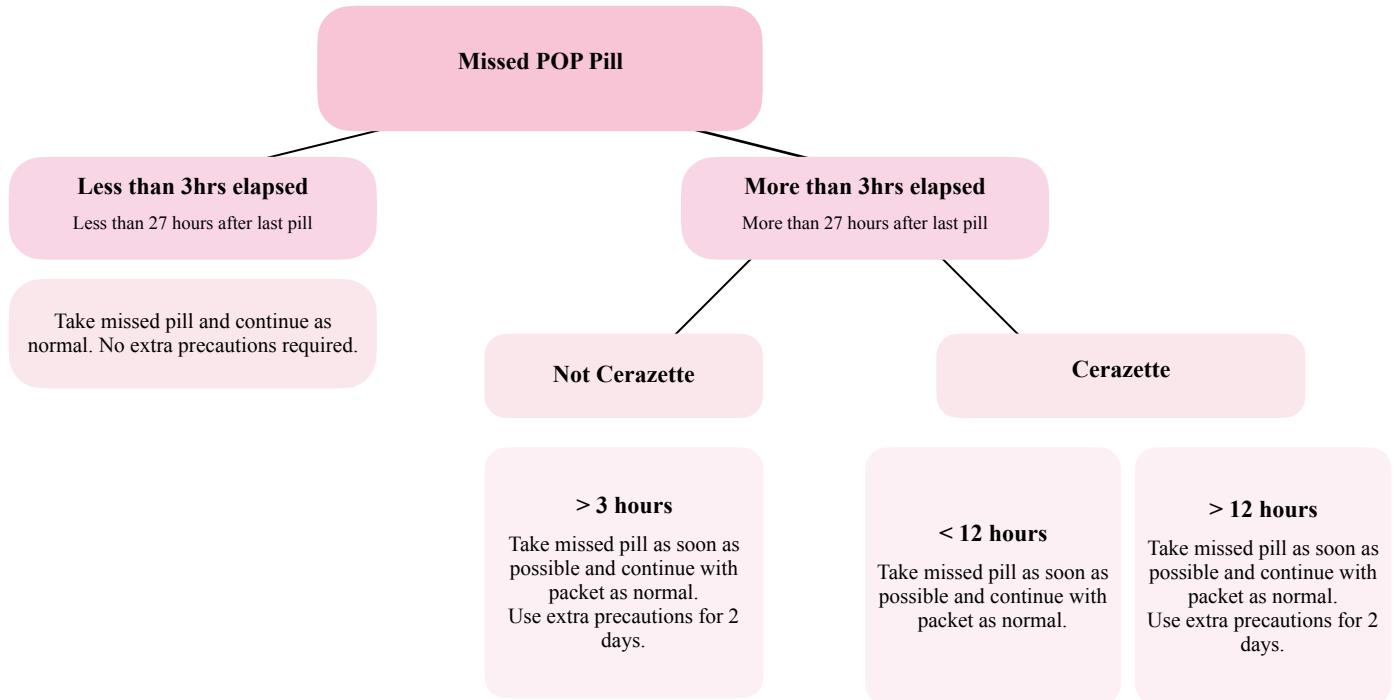
Starting at the start of your period provides instant protection. If starting at another time in your cycle, you will not be protected until you have taken 2 pills (POP)

Not protected from pregnancy if:

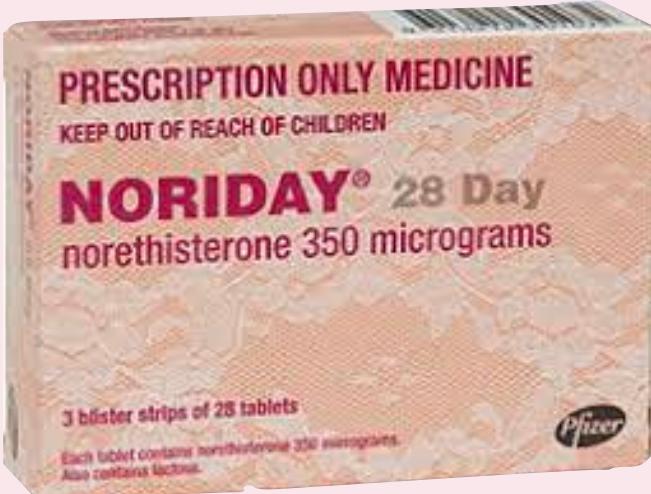
- Missed a pill and took it more than 3 hours after normal time (12 hours for Cerazette)
- Vomiting/Diarrhoea within 2 hours of taking pill or continued vomiting

What to do if this happens:

- Need to abstain or use condoms for next 2 days for traditional POP and 7 days for cerazette
- If unprotected sex has occurred after the missed pill and within 48 hours of restarting the POP, need ECP



Products Available

PROGESTERONE ONLY PILL FORMULATIONS AVAILABLE IN NZ	
Progesterone (Progestogen/Progestin) Dose	Brand Name
Levonorgestrel 30 micrograms	Microlut (3hrs)   <p>— 0.03 mg — 35 tabletas — Oral</p>
Norethisterone 350 micrograms	Noriday 28 (3hrs) 
Desogestrel 75 micrograms	Cezarette (12hrs) 

Emergency Contraceptive Pill (ECP)

PSNZ ECP Guidelines

Description

New Zealand has one of the highest rates of adolescent pregnancies. The emergency contraceptive pill (ECP), also known as the ‘morning after pill’ or ‘Plan B’, is a pill that contains 1.5mg of Levonorgestrel and is taken to prevent a potential pregnancy. It is important to note that many situations can lead to the need for its use:

1. Unprotected sex
2. Contraceptive failure e.g. missed pills



Not an Abortifacient!

The ECP cannot be used to terminate a pregnancy - only prevent one. It is thus important to ensure there isn't a chance the patient could already be pregnant.

Mechanism of Action

The ECP is essentially a higher dose of progesterone - it stops or delays the release of an egg from your ovaries until the sperm aren't active in your body any more. It also prevents the sperm from fertilising an egg by changing the way the sperm moves in your body.

Pharmacological Treatment

The emergency contraceptive pill is not the only form of emergency contraception that exists - in fact three options are available.

1. ECP (pharmacist-only medicine)
2. Copper IUD
3. *Ulipristal (progesterone antagonist) — Not in NZ*

EMERGENCY CONTRACEPTIVE FORMULATIONS		
	Postinor-1 (Levonorgestrel)	Copper IUD
Mechanism of Action	A large dose of levonorgestrel will stop/delay the release of the egg until the sperm is no longer active in the body. Thus the ECP must be taken pre-fertilisation as it is not an abortifacient	Copper ions interfere with sperm motility
	Works up to 4 days post UPSI but only registered up to 72 hours.	Works up to 5 days after UPSI. Can be left in situ for future contraception up to 10 years.
Dosing	1.5mg orally within 72 hours of intercourse Dose is doubled if weight > 70kg or BMI >26	Efficacy is not affected by body mass index or weight. Thus this is the recommended form of ECP in weight > 70kg or BMI >26

Efficacy	<ul style="list-style-type: none"> Efficacy is 98-99%. 85% of expected pregnancies are prevented if taken within the first 24 hours. <p><i>Factors that increase risk of failure</i></p> <ul style="list-style-type: none"> High fertility (UPSI occurred a few days before ovulation or missed COC pills were in the 1st week) Subsequent UPSI in the same cycle??? High BMI/weight Taken post-fertilisation 	<p>Most effective form of ECP (almost 100%).</p> <p><i>Note: Mirena is not a suitable form of ECP (no evidence)</i></p>
Brand Qualities	<ul style="list-style-type: none"> Pharmacist accreditation required Funded brand (without prescription) Pharmacist may charge a consultation fee (<i>see consultation checklist below</i>) 	<ul style="list-style-type: none"> Must be fitted by an expert (e.g. GP, family planning clinic) Funded brand
Contraindications	<ul style="list-style-type: none"> Potential enzyme induction: Carbamazepine, Phenytoin, Topiramate, St John's Wort — double dose or recommended copper IUD 	<ul style="list-style-type: none"> Have uterine abnormalities Have a pelvic infection e.g. PID Have uterine or cervical cancer Unexplained vaginal bleeding
Side Effects	<ul style="list-style-type: none"> May delay next period (menstrual irregularities) N&V Headache, dizziness, breast discomfort. 	<ul style="list-style-type: none"> Uterine or cervical perforation Displacement, expulsion Menorrhagia, intermenstrual bleeding, dysmenorrhoea
Counselling	<ol style="list-style-type: none"> Repeat dose if vomiting occurs within 3 hours of taking ECP. Next period may be early or late; if >5 days late, abnormally light, heavy or brief, take pregnancy test. Pregnancy risk is increased after taking ECP as it can delay ovulation Seek medical attention ASAP if any lower abdominal pain occurs (ectopic pregnancy) Need STI, sexual assault or OC counselling/referral? 	<ol style="list-style-type: none"> Need STI, sexual assault or OC counselling/referral? Seek medical attention ASAP if any lower abdominal pain occurs (ectopic pregnancy)
On Regular OC	Continue contraceptive immediately + 7 days abstinence/barrier (2 days for POP)	

Emergency Supply of the ECP - How to Assess A Patient

There are a few requirements and questions that need to be sorted through in order for the ECP to be provided - the purpose of this is to ensure the suitability of the drug for the woman.

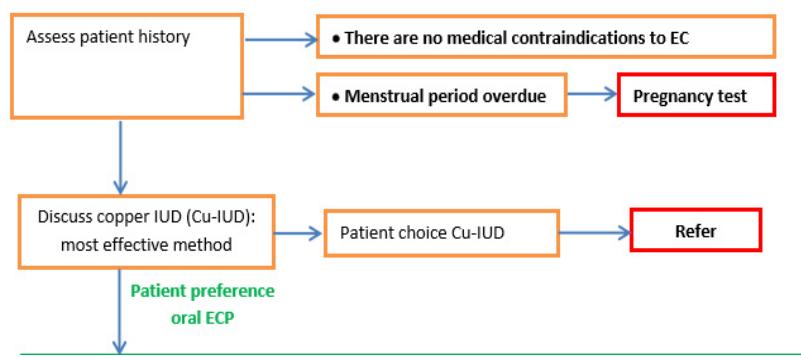
1. Pharmacist must be ECP accredited and go through the consultation form and advice checklist (see next page)
2. Supply is funded (without a prescription): \$5 co-pay + Consultation fee
3. Woman must be seen personally, assessed and directly supplied the pill
4. Sale must be recorded as a pharmacist only medicine
5. Education must be provided regarding the limitations of the pill as an ongoing method of contraception and when to take a pregnancy test.

PHARMAC will fund a **maximum of TWO** tablets per prescription. Please note that pharmacists are **not** prevented by law from supplying the ECP, nor providing contraceptive advice, to people **under the age of 16 years**.

Note: ECP Accredited pharmacists can supply prochlorperazine for nausea associated with the pill

Assessment for ECP

6.



ADVICE CHECKLIST

- THE ECP DOES NOT PREVENT PREGNANCY IN EVERY SITUATION**
 - It is 95% effective if used within 24 hours of unprotected sex.
 - It is 85% effective if used within 25 – 48 hours of unprotected sex.
 - It is 50% effective if used within 49 – 72 hours of unprotected sex.
- TIMING**
 - The ECP is most effective when it is taken as soon as possible and no later than 72 hours after unprotected sex.
- The ECP is unlikely be effective in women who weigh more than 70kg or have a BMI greater than 26. If you weigh more than 70kg or have a BMI greater than 26 a copper IUD would provide more effective emergency contraception. Please see your doctor or family planning clinic.
- POSSIBLE SIDE EFFECTS**
 - Nausea, tiredness, headache, dizziness, breast tenderness, vomiting. These should resolve within a few days.
 - If vomiting occurs within three hours of taking the ECP, another dose should be taken immediately. You will need to obtain another supply of the ECP.
- THE ECP IS FOR EMERGENCY USE ONLY**
 - It is not a substitute for regular contraception.
- USE OF CONTRACEPTION AFTER TAKING THE ECP**
 - Barrier method recommended until your next period starts and regular method of contraception begins.
 - If using the contraceptive pill, keep taking the hormonal pills as normal and use additional barrier protection for seven days.
 - If there are less than seven hormonal pills left in the packet, you should continue with the next pack omitting the seven day break or placebo (sugar) tablets.
- POSSIBLE CHANGE TO TIMING OF NEXT PERIOD**
 - It may be a few days earlier or later than usual.
- SEE YOUR DOCTOR OR FAMILY PLANNING CLINIC**
 - if your next period is unusually light or heavy, more than 5 days late or, for those taking oral contraceptives, there is no bleeding in the pill-free interval.
 - if you have any lower abdominal pain.
- THE ECP DOES NOT PROTECT AGAINST SEXUALLY TRANSMITTED INFECTIONS (STIs)**
 - If you have any concerns, see your doctor or Family Planning Clinic.
- RECOMMEND FOLLOW-UP APPOINTMENT WITH DOCTOR OR FAMILY PLANNING CLINIC**
 - about two to three weeks after taking the ECP to check that it has worked, to screen for STIs (if indicated) and to discuss regular methods of contraception.
- BREASTFEEDING**
 - While the ECP is not considered harmful, to reduce the amount the baby ingests, either express milk immediately before taking the ECP or take it immediately after feeding the baby.
- PATIENT INFORMATION LEAFLET PROVIDED**

As ovulation is delayed, you are at a higher risk of pregnancy following its taking!

Consultation Record

Pharmacy Guild of New Zealand (Inc) October 2017

Emergency Contraceptive Pill

NAME: _____ SCRIPT NO. _____

ADDRESS: _____

WEIGHT: _____ HEIGHT: _____ BMI: _____

DISCLAIMER: This document should be used in conjunction with the Practice Guidelines for Pharmacist supply of the Emergency Contraceptive Pill (ECP).

QUESTIONS	RESPONSE	COMMENTS
Is the ECP for your own use? If not, who is it for?		
Have you had unprotected sex or possible contraceptive failure?		
How long ago did this happen?		
When did you have your last period? Was it lighter, shorter or different than usual?		
Have you had unprotected sex at any other time since your last period?		
Have you used the ECP already since your last period?		
Are you taking any other medicines or herbal products - prescribed or that you have purchased? Refer to <i>Guidelines if patient is taking any of the below medicines.</i> Enzyme inducers - barbiturates, primidone, phenytoin, carbamazepine, topiramate, rifampicin, rifabutin, ritonavir, nevirapine, nelfinavir, tacrolimus, griseofulvin, St John's wort. Ciclosporin - toxicity increase		
Do you have, or have you ever had, any medical conditions? e.g. Bowel disease, severe liver disease, high blood pressure, diabetes, heart disease/stroke, breast cancer		
Have you ever had an allergic reaction to, or vomited after taking, the ECP?		
Are you breastfeeding?		

PHARMACIST RECORD

- ECP supplied (1.5mg) ECP supplied (3mg) Patient referred to GP or FPC
 ECP not appropriate Informed consent given to supply ECP YES NO

Pharmacist _____ Date _____



Monitoring

Note: If the Copper IUD is provided as emergency contraception, a pregnancy test should be done 3-4 weeks following the fitting (to confirm that they have really missed their period)

Note: A pregnancy test should be done following the supply of the ECP if the next period is later than 5 days, is unusually light or heavy or if there is any sharp abdominal pain. However if you have any suspicions that you might already be pregnant do a pregnancy test 3-4 weeks following the ECP.

OSCE Points

1. What is the reason behind needing the ECP?
2. Is the patient already pregnant? (When was the last period? Late period? Was the period different or unusual?). If pregnancy is suspected, a pregnancy test could be offered.
3. Usual method of contraception? Patients may not need emergency contraception

Non-Oral Contraception

Male Contraception

Description

Aside from a vasectomy and the condom, there are no other forms of reversible contraception available for men. While a few pill formulations are currently in clinical trials, there is no male contraceptive pill that has been approved.

While the majority of men/women from all nationalities/religious groups welcome the male pill, there are many reasons why the male pill has lagged behind the females'

1. >50% of women in a stable relationship would not trust their partner to use contraceptive.
2. Plenty of safe/effective options already available for females.
3. Stricter safety/efficacy standards for new medicines compared to 50 years ago
4. Harder to stop the production or to inactivate sperm.

Pill

The pill mimics negative feedback of endogenous testosterone.

Benefit: Has undergone Phase 1 Trials and stopped sperm production for all.

Risk: found to decrease sex drive and induce erectile dysfunction in some

Injection

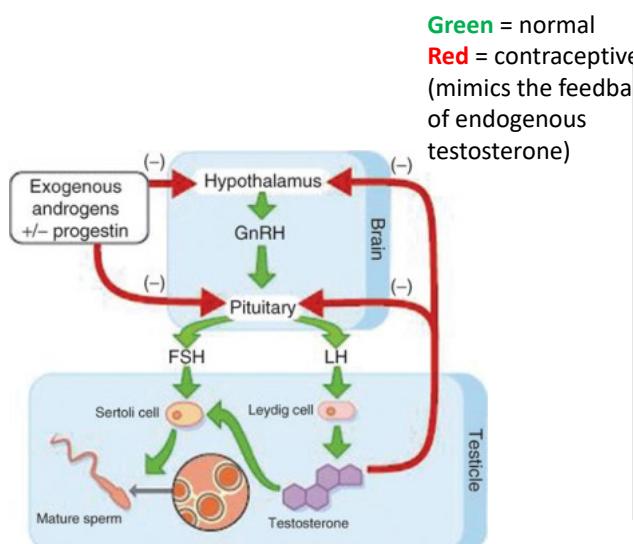
Benefit: Longer acting

Risk: Was stopped as it was found to increase depression and mood disorders.

Body Gel

Benefit: Absorbed by being rubbed on back and shoulders

Risk: N/A — currently moving onto the next phase



Intrauterine Devices (IUD)

Description

IUDs are small plastic objects inserted into uterus (STI checks are to be done before insertion). IUDs have fine plastic threads attached that hang slightly out of cervix into the vagina for removal. They have a very high continuation rate compared to other methods. Two types that exist:

Hormone Releasing

*Mirena (5 years), Jaydess (3 years)
Progesterone (Levonorgestrel) IUD*

Copper Releasing

Copper IUD (10 years)

TYPES OF IUDS		
	Levonorgestrel IUD	Copper IUD
Uses	<p><i>Other uses</i></p> <ol style="list-style-type: none"> Can be used as HRT for menopause Prevent endometrial hyperplasia from estrogen in menopause treatment To reduce heavy menstrual bleeding (~90%) - better than endometrial ablation, medications (e.g. progestins, NSAIDs) 	<p><i>Other uses</i></p> <ol style="list-style-type: none"> Can be used as EC Reduces risk of endometrial cancer (hormonal cancer 40% reduction)Note: Copper IUD can cause heavy and unpredictable periods.
MoA	<p><i>Mechanism of Action</i></p> <p>IUD releases ~20mg of progesterone per day</p> <ol style="list-style-type: none"> Inhibits fertilisation Thickens cervical mucous Inhibits sperm function Thins/suppresses endometrium 	<p><i>Mechanism of Action</i></p> <ol style="list-style-type: none"> Inhibits fertilisation Cu^{2+} ions reduce sperm motility May disrupt the normal division/formation of oocytes and formation if fertilisable ova
Duration	Can be used for up to 5 years (pregnancy rate is < 1 %)	Can be used for up to 10 years (pregnancy rate is < 2 %)
IUDS ADVANTAGES vs DISADVANTAGES		
	Advantages	Disadvantages
<i>Duration</i>	<ol style="list-style-type: none"> Copper: good for up to 10 years Hormone: good for up to 5 years 	
<i>Overall Use</i>	<ol style="list-style-type: none"> Long-term protection Very effective and easy adherence (essentially no “user error”) No interruption of sexual activity Can be used during breastfeeding (or where estrogen is contraindicated) 	<ol style="list-style-type: none"> Cost of family planning visits (can also get assistance from work and income if have a CSC) No STI protection Risk of PID usually within first 1-2m following insertion Rare incidence of perforating uterine wall Copper IUD can cause heavy and unpredictable periods.
<i>No concerns about infection/infertility:</i>	<ol style="list-style-type: none"> Upon discontinuation, person has rapid return to fertility, unlike with the pill where it takes a year Prophylactic antibiotics may be prescribed at the time of insertion to prevent infections — except if woman had a high prevalence of STIs No increased risk of upper genital tract infection during insertion 	

Contraindications to IUD

1. Pregnant
2. Vaginal bleeding of unknown etiology
3. Acute reproductive tract infection (treat infection first before IUD insertion)
4. Prior ectopic pregnancy
5. STI history in the past 3 months (possibility of sub-clinical infection)
6. Anatomic anomaly e.g fibroid of uterus (higher risk of IUD dislodging and therefore contraceptive failure)
7. Mirena: current breast cancer
8. Copper: copper allergy, Wilson's disease, menorrhagia (as the copper can worsen this)



Important Counselling Point for IUDs

Women are recommended to periodically feel their cervix for the IUD strings to ensure 'silent spontaneous expulsion' of the device has not occurred.

Implant (Jadelle)

Description

Jadelle is a progesterone (levonorgestrel) implant available in New Zealand. Two rods are implanted subcutaneously under the skin of the upper arm and last about **5 years**.

Progesterone

Inhibits the secretion of LH and *thus prevents ovulation*.

Makes the cervical mucus *less suitable for the passage of sperm*

Mechanism of Action

- Prevents implantation
- Thickens cervical mucus

Injectable (Depot)

Description

Depo Medroxyprogesterone acetate (Depo-Provera) is an IM progestin-only injection every **3 months (12 weeks)**. If this is delayed over 14 weeks, we need to consider pregnancy risk.

Progesterone

Inhibits the secretion of LH and *thus prevents ovulation*.

Makes the cervical mucus *less suitable for the passage of sperm*

Side Effects

- Breakthrough bleeding can be problematic
- Bone mineral loss is **NOT** a concern but there can be some

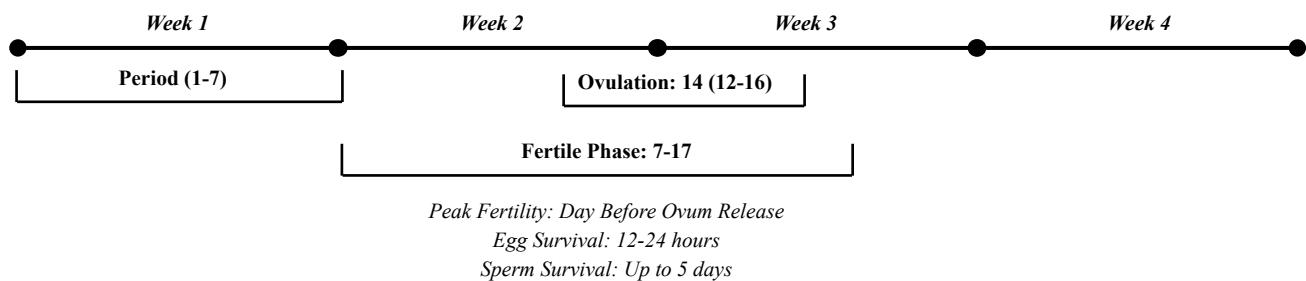
Non-Hormonal Contraception

Fertility Awareness Methods

Calendar Method 28 day Cycle (Ok)

Fertility Basic Principles (28 Day Calendar)

Women could study their cycle and predict when they would be the least likely to get pregnant. Highest rate of effectiveness of natural family planning methods



Nursing (Not Good)

Amenorrhea is common for a brief period after birth while breastfeeding. However, breastfeeding only prevents pregnancy for up to **6 months**. 80% of women ovulate before their first period (and so do not know that they are fertile).

Withdrawal Method (Not Good)

1. Difficult to judge when to withdraw
2. Anxiety may lower pleasure for both partners
3. Cowper's gland fluid may carry sperm
4. Any sperm on vulva may travel into vagina/uterus

Douching (Not Good)

1. Sperm reaches uterus in 1-2 minutes
2. Douching may speed sperm along
3. Irritates vaginal tissue



Note

As you would've have noticed, generally, natural methods of preventing pregnancy, unless involve abstinence, are generally not effective - consider relaying this information to patients adamant on using these methods (particularly if they are on teratogenic medicines e.g. anti-epileptics, isotretinoin)

Barrier Methods

Description

Barrier methods have assumed greater importance in recent years due:

1. To their ability to **reduce the risk of sexually transmitted infections (STIs)**
2. They are commonly used with other methods of contraception (the OC/condom most common)
3. Particularly appropriate for women in stable relationships who can predict when they will have intercourse

BARRIER METHODS	
Method	Description
Condoms	<p>Recommended</p> <p><i>Condoms are a sheath that fits over the erect penis and is:</i></p> <ol style="list-style-type: none">1. Currently the only temporary method of birth control for men2. The only form of contraception that effectively reduces STI transmission <p><i>Components</i></p> <ol style="list-style-type: none">1. Made of thin latex, polyurethane, or natural membrane2. Many varieties - different features, shapes, textures, colours, flavours3. Some “extended pleasure” types have a desensitising agent on the inside to delay ejaculation4. Can be lubricated or non lubricated5. Average shelf life is 5 years; don’t store latex condoms in hot places, heat can deteriorate the latex
Diaphragms	<p>Not Recommended</p> <p><i>Composition</i></p> <p>A diaphragm is a cap that fits inside your vagina and prevents sperm passing through the cervix (the entrance of your womb). It is positioned to completely cover the cervix, fitting behind the pubic bone and the posterior vaginal fornix.</p> <ol style="list-style-type: none">1. Available in several materials, styles and sizes2. Prescription-only; fitted by a health professional3. First-year pregnancy rate for typical use is 16%4. Should be used with a spermicide (gel)5. May be used with a condom. <p><i>Side effects:</i></p> <ol style="list-style-type: none">1. UTIs (could switch to a smaller diaphragm or one with a different rim)2. Vaginal irritation3. Recurrent yeast infections, and bacterial vaginosis
Spermicides	<p>Not Recommended</p> <p><i>Chemical Contraceptive Barrier - not available in NZ</i></p> <ol style="list-style-type: none">1. Surfactants (nonoxynol-9, octoxynol-9) that destroy sperm’s cell membrane2. Apply 15-30 minutes before sex, most spermicides are only effective for 60 minutes, never wash out or remove spermicide after having sex.3. Failure rate during the first year of typical use of spermicides alone is approximately 29%4. Efficacy may be dose-related, based on concentration of spermicide5. Spermicides do not protect against STIs and HIV

Sterilisation

Description

Sterilisation is a permanent method of sterilisation — except for vasectomies which are reversible. It has no effect on hormones or desire of sexual functioning. Female sterilisation aims to prevent the eggs from reaching the sperm while male sterilisation aims to prevent release of sperm.

MALE & FEMALE STERILISATION	
Female	Male
<p>Tube Tying Tubes are often tied following a C-section upon the woman's request.</p> <p>1. <i>Tubal Sterilisation</i> • Fallopian tubes are severed to block passage of sperm & eggs</p> <p>2. <i>Transcervical Sterilisation</i> • A tiny coil is inserted through cervix into the fallopian tubes to promote tissue growth — this will block the fallopian tubes after 3 months.</p>	<p>Vasectomy</p> <ol style="list-style-type: none">1. Safer, less expensive2. Reversible3. Fewer complications than female sterilisation <p>Vas deferens (ducts that carry sperm) are cut on each side, a small section is removed and the ends are tied off or cauterised. However, a number of ejaculations after the surgery is needed to release the stored sperm.</p>

HORMONE-RELATED CONDITIONS

Introduction

We will first look into women's hormonal conditions e.g. menopause, endometriosis, PCOS and then men's e.g. BPH, Androgenic Alopecia. Please note that generally hormonal-related conditions that afflict women can be treated or relieved with an exogenous supply of female hormones.

Women's Hormonal Conditions

Menopause

[NZF Menopause](#), [NICE Guidelines Menopause](#)

Description

Menopause is the permanent cessation of menses following loss of ovarian follicular function - it is associated with the natural decline in reproductive hormones, which begins to occur when a woman reaches 40-58 years (mean age is 52).



Premature Menopause

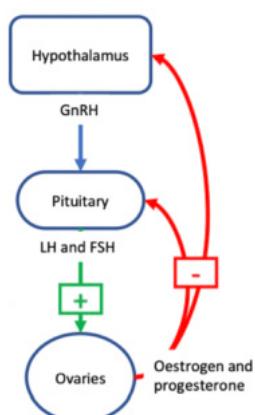
Premature menopause is menopause that occurs before 45 years of age. It is associated with:

- Earlier onset of CVD episodes and osteoporosis
- Reduced breast cancer risk compared to menstruating peers

For this reason, prematurely menopausal women are strongly advised to consider **HRT** until the age of **50**

Pathophysiology

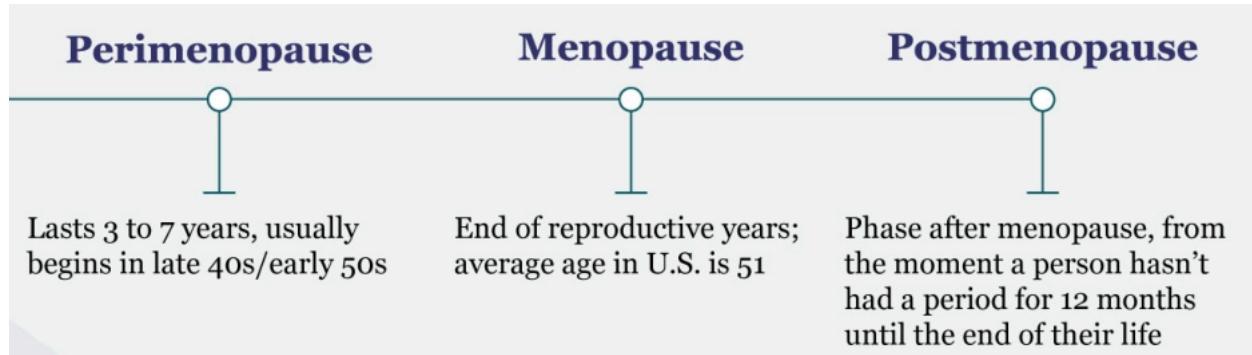
Hypothalamus (GnRH) Pituitary (FSH & LH) Ovarian (Estrogen & Progesterone) Axis



1. Declining ovarian follicular function causes less amounts of estrogen and progesterone to be produced. Subsequent decreased (-) feedback reflexively increases FSH and LH concentrations.
2. The remaining follicles require higher FSH concentrations to mature and ovulate — until ovulation eventually ceases.
3. However, the increase in FSH and LH causes menopausal symptoms. We need to provide an external source of estrogen and progesterone to increase negative feedback and minimise these symptoms (decrease in FSH & LSH).

The transition into menopause occurs in the following way:

1. *Peri-menopause*: a transition period that occurs 2-8 years prior to menopause. Hormonal and biological changes occur and physical symptoms may be observed (e.g. irregular menstrual cycles, ↓cycle length)
2. *Menopause*: permanent cessation of menses following loss of ovarian follicular function



Signs & Symptoms

Menopause can cause symptoms such as:

Vasomotor Symptoms

- Lasts 5 years
- Hot Flushes
- Night Sweats

Other Symptoms

- Vulvovaginal Atrophy
- Vaginal Dryness & Itchiness
- Dyspareunia

Less Common

- Mood Swings, Depression,
- Insomnia, Arthralgia,
- Myalgia, Urinary Frequency,
- Decreased Libido, Dermatological

A Note on Vasomotor Symptoms

Vasomotor symptoms are the most commonly experienced symptoms in menopause (~70%) — they are a form of temperature dysfunction that occur due to an increased hypothalamus sensitivity in response to the changes in body temperature. Women often describe hot flushes as a feeling of sudden warmth to the face, neck and chest for about 4 minutes.

They vary in severity, diminish over time (~5.2 years) before they disappear completely. While all symptoms respond well to external estrogen replacement, vasomotor symptoms respond extremely well.

Diagnosis

- Amenorrhoea (no period) for **12 consecutive months**
- Lab: Increase in FSH level

Pharmacological Treatment

BPAC Menopause Treatment Guidelines

Hormone Replacement Therapy (HRT) relieves some of the menopausal symptoms by providing an external source of the hormones the ovaries no longer make.

1. *Progesterone* prevents growth of the endometrium into cancer
2. *Estrogen* provides an exogenous source to reduce menopausal symptoms

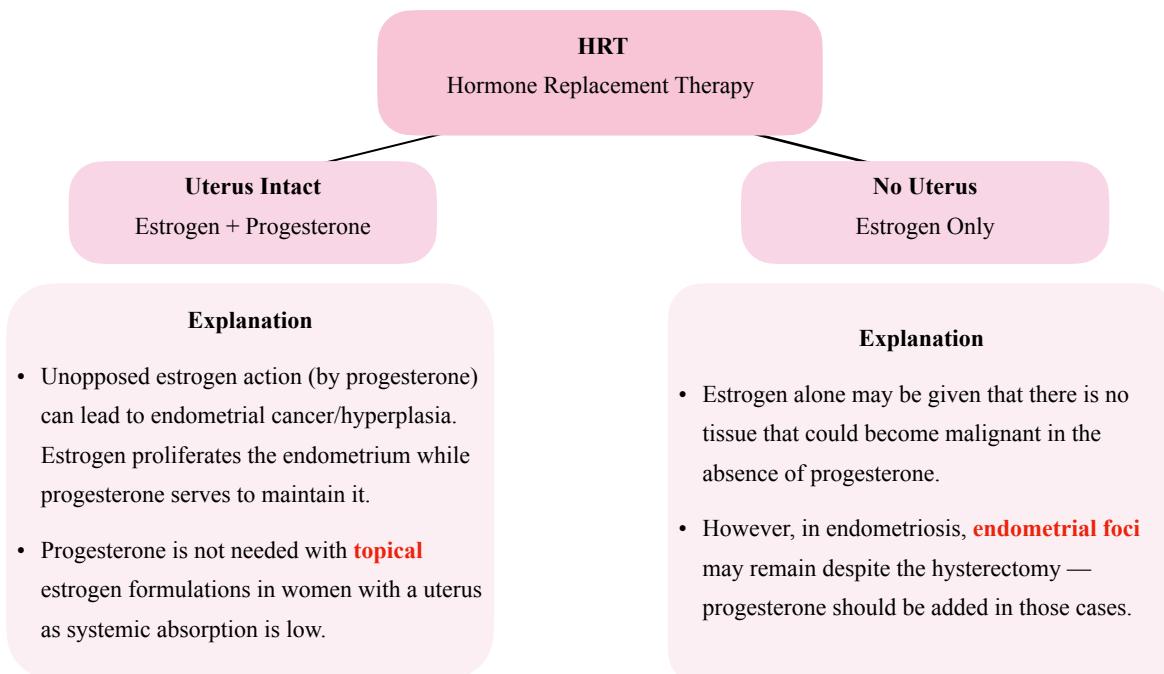


Topical Estrogen

Topical forms of estrogen can be used for **localised symptoms** e.g. urogenital symptoms (vaginal dryness, soreness, dyspareunia, increased urinary frequency and urgency)

The hormones given depend on:

1. Whether the woman still has her uterus
2. Her age and
3. What other medical conditions she has.



Treatment Recommendation

- There is no single recommendation for optimum duration of treatment for HRT. For most women, short-term treatment will be sufficient to relieve vasomotor symptoms; for others, HRT may need to be continued for longer.
- Women can have a 3 month trial of HRT, then consider further treatment. Therapy is generally stopped within **2 years** if symptoms have resolved, and is stopped abruptly or withdrawn slowly.
- The lowest effective dose should be used for the shortest possible time, and the need to continue HRT should be reviewed at least yearly, taking into consideration the change in balance of risks and benefits.

HORMONE REPLACEMENT THERAPY	
	<p>Oral Formulations</p> <ol style="list-style-type: none"> 1. Estradiol Valerate (<i>Progynova</i>) 2. Estradiol (<i>Estrofem</i>) 3. Estriol (<i>Ovestin</i>) 4. Tibolone: synthetic steroid with weak estrogen, androgen and progesterone actions (<i>Livial</i>) 5. Bazedoxifene (SERM) + Estrogens Conjugated Equine (<i>Duavive</i>)* 6. Estrogens Conjugated Equine (<i>Premarin</i>)
Estrogen	<p>*Note on <i>Duavive</i>: used in menopausal women with uteruses who have <i>contraindications to progestogens</i></p>
	<p>Transdermal</p> <ol style="list-style-type: none"> 1. Estradiol (<i>Estradot, Climara Patches</i>)
	<p>Topical Formulation</p> <ol style="list-style-type: none"> 1. Estriol (<i>Ovestin Cream or Pessaries</i>) <p>*Note: Creams are more commonly used but can <i>damage condoms</i></p>
Progesterone	<p>Oral Formulations</p> <ol style="list-style-type: none"> 1. Medroxyprogesterone Acetate (<i>Provera</i>) 2. Norethisterone (<i>Primolut N</i>) 3. Progesterone (<i>Crinone, Utrogestan</i>) <p>Intra Uterine Formulations</p> <ol style="list-style-type: none"> 1. Levonorgestrel IUD (<i>Mirena</i>)
Estrogen + Progesterone	<p>Oral Formulations</p> <ol style="list-style-type: none"> 1. Estradiol + Norethisterone (<i>Trisequens, Kliogest, Kliviance</i>) 2. Medroxyprogesterone + Estrogens Conjugated Equine

	Route of delivery	Funding status*	Dose forms (refer to NZF for dosing regimens)
Oestrogen only products[†]			
Estradiol patch	Transdermal	●	25, 50, 75 or 100 micrograms/24 hours (applied twice weekly)
Estradiol valerate tablets	Oral	●	1 mg, 2 mg
Estradiol tablets		●	1 mg, 2 mg
Estriol		●	2 mg
Ethinylestradiol		●	10 micrograms
Conjugated equine oestrogens		●	300, 625 micrograms
Progesterogen only products			
Medroxyprogesterone acetate	Oral	●	2.5 mg, 5 mg, 10 mg
Norethisterone tablets (unapproved indication)	Oral	●	350 micrograms (<i>Noriday</i>), 5 mg (<i>Primolut N</i>)
52 mg levonorgestrel IUD (<i>Mirena</i>) [‡]	Intrauterine	●	20 micrograms/day
Progesterone capsule (micronised – <i>Utrogestan</i>)	Oral	○**	100 mg
Combination products			
Estradiol + norethisterone tablets	Oral	●	2 mg estradiol + 1 mg norethisterone
		●	1 mg estradiol + 0.5 mg norethisterone
		●	Cyclical (three doses): <ul style="list-style-type: none"> • 2 mg oestradiol • 2 mg oestradiol + 1 mg norethisterone • 1 mg oestradiol
Conjugated equine oestrogens + bazedoxifene	Oral	○	450 micrograms conjugated equine oestrogens + 20 mg bazedoxifene

RISK & BENEFITS OF HORMONE REPLACEMENT THERAPY	
Breast Cancer	Increase <ul style="list-style-type: none"> All types of HRT increase this risk within 1-2 years of initiating treatment Risk disappears within 5 years of stopping Mammographic density increases with HRT use, resulting in difficulty in detecting cancer radiologically
Endometrial Cancer	Increase or reduced risk <ul style="list-style-type: none"> Increased risk with estrogen (except Duavive) Decreased risk with combination HRT (intact uterus)
Ovarian Cancer	Small Increase <ul style="list-style-type: none"> With long term use (5-10 years) Risk disappears within a few years of stopping
VTE	Increase <ul style="list-style-type: none"> All types of HRT increase this risk within the first years of initiating treatment Be careful of pre-disposing factors that may increase this risk even more!
Stroke/CHD	Small Increase <ul style="list-style-type: none"> Risk of stroke increases with age regardless thus older women already have a greater absolute risk HRT slightly increases this
Adverse Effects	<p>These adverse effects usually decrease overtime, if not, lowering dose of HRT may be needed.</p> <ul style="list-style-type: none"> Irregular bleeding with combined regimens Nausea and breast tenderness
Weight Gain	Does not cause weight gain if combination estrogen + progesterone is used

The risk for blood clots stroke and breast cancer while taking MHT is very small and lower than for many risk factors such as being overweight.

OSCE Points - How to use Estrogen (Ovestin) Cream

- Insert 1 application daily in the evening, for up to 4 weeks, then reduce gradually to a maintenance dose of 1 application twice a week
- Screw applicator onto the tube of cream and draw up to the line
- Insert applicator up to the vagina high up and squeeze the cream
- Do not stand up as cream may leak out
- Cream may damage condoms (important for STI prevention)
- Wash applicator in warm soapy water
- If you miss a dose, take it as soon as you remember **unless** it is day of the next dose (in this case miss the dose completely and just continue as usual). Two doses must not be administered on the same day.

Endometriosis

Description

Endometriosis is defined as the presence of endometrial glands and stroma outside of the uterus (e.g. ovaries, fallopian tubes), causing ectopic lesions in the pelvic cavity.



Pathogenesis

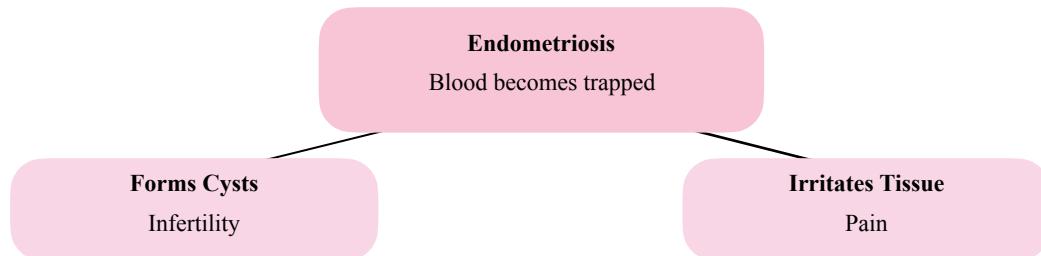
Estrogen aims to proliferate the endometrial tissue while progesterone maintains it to prevent its excess growth. Endometriosis was found to have high levels of estrogen, as well as progesterone resistance (target tissue responds less to bioavailable progesterone).

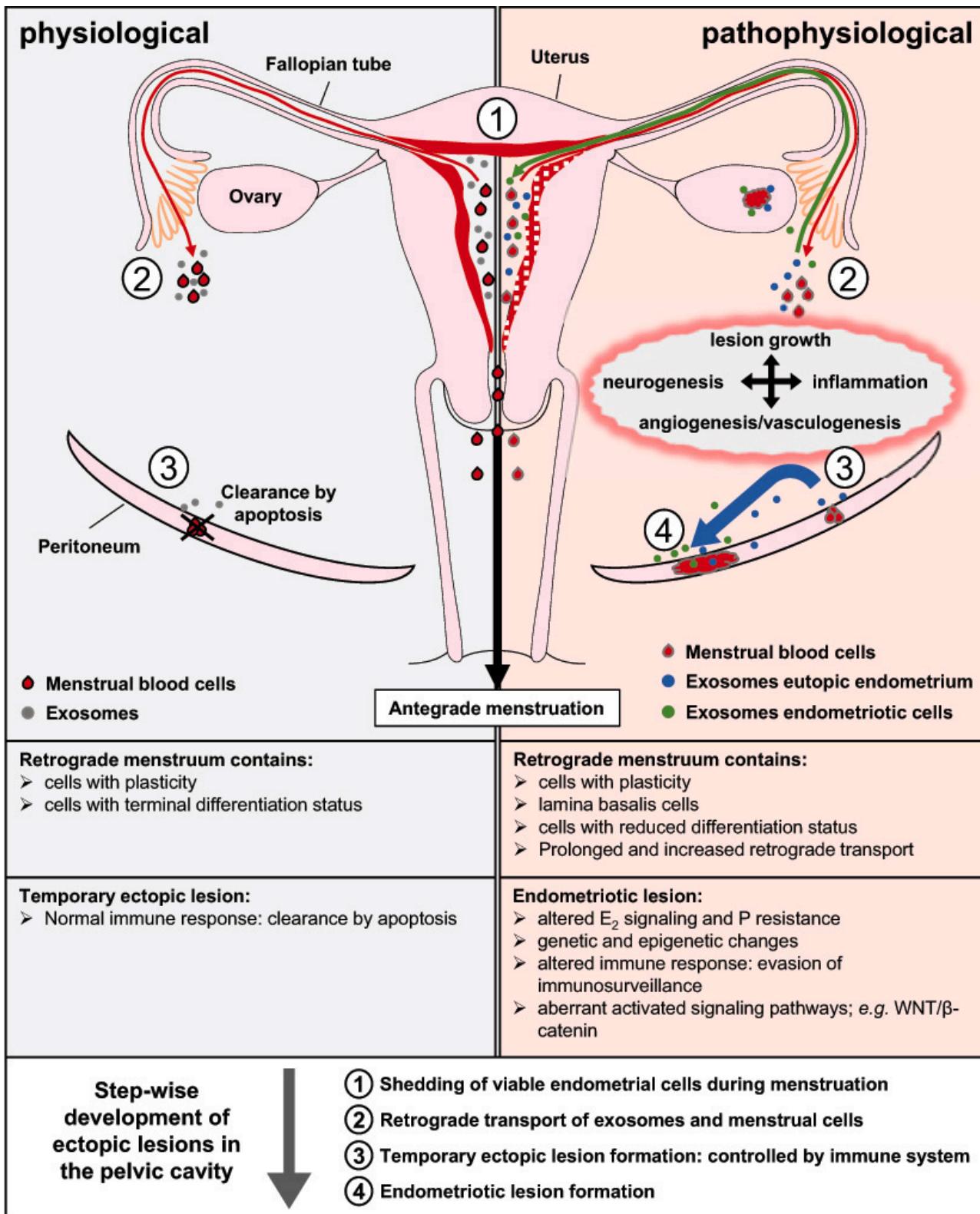
Although the mechanism is not very well understood, there are three theories that have been proposed for the development of endometriosis — no one theory applies to all individuals and all three cause blood to be trapped, forming cysts that cause pain and infertility.

PATHOGENESIS THEORIES OF ENDOMETRIOSIS	
Theory 1 Implant Theory	Tissue travels via retrograde menstruation or surgery/deliveries Upon failure of the egg to implant, the endometrium begins to shed to form the menstrual cycle. However we theorise that some of this blood travels upwards to other parts of the female reproductive tract and grows there. In females with normally functioning immune system, this blood is cleared out. If it isn't, it can lead to endometriosis.
Theory 2 Lymphatic/Vascular Theory	Explains distant location It is possible that pieces of the endometrium travel in the <i>lymphatic</i> system — which would explain the location of cysts on the <i>bladder</i> and other parts outside the female RT.
Theory 3 Metaplasia Theory	Undifferentiated cells transform into endometrial tissue It is possible that stem cells randomly differentiate into endometrial tissue in random places.

Complications

1. **Adhesions** can cause pain, structural changes to the pelvic/reproductive organs, and bowel obstruction
 - The trapped blood form cysts and can cause infertility
 - If the lesions grow big enough, they irritate surrounding tissue and cause pain
 - They can also begin to attach parts of the RT to each other, causing further complications
2. Ovarian failure post-surgery





Risk Factors

Endometriosis can affect any woman of reproductive age (thus that menstruates) but it is more common in the 30s-40s. Other risk factors include anything that **predisposes the woman to longer periods of menstruation:**

- Being infertile
- Being nulliparous (women who've never had children)
- Menstrual periods that last 7+ days
- Short menstrual cycles (≤ 27 days)
- Genetic predispositions (family history)

Co-morbidities

A large percentage of women experience the following ***co-morbidities***. This is because although endometriosis isn't an autoimmune disease, it slightly behaves like one (i.e. due to the immune system not being able to clear the endometrial tissue?) — increasing your risk for others:

- Fibromyalgia (muscle aches)
- Hypothyroidism
- Chronic Fatigue Syndrome (CFS)
- Allergies, Asthma
- MS, Lupus, RA

Signs & Symptoms

Common

- Dysmenorrhea (painful and heavy bleeding)
- Constant/intermittent, or cyclical pelvic, and/or low back pain (unilateral or bilateral)
- Dyspareunia (pain during sexual intercourse)
- Sub-fertility/Infertility
- Pelvic mass (ovarian endometriomas — chocolate cysts)
- Endometrial **pain** — however, this does **not** correlate with the severity of the disease

Uncommon

- Dyschezia (painful bowel movements, particularly during menstruation)
- Dysuria

Diagnosis

Making a clinical diagnosis of endometriosis can be difficult as symptoms are often non-specific and there can be limited clinical signs on examination.

1. *Ultrasound* (usually transvaginal)
2. *Laparoscopy* (definitive diagnosis): direct visualisation with biopsy-confirmed endometrial glands or stroma outside of uterine cavity. However, it is invasive and associated with many complications.

Classification of Endometriosis

CLASSIFICATION OF ENDOMETRIOSIS	
Minimal Stage I Endometriosis	Typically small patches, surface lesions or inflammation on or around organs in the pelvic cavity.
Mild Stage II Endometriosis	More extensive than stage I but infiltration of pelvic organs still very limited, without a great deal of scarring or adhesions.
Moderate Stage III Endometriosis	Sometimes more widespread and starting to infiltrate pelvic organs, peritoneum (pelvic side walls) or other structures. Sometimes there is also scarring and adhesions.
Severe Stage IV Endometriosis	Infiltrative and affecting many pelvic organs and ovaries, often with distortion of the anatomy and adhesions.

Goal of Treatment

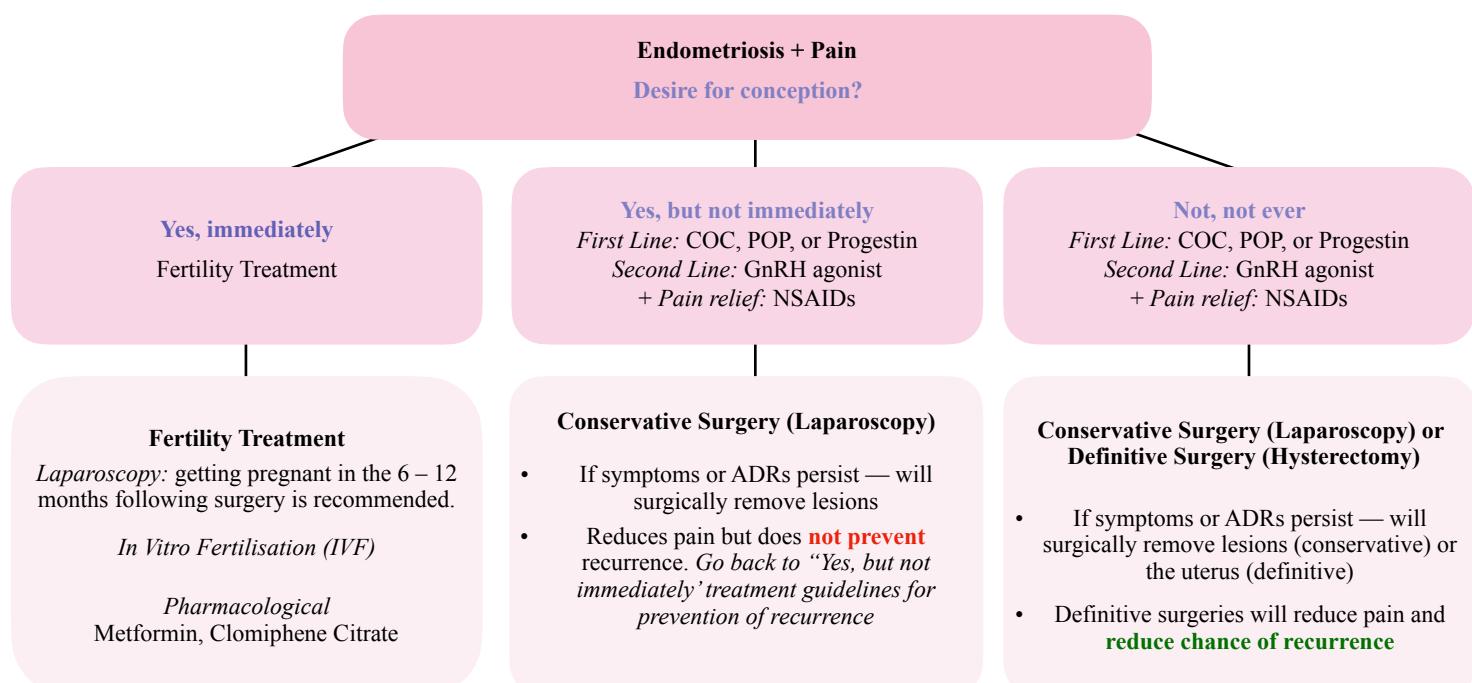
1. Control symptoms, either prior to, alongside or instead of more curative surgical interventions
2. Stop the lesions from growing via hormonal suppression of endometriotic lesions, this is particularly effective when amenorrhoea occurs.

Pharmacological Treatment

BPAC Endometriosis Treatment Guidelines

Endometriosis is a chronic and often recurrent condition — long-term treatment is usually required.

Approximately 50% of women will have a **recurrence of symptoms** within five years if medical management is stopped. Treatment option depends on whether the women desires conception.



TREATMENT OPTIONS (HORMONES)						
	First Line Progesterone (P4) Signaling Modifiers <i>Progesterone resistance occurs in endometriosis</i>		Second Line Estrogen (E2) Signaling Modifiers <i>Estrogen is elevated in endometriosis</i>			Additional Analgesia NSAIDs
	COCs	Progestins	GnRH Agonists	GnRH Antagonist	Aromatase Inhibitor	
Indication	Decrease progesterone resistance		For women who do not respond to oral contraceptives or progestins			Pain relief
Options	1. Levlen ED (Ethynodiol + Levonorgestrel) 2. Any other COC they have previously used	1. POP 2. Implant (<i>Jadelle</i>) 3. Injection (<i>Depot-Provera</i>) 4. IUD (<i>Mirena, Jaydess</i>)	1. Goserelin 2. Leuprorelin Acetate (depot) 3. Buserelin Acetate	1. Cetrorelix 2. Ganirelix	1. Exemestane 2. Anastrozole 3. Letrozole	All NSAIDs have similar efficacy for endometriosis 1. Ibuprofen 2. Naproxen 3. Mefenamic Acid
MoA	Suppress ovarian steroid production and supplement P4 levels	Supplement P4 Levels	↓ E2 production through (-) feedback	↓ E2 production by competing for GnRH receptors	↓ E2 production by inhibiting peripheral conversion of androgens to E2	↓ prostaglandins, provides acute pain relief
Therapeutic Effect	<ul style="list-style-type: none"> Reduce endometriosis pain (significant dysmenorrhea relief within 4 months) + reduce recurrence. Continuous administration with OCs may be more beneficial for pain (as no blood is getting trapped) but additional pain relief can be given 		<ul style="list-style-type: none"> Reduce endometriosis pain (significant dysmenorrhea relief within 4 months) + reduce recurrence. <i>GnRH Agonists:</i> Cannot use long-term (>6 months) without hormone add-back therapy (e.g. norethisterone or conjugated estrogen + medroxyprogesterone) <i>Aromatase inhibitors:</i> Often used in conjunction with COC or progestin. 			A safer alternative to long-term opioid use (should be avoided in endometriosis)
Side Effects	<p>Progesterogen (not IUD):</p> <ul style="list-style-type: none"> Loss of bone mineral density Prolonged delay in resumption of menses/ovulation when woman is trying for a baby Breakthrough bleeding 		<p><i>GnRH agonists — Initial flare (2-4 weeks)</i></p> <ul style="list-style-type: none"> Induces hypoestrogenism (menopause symptoms: hot flashes, insomnia, vaginal dryness, libido loss, bone mineral density loss) 			GIMIRI

Poly cystic Ovarian Syndrome (PCOS)

Description

PCOS is a hormonal disorder associated with an excess of insulin and testosterone. This causes enlarged ovaries with small cysts on the outer edges. It is a collection of signs and symptoms — it is a **syndrome** so no single test or feature is diagnostic. **Polycystic Ovaries ≠ PCOS (Rule of 20%)**

Polycystic Ovaries ≠ PCOS (Rule of 20%)		
	Polycystic Ovaries	No Polycystic Ovaries
PCOS	20%	20%
No PCOS	20% <i>Examples: hypothalamic amenorrhea, adolescents, hyperprolactinemia</i>	-

Pathophysiology

1

2

3

Neuroendocrine Derangement

- Increased pulsatile release GnRH causes ↑ LH relative to FSH (↑ LH:FSH ratio)
- No FSH/LH spike to trigger ovulation

Hyperinsulinaemia

- Insulin resistance (action/secretion) leads to hyperinsulinaemia which feeds into ovarian dysfunction

Androgen Excess

- Ovarian dysfunction leads to excess production of testosterone (and impaired ovulation)

PCOS begins with risk factors which cause a neuroendocrine derangement (increased LH:FSH ratio) and hyperinsulinaemia (insulin resistance). These two factors exacerbate androgen excess, which leads to:

1. *PCOS symptoms:*
 - Hirsutism, acne, alopecia, depression
2. *Follicle development arrest:*
 - Anovulation: no follicle development so no egg release (absence of progesterone due to no corpus luteum), resulting in fertility issues
 - Polycystic ovaries (cysts on outside of ovaries)

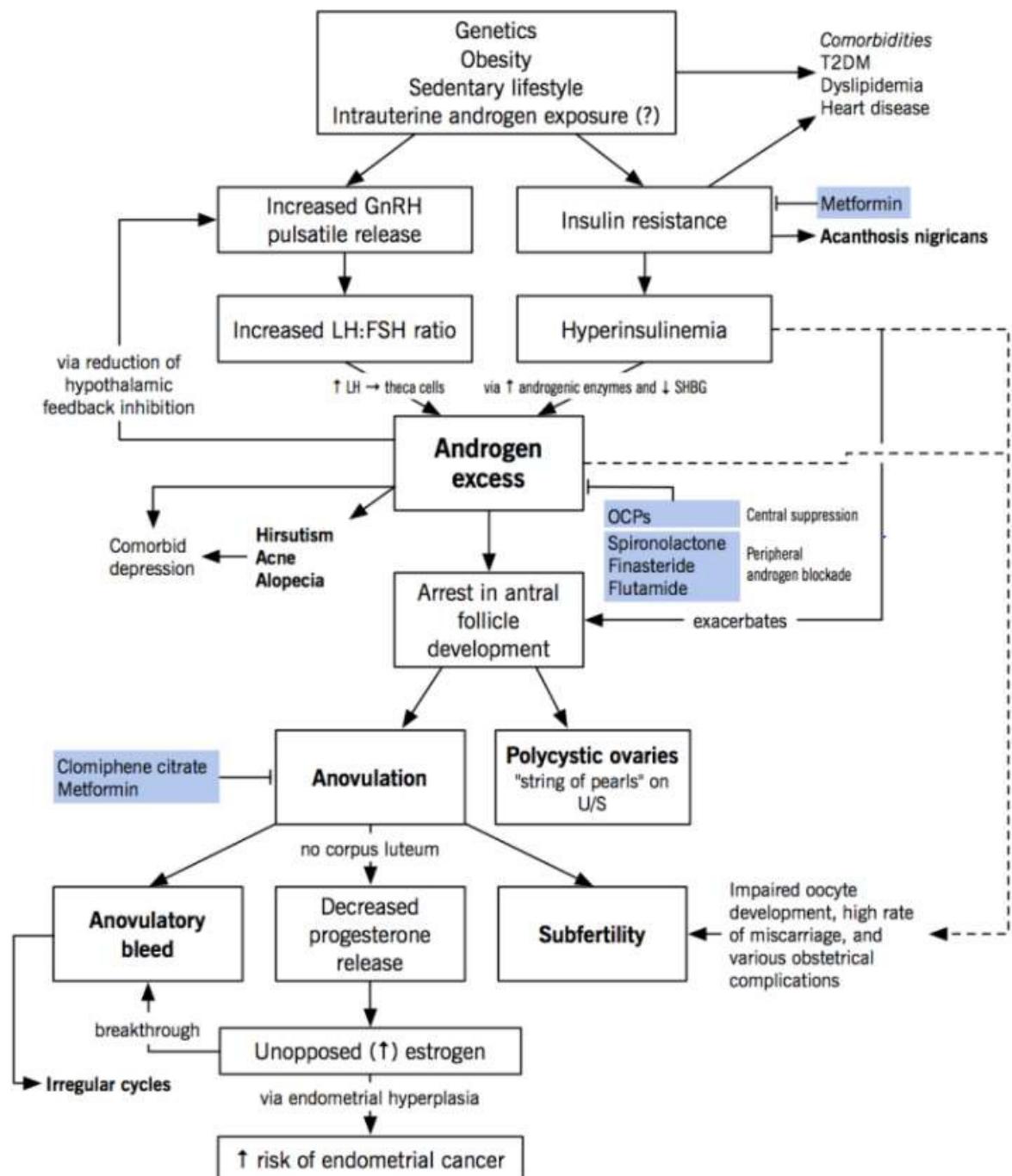
Complication: Similar to endometriosis, we have little progesterone release and unopposed estrogen action (due to anovulation). This increases the risk of endometrial hyperplasia/cancer.

Risk Factors

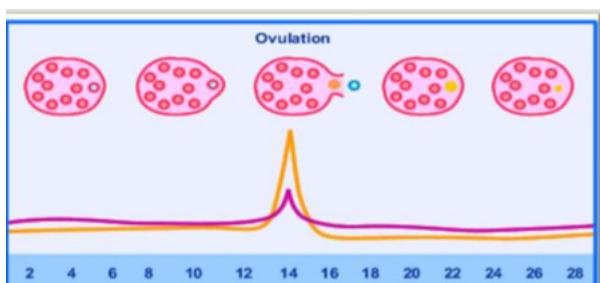
- Most common endocrine disorders among reproductive aged women
- Genetic predisposition
- Metabolic syndrome

Pathophysiology of PCOS

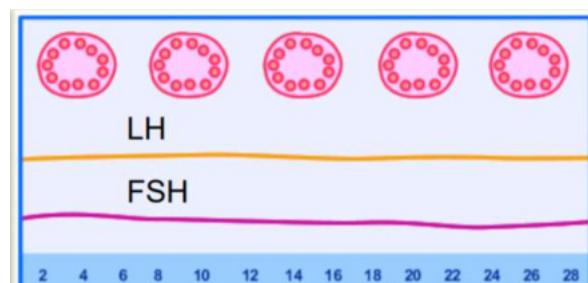
Alex Rotstein, Ragini Srinivasan, and Eric Wong



NORMAL



PCOS



Signs & Symptoms

The clinical presentation of PCOS is a collection of signs and symptoms that are often the presenting conditions of many women.

	Biochemical Abnormality	Signs & Symptoms	Consequences
Neuroendocrine Derangement	• Chronic Estrogen Excess	• Irregular Menstrual Cycles • Menorrhagia • Dysfunction Menstrual Bleeding	• Endometrial Hyperplasia or Cancer • Ovarian Cancer
Hyperinsulinaemia	• Impaired Glucose Tolerance • Insulin Resistance • Diabetes	• Acanthosis Nigricans • Obesity (particularly truncal)	• Diabetes • Gestational Diabetes • Hypertension • Pre-eclampsia
	• Dyslipidaemia	• Abnormal Lipid Panel	• Coronary Artery Disease (CAD)
Hyperandrogenism	• High androgens • Low Sex Hormone Binding Globulin (SHBG)	• Hirsutism • Acne • Alopecia (frontal balding)	• Anovulation • Infertility • Polycystic Ovaries (ultrasound)

Diagnosis

No single test or diagnostic feature exists for PCOS. Its presentation is:

- A collection of signs and symptoms
- Heterogeneous
- Changes with age

Rotterdam Criteria

ROTTERDAM CRITERIA FOR THE DIAGNOSIS OF PCOS	
Exclusion of other Aetiologies	Presence of at least 2 of the following:
Exclusion of other aetiologies • Congenital adrenal hyperplasia • Androgen-secreting tumours • Cushing's syndrome	<ol style="list-style-type: none"> Hyperandrogenism <ul style="list-style-type: none"> • Clinical (hirsutism, acne, frontal balding) • Biochemical (high serum androgen concentrations) Menstrual Irregularity <ul style="list-style-type: none"> • Absent/Infrequent Periods Polycystic Ovaries <ul style="list-style-type: none"> • Remember rule of 20%

Goal of Treatment

1. Identify and monitor co-morbidities: hyperlipidaemia, diabetes, endometrial hyperplasia
2. Modify associated long term health risks: diet, exercise, induce cyclic bleeding, medications
3. Treat patient concerns: hirsutism, infertility, cycle regulation

Non-Pharmacological Treatment

Lifestyle modification to reduce weight is the most effective first line treatment in PCOS. A modest weight loss of 5% will reduce insulin resistance, central obesity, reduce risk of GDM and improve endocrinological abnormalities (e.g. menstrual irregularities). Note that weight loss is not necessary if BMI is within normal range.

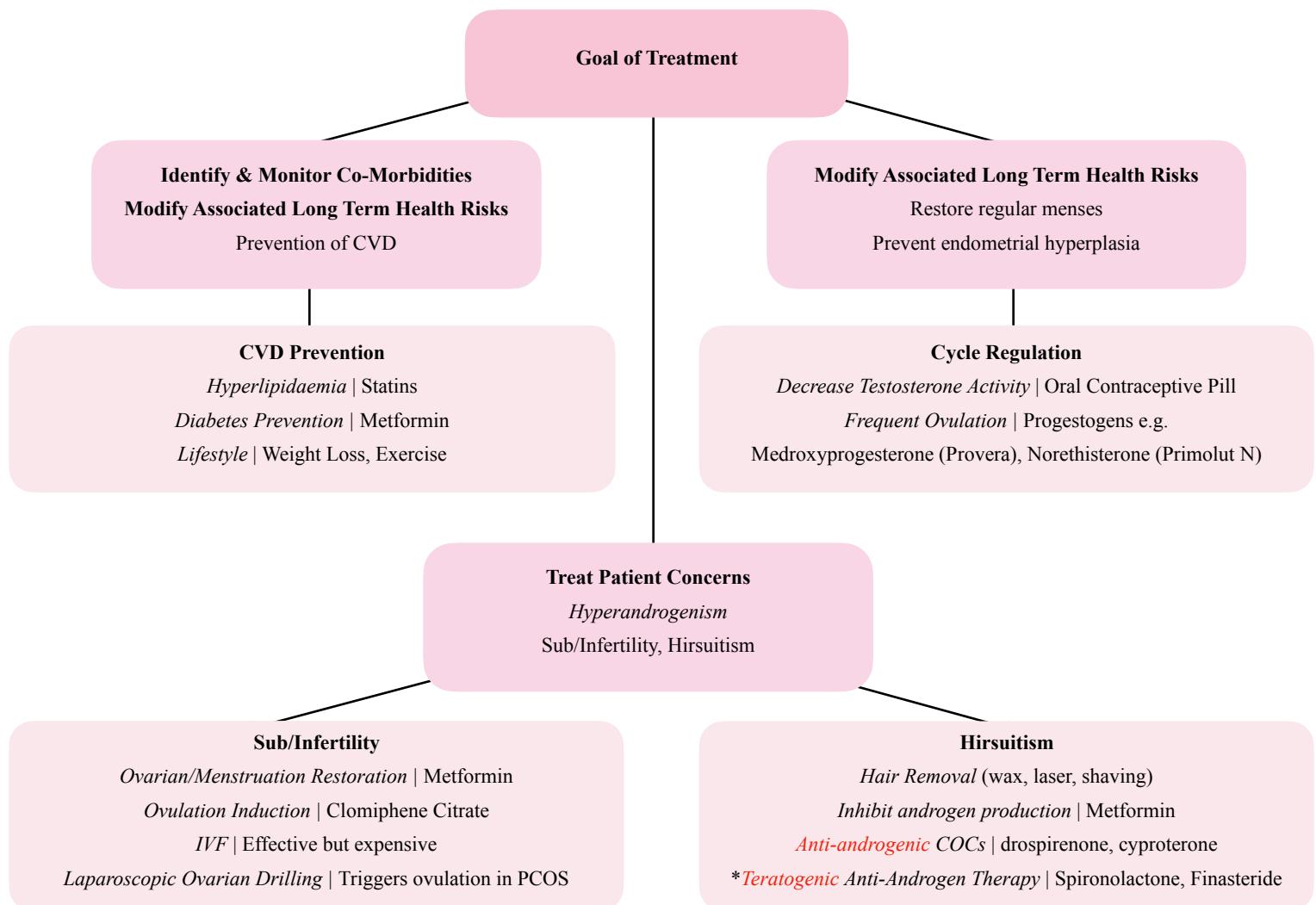
Pharmacological Treatment

[BPAC PCOS Treatment Guidelines](#)



Warning: Teratogenic Therapy

Teratogenic anti-androgenic therapy (spironolactone, finasteride) requires co-prescribing of a contraceptive.



Men's Hormonal Conditions

Benign Prostate Hyperplasia (BPH)

NZF Benign Prostate Hyperplasia

Description

BPH describes the gradual enlargement of the prostate as men age. It is not linked to cancer, however if untreated it can lead to other health issues (urinary issues, bladder or kidney damage, UTIs, kidney stones).

Pathophysiology

The pathophysiology of BPH is not very well understood. However the two theories that exist hypothesise a decrease in relative testosterone levels.

Theory 1 Unchanged Estrogen & Decreased Testosterone	= Estrogen, ↓Testosterone Testosterone, a hormone made by both the testes and adrenal glands, acts on the prostate. As men age, there are decreasing levels of testosterone in the blood. The unchanged production of estrogen relative to the decrease in testosterone gives the illusion that there is an excess of it - this is thought to cause BPH.
Theory 2 Increase in DHT & Decreased Testosterone	↑DHT, ↓Testosterone The second theory hypothesises that BPH is caused by older men having higher concentrations of DHT (a potent version of testosterone that supports the development of the prostate) and decreased levels of testosterone.

Risk Factors

- *Genetics*: Family history
- *Biology*: Hormonal changes, **ageing**
- *Lifestyle*: Obesity, lack of exercise

Signs & Symptoms

- Urinary frequency or urgency, difficulty starting urination, weak urine stream or a stream that starts and stops, dribbling at the end of urination, inability to completely empty the bladder
- Pain in the groin/pelvic area/genitals
- Discomfort or painful ejaculation

Diagnosis

- *Digital Rectal Examination (DRE)*: subjective examination
- *Prostate Specific Antigen (PSA)*: unspecific, may indicate BPH, prostatitis, or prostate cancer
- *Biopsy*

Lifestyle Modifications

- Limit excessive fluid uptake to avoid urination during the night (particularly caffeine and alcohol)
- Limit decongestants or antihistamines (antimuscarinic)
- Respond to urge, schedule bathroom visits
- Healthy diet, active lifestyle, keep warm

Pharmacological Treatment

BPAC Urinary Incontinence Treatment Guidelines

1. *Alpha-blockers*: doxazosin, tamsulosin, prazosin, terazosin
2. *5α-reductase inhibitors*: finasteride, dutasteride
3. *Surgery*: prostate removal

Note: *Combination alpha-blocker and 5α-reductase inhibitors*: finasteride + doxazosin

Medicine	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Alpha-blockers</i> Doxazosin, tamsulosin, prazosin, terazosin	Alpha-blockers relax the muscle of the prostate and bladder neck, which allows urine to flow more easily.	Postural hypotension	Dizziness, headache, retrograde ejaculation, dry mouth, gastro-intestinal disturbances, hypotension
[PRESCRIPTION] <i>5α-reductase inhibitors</i> Finasteride (Ricit) Dutasteride (Terod)	Inhibits the enzyme 5-alpha reductase, which metabolises testosterone → DHT. Decreased DHT levels leads to reduction in prostate size i.e. improves symptoms, increases urinary flow rate, and prevents BPH outcomes by reducing prostate enlargement through hormonal mechanisms	May take up to 6 months for it to work	Impotence, decreased libido, ejaculation disorders, breast tenderness and enlargement, mood changes

Baldness (Androgenic Alopecia)

[NZF Dermnet Hair Loss](#)

Description

Baldness typically refers to the excessive loss of hair from the scalp. This loss is usually and most commonly hereditary with age.

Pathophysiology

95% of hair loss in men is caused by androgenetic alopecia. This inherited trait that tends to give guys a receding hairline and a thinning crown is caused by genetic sensitivity to a byproduct of testosterone called dihydrotestosterone (DHT). It can manifest as:

1. Gradual thinning on top of the head
2. Circular or patchy bald spots

Risk Factors

Androgenic alopecia, genetics, *perceived* hair loss post-menopause, stress, iron deficiency, thyroid disorders, medicines.

Signs & Symptoms

Men: begins at the front and recedes back

Women: generalised and diffuse hair loss

Pharmacological Treatment

1. Minoxidil Solution (liquid or foam)
2. Finasteride Tablets

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PHARMACY ONLY] <i>Minoxidil 2% or 5%</i> Regaine	Prolong anagen growth phase of hair follicles This stimulates them to produce stronger, thicker hair. At stronger concentrations of around 5%, Minoxidil also increases blood flow to hair follicles, strengthening them.	<ul style="list-style-type: none">• Liquid or foam to rub into scalp daily• May cause hair to shed at first. New hair may be shorter and thinner than previous hair. May take 4 months before effect is seen. Discontinue treatment if no improvement after 1 year• Liquid must remain in contact with scalp for at least 4 hours	<ul style="list-style-type: none">• Local irritation, unwanted hair growth on adjacent skin, headache, change in hair colour and texture
[PRESCRIPTION] <i>Finasteride 1mg</i> Profal, Propecia	Increase testosterone levels 5α-reductase inhibitor (anti-androgen) which metabolises testosterone to DHT, therefore increases hair growth on the scalp.	(Not indicated for use in women) <ul style="list-style-type: none">• May take 3-6 month to see effect• Contact your doctor if you notice any changes in breast tissue such as lumps, pain, or nipple discharge.• Finasteride is excreted in semen—use a condom if sexual partner is pregnant or likely to become pregnant (may cause androgen excess in baby)	<ul style="list-style-type: none">• Impotence, decreased libido, ejaculation disorders, breast tenderness and enlargement

LGBTQIA+ RELATED CONDITIONS

Overview of Sexuality, Gender & Minority Stress Theory

Introduction to Sexuality & Gender

[LGBTAQI+ Health Navigator](#)

The LGBT community is a loosely defined grouping of lesbian, gay, bisexual, transgender, and other queer individuals united by a common culture and social movements. These communities generally celebrate pride, diversity, individuality, and sexuality.

Definitions of Sexuality <i>"Who you go to bed with" i.e. attraction</i>	
Gay	Sexual/romantic attraction to the same gender (predominantly male)
Lesbian	A person who identifies as female and displays sexual/romantic attraction to females
Bisexual	A person who displays sexual/romantic attraction to same and different genders
Demisexual	Only experiencing sexual attraction to people they have an emotional connection
Pansexual	Sexual/romantic attraction is based on personality/connection/physical characteristics regardless of the others assigned sex or gender identity
Asexual	A person who experiences no sexual attraction but with differing desires for sexual activity
Definitions of Gender <i>"Who you go to bed as"</i>	
Cisgender	Gender identity corresponds to birth sex
Transgender (MtF/FtM)	Gender identity differs from the sex which was assigned at birth
Non-binary	Gender identity that is neither male or female
Gender fluid	Does not identify as having a fixed gender
Gender non-conforming	Gender expression not limited by stereotypical masculine/feminine gender norms.
Intersex	Born with sex chromosomes, external genitalia and/or reproductive organs or both sexes

Health Disparities & Minority Stress Theory

HEALTH DISPARITIES FOR THE LGBTQIA+ COMMUNITY	
Problem	Explanation
General Health Care	Inequities, social stigma, hostile, low cultural competency from clinicians all create a legacy of distrust and avoidance
Aged Care	<ul style="list-style-type: none">LGBTQ+ are affected by distinct health-related issues, including same-sex partner separation in residential care, pressure on older trans people to transition back, end of life decision making<i>Privacy</i>: older adults may feel forced to conceal their identity and feel vulnerable due to historical stigma/abuse
HIV	<ul style="list-style-type: none">Highest risk in men who have sex with men (MSM)Need education, safe sex, PrEF, access to treatment
Mental Health	<ul style="list-style-type: none">Higher risk of experiencing distress, addiction, suicideServices are not adequate (e.g. long wait times, accessibility issues, trained providers)'Minority Stress' Theory: Stigma, prejudice, discrimination create hostile and stressful social environments that cause mental health problems
Gender-affirming Health Care	<ul style="list-style-type: none">Unmet needs: delivery of services are not kept up with demands

A note on Māori sexuality:

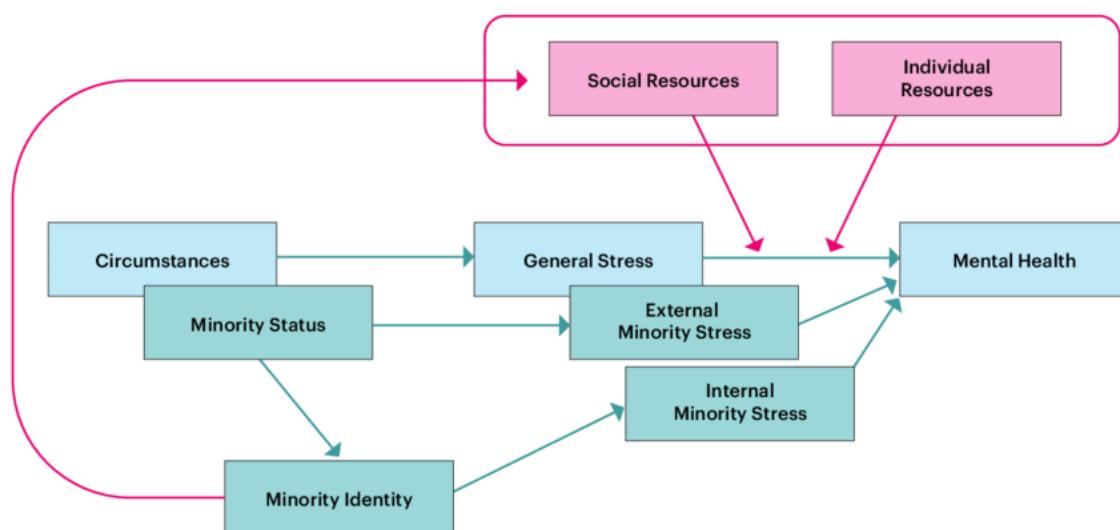
Takatāpui is a Māori term used in a similar way to LGBTQI+, demonstrating that this was openly accepted by Māori culture. However, the Impact of Colonisation;

- Religion (Christianity), British Law and social expectations all changed with colonisation.

Minority Stress Theory

Minority stress theory proposes that sexual minority health disparities can be explained in large part by stressors induced by a hostile, homophobic culture, which often results in a lifetime of harassment, maltreatment, discrimination, and victimisation (**in addition** to the general stressors of everyday life).

The theory thus proposes that difficult social situations cause stress for minority individuals, which accrue over time, resulting in long-term health deficits (e.g poor mental and physical health).



MINORITY STRESS THEORY	
Circumstances in the environment	The following circumstances are interconnected: 1. <i>General circumstances in the environment</i> : socioeconomic circumstances, living conditions 2. <i>Minority status</i> : sexual orientation, race, ethnicity, gender
Minority Status	These lead to stressors including: general stressors and minority stressors (internal and external)
General Stressors	Stressors experienced by all individuals. • E.g. job loss, death of a loved one
Distal (external) Processes	These stressors are exacerbated for minorities . • External Stressors: Distal stressors placed onto you by others • E.g. Losing a job due to discrimination or prejudice & violence
Proximal (internal) Processes	• Internal Stressors: Proximal processes that occur following exposure to distal processes, and affect your central thoughts/feelings • E.g. Fear of rejection, rumination, distaste for your own minority group
Coping & social support	Stressors are moderated by the following: 1. <i>Coping/Social Support</i> : • E.g. enhanced in-group identity, group solidarity/gay-affirming church 2. <i>Characteristics of Minority Identity</i> • E.g. how important is the identify to the individual) <i>Example: If an individual is exposed to a minority stressor (e.g., called a discriminatory name) but does not identify strongly with that identity, it is perhaps less likely to affect that individual's mental health patterns.</i>
Mental Health outcomes	All of the above eventually lead to poorer mental and physical health outcomes.

The Role of The Pharmacist

1. Create a safe, non judgmental environment for the individual to return to (e.g. using correct pronouns, not being judgmental, being culturally aware and sensitive)
2. Being aware of the many health disparities that afflict them.

Transgender Therapy

Masculinisation & Feminisation Therapy

NZF Hormone Treatments

Description

Gender-diverse, transgender, or trans describe individuals whose gender identity differs from the sex designation assigned to them at birth.

EFFECTS OF TREATMENT	
Male to Female (Transwomen)	Female to Male (Transmen)
<ul style="list-style-type: none">• Breast growth• Softening of the skin• Reduction and fining of body hair• Change in body fat distribution• Reduced muscle mass and strength in the upper body• Emotional change• Decline in libido• Decreased spontaneous erections• Testicular shrinkage and cessation of spermatogenesis	<p>Menstruation typically ceases in the first 3–6 months of testosterone treatment. In cases where this is delayed or distress arises from menstruation, progesterone can be used.</p> <p>There can be cyclical effects of aggression or an expansive mood at the start of the cycle and fatigue and irritability at the end.</p> <ul style="list-style-type: none">• Deepening of the voice• Increased muscle mass and strength (particularly upper body)• Change in body fat distribution• Increased hair growth (body and face)• Increase in skin oiliness and body odour• Atrophy of breasts, vulval and vaginal tissues• Clitoral enlargement• Cessation of menstruation

Complications

Being transgender or gender-diverse is associated with an increased risk of psychological harm, social exclusion, and discrimination. These people are at higher risk of experiencing mental health problems.

Additionally, many gender affirming treatments, including testosterone, gonadorelin analogues, and spironolactone are on the World Anti-Doping Agency Prohibited List for use in sport.

Pharmacological Treatment

Transgender Patients Prescribing Guidelines

In both genders, changes begin to appear in the first few months of treatment and usually reach a maximum after three to five years. Starting treatment after puberty will reverse or regress many primary and secondary sexual characteristics, but obviously some will persist to the extent that reassignment surgery might also be sought by some individuals.

Medical treatment should only occur after:

1. A thorough psychosocial assessment has been undertaken by a clinician experienced in the field (e.g. grading of gender dysphoria)
2. Informed consent has been obtained from the patient

Endocrinologist referral will then proceed to assess eligibility

1. Cardiovascular issues
2. History of clotting disorders
3. Smoking

*Standard treatment in adults is based on a **gender-affirming** hormone:*

1. Female to male: Testosterone
2. Male to Female: Estrogen, supplemented by an anti-androgen (spironolactone, cyproterone acetate)

Note: Puberty blockers can be used to prevent development of secondary sex characteristics during teen years e.g. GnRH analogues.

Complications of medicines

MALE TO FEMALE (FEMINISATION TRANSGENDER THERAPY)		
	Dosing	Side Effects
Estrogen	<p>Estradiol is preferred and is prescribed similar to HRT but at <i>higher doses</i>. Ethinylestradiol and conjugated equine estrogen's are avoided due to increased risk of VTE.</p> <p><i>Tablets</i></p> <ul style="list-style-type: none"> • Estradiol valerate tablets can be given in divided doses if nausea occurs <p><i>Patches</i></p> <ul style="list-style-type: none"> • Patches can be used for any age but are preferred in transwomen of > 40 years to reduce risk of VTE <p><i>Implants</i></p> <ul style="list-style-type: none"> • Dose depends on BMI <p><i>Creams</i></p> <ul style="list-style-type: none"> • Creams are insufficient for transgender therapy 	
		N/V, headache Tachyphylaxis can develop with long-term implant use, abdominal cramps, breast cancer, changes in skin
Anti-Androgens	<p>Cyproterone and spironolactone Suppress production and effects of endogenous androgens to reduce masculine characteristics at higher doses.</p>	<p><i>Cyproterone</i> Mood swings, weight changes, changes in hair pattern, fatigue, acne improvement</p> <p><i>Spironolactone</i> Polyuria, polydipsia, postural hypotension, GI disturbances, fatigue</p> <p>Hyperkalaemia is also possible, particularly in patients with impaired kidney function or taking potassium-retaining drugs such as ACE inhibitors.</p>
Progesterone	<p>Progesterone is used by some clinicians in addition to estrogens and anti-androgens.</p> <p>May improve breast development.</p>	Depression, weight gain, increase in lipids

FEMALE TO MALE (MASCULINISATION TRANSGENDER THERAPY)

	<p>Testosterone is available in a range of formulations and doses aim to reach male physiological concentrations.</p> <p><i>Injection (First choice)</i> Administered every 2-3 weeks by HCP or patients if suitable.</p> <p><i>Tablets</i> Unsuitable in gender affirming therapy as it is unlikely to achieve physiological concentrations or suppress menstruation.</p> <p><i>Patches</i> Similar evidence of masculinisation compared to injections/tablets but take a longer time thus are less preferred.</p> <p><i>Gels & Creams</i> Less commonly used due to practicality e.g swimming/bathing restrictions following applications and fear of contaminating women/children.</p>	Acne, sleep disorders, fluid retention
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General Monitoring

Individuals receiving hormone treatments should be assessed before treatment and regularly during treatment for conditions which may be exacerbated by administration of sex hormones, or suppression of endogenous hormones.

- *ADRs*: At 4 months, then every 6-12 months
- *Cardiovascular risk factors*: Weight, blood pressure, lipid profile, smoking status, diabetes screening
- *Organ function*: Liver function, Renal function
- *Electrolytes*: Annually, more frequently if using spironolactone as androgen suppression
- *Bone mineral density*: If risk factors for osteoporosis e.g. those who stop hormone therapy after gonadectomy or are non-compliant with hormone therapy

Counselling Points

- Need to take medications life-long
- Reduces fertility

MONITORING OF FEMINISING HORMONE TREATMENTS		
What	Description	When
Serum-Testosterone Concentration	Ensure adequate suppression of endogenous testosterone	Every 3–6 months for the first year and then annually thereafter
Serum-Estradiol Concentration	Ensure levels remain within the normal physiological range for females.	Every 3–6 months for the first year and then annually thereafter
Prolactin Levels	Baseline measurement and periodic monitoring	Every 2 years: for prolactinoma associated with estrogen treatment.
Prostate and Testicular Disease	Monitor if tissues are present.	-
Breast cancer screening	Recommended for non-transgender females and offered if on estrogen.	-
Medicines	BP & Hyperkalaemia with Spironolactone	-
Other	Clotting risk (DVT, PE, Stroke), bone mineral density, migraines with aura	-

MONITORING OF MASCULINISING HORMONE TREATMENTS		
What	Description	When
Serum-Testosterone Concentration	Ensure levels remain within normal physiological range for males.	Every 3–6 months for the first year and then annually thereafter
Haematocrit and haemoglobin	Before treatment, increased risk of clotting.	At 3, 6, and 12 months after initiation, and then annually thereafter
Breast cancer screening	Advised where surgical removal of tissues is incomplete	Annual sub- and peri-areolar breast examination is recommended if mastectomy performed

Renal Function and Hormonal Gender-Affirming Therapy

Duration of Hormonal Gender-Affirming Therapy	Recommendation for IBW Dosing	Recommendation for Estimation of Renal Function
Patient is not taking gender-affirming hormonal therapy <i>or</i> started therapy <1 mo prior to admission	Calculate IBW based on sex at birth.	Calculate renal function based on sex at birth.
Initiation of therapy <6 mo prior to admission	Consider calculating IBW based on sex at birth.	Consider calculating estimated renal function based on sex at birth.
Initiation of therapy ≥6 mo prior to admission	Consider calculating IBW based on gender identity.	Consider calculating estimated renal function based on gender identity.

PREGNANCY & BREASTFEEDING

Introduction to Pregnancy

Drugs in Pregnancy & Breastfeeding by Briggs (11th Edition)

When an egg is fertilised by sperm in the fallopian tubes, a zygote is formed. Within 3-5 days, if implantation occurs on the endometrial wall of the uterus, a woman is said to be pregnant.

Diagnosing a Pregnancy

There are multiple ways to diagnose a pregnancy and at different stages of the pregnancy. However the first sign should be a missed period.

1. *Blood Test (more sensitive)*: human chorionic gonadotropin (hCG) detectable **6-8 days** from the time of suspected conception. Also high estrogen and progesterone levels.
2. *Urine Test*: depending on test sensitivity, hCG detectable at **10 days**
3. *Gynaecologist visit*: ultrasound at **6-7 weeks**

Lead Maternity Career (LMC)

Pregnant women choose one lead professional (independent or hospital based midwife, GP, private obstetrician) to provide and coordinate care throughout pregnancy, and for 4-6 weeks after birth (FUNDED by MOH). Services include counselling, psychological support, education & advice, health promotion, antenatal screening, risk assessment & treatment when required.



Note

It is important for pregnant women to discuss with the GP any changes needed in medicines.

Pregnancy Stages & Physiological Changes

Development from Fertilisation				
Timeline	N/A	Gestational period (between fertilisation and birth) Estimated to be 38 (± 2) weeks from the first day of your last menstrual period		
		Fertilisation	Gestation to 9 weeks	Birth to 6 weeks post-gestation
Developmental stage	Egg	Zygote → Blastocyte → Embryo Cells at the implantation site develop to form the placenta	Fetus *A chance of viable birth begins at 23 weeks.	Neonate
Types of Birth	1. Natural delivery 2. Caesarean birth (C-section; surgical incision through abdomen and uterus)			

Stages of Pregnancy	
	Description
First Trimester (1-3 months)	<p>Weeks 0 - 12</p> <ul style="list-style-type: none"> This is the most important trimester. All vital structures (e.g. organs) form but are not all yet fully functional. Heart, brain, lungs, eyes, arms, legs, placenta and umbilical cord. Embryo grows to 4cm. Miscarriages are likely at this stage.
Second Trimester (4-6 months)	<p>Weeks 13 - 28</p> <ul style="list-style-type: none"> Organs continue to develop and movement can be felt. The fetus recognises voices and grows hair and nails. By the end of the 2nd trimester, the fetus is about 36cm long and about 1kg weight. Amniocentesis is performed here
Third Trimester (7-9 months)	<p>Weeks 29 - 40</p> <ul style="list-style-type: none"> The fetus gains most of its weight during this trimester and is able to grasp objects as well as open and close its eyes. This is the safest trimester for medicines.

Important Structures during Pregnancy	
	Description
Placenta	<ul style="list-style-type: none"> Develops in the uterus during pregnancy, and is connected to the embryo via the umbilical cord. Provides nourishment, oxygen, substances from the mother to baby. Removes waste It is eventually expelled out of the body following birth. However, if it is obstructing the birth canal, a C-section may be required.
Amniotic Fluid	<ul style="list-style-type: none"> The watery substance surrounding the fetus in the womb It helps to cushion the baby from external force. Standard amniocentesis performed 15 - 20 weeks gestation to test for genetic abnormalities & gender Sac will typically rupture at the beginning of labour — “the water is breaking”

Physiology during Pregnancy	
	Description
Medicines	<p>Medicines doses may need to be increased and dosed more frequently due to changes during pregnancy:</p> <ol style="list-style-type: none"> ↑ Plasma volume, ↑ Volume of distribution, ↑ Cardiac output Kidneys: ↑ GFR Metabolism: ↑ Hepatic enzymes, ↑ Metabolism of drugs (particularly anti-epileptics)
Coagulation	Pregnancy renders the woman in a hypercoagulable state. Careful monitoring of coagulation parameters and an adjustment (increase) of anticoagulants is required
Thyroid Function	Thyroid medicine doses may need to be increased as pregnancy increases thyroid function
Placental Transfer	Medication of low MW and high lipophilicity are more likely to transfer to baby
Teratology	<p>See FDA Classification system for teratogenicity classification</p> <ol style="list-style-type: none"> Thalidomide (first trimester → phocomelia) Warfarin ACEI Valproic acid (lamotrigine is safe in pregnancy) Carbamazepine

Maternal & Neonatal Immune System		
	Maternal	Neonatal
Description	<p>Has two main roles to facilitate foetal development.</p> <p>However, this increases susceptibility to and/or severity of diseases where cellular responses are important (only innate immune system functions)</p>	<p>The newborn immune system is underdeveloped, such that it is tolerogenic, non-reactive, and immunologically naive, with the absence of memory and underdeveloped microflora so that it doesn't kill the mom</p> <p>New born infants and children >2yo are thus highly susceptible to infections. Premature babies even more so.</p>
Roles	<ol style="list-style-type: none"> 1. <i>Don't kill the foetus</i> <ul style="list-style-type: none"> • As the foetus is a foreign object, the maternal immune system modifies itself to prevent its murder. • Dampening of acquired immune response occurs (immune cells CD4, CD8, T and B cells) with increasing levels of progesterone at later stages in the pregnancy. 2. <i>Protect foetus/newborn</i> <ul style="list-style-type: none"> • Protection from in utero congenital infections • Transfer of maternal immunity 	<p><i>Maternal immunity protects the child</i></p> <ol style="list-style-type: none"> 1. <i>During gestation:</i> crossing of Maternal IgG across the placenta. By 20 weeks gestation, the baby has a full T cell repertoire. 2. <i>After birth:</i> breast milk contains IgA and leukocytes while the baby produces only IgM for the first 6 months. Full term baby is born with all of their T cells. 3. <i>After 1 year:</i> all maternal IgG is absent

Introduction to Breastfeeding

Recommendations

The WHO recommends that all babies be exclusively breastfed for 6 months, then gradually introduced to appropriate foods after 6 months while continuing to breastfeed for 2 years or beyond. Breastmilk changes as your baby's needs change (provision of antibodies to provision of nutrients, etc...)

Benefits

Breastfeeding has many benefit, including reducing constipation (easily digested), decreasing fat storage in the baby, provides protection against infections (particularly mother's first milk; colostrum), and reduces the risk of allergies.

Breastfeeding Hormones

	Trigger for release	Medical Uses
Oxytocin	<p>There are 4 triggers for oxytocin release which occurs via stimulation of the hypothalamus and posterior pituitary:</p> <ol style="list-style-type: none"> 1. <i>Uterine stretch</i> (indicates the baby is too big) → induces contractions 2. <i>Cervical dilation</i> → Labour (induces oxytocin positive feedback loop) 3. <i>Suckling</i> → Mammary Gland for Milk production 4. <i>Sexual stimulation</i> → CNS for Mating & Parenting behaviour 	Induction of labour
Prolactin	<p>Prolactin release occurs via stimulation of the hypothalamus (PFT or TRH) and anterior pituitary:</p> <ol style="list-style-type: none"> 1. <i>Sucking</i> → Mammary Gland: <ul style="list-style-type: none"> • Milk-let down (in 1-2 days) • Development of mammary tissue during pregnancy • Inhibition of GRH to prevent ovulation 	<p>Domperidone (Dopamine Antagonist)</p> <ul style="list-style-type: none"> • Milk expression
Dopamine	Dopamine inhibits the pathway for prolactin secretion	<p>Bromocriptine (Dopamine Receptor Agonist)</p> <ul style="list-style-type: none"> • Prevents prolactin production (prevents lactation)

Recommended Lifestyle, Immunisations & Supplements

Recommended Lifestyle

In Pregnancy

- Consume foods and beverages rich in folate, iron, calcium, and protein.
- Eat breakfast everyday.
- Consume pre-natal supplements (see below)
- Smoking, alcohol, drug cessation, light to moderate exercise (enough to talk, but not sing)
- Eat foods high in fibre and drink fluids (particularly water) to avoid constipation.
- Vaccinations — what are recommended prior to conception and during pregnancy
- Maintain healthy BMI (high BMI could lead to eclampsia)

In Breastfeeding

Any dietary restrictions you were on when pregnant **don't** apply during breastfeeding

- Include protein foods 2-3 times a day (meat, poultry, fish, eggs, beans, nuts, etc..)
- Eat 3 servings of vegetables
- Include whole grains (oatmeal, whole bread)
- Drink water to avoid dehydration
- If you are on a vegetarian diet, you are likely to need B12 supplementation.
- Natural foods that increase milk supply (fenugreek, fennel, alfalfa, blessed thistle, brewer's yeast, moringa, shatavari, milk thistle, goat's rue, vitex, pumpkin, protein rich foods (chicken, eggs, tofu, lean meat)

Recommended Immunisations

1. Pre-conception (*live vaccines*)

- MMR
- Chickenpox
- Pneumococcal

2. Before /during pregnancy

- Pertussis: from 16 weeks onwards
- COVID: anytime
- Flu: anytime

Recommended Supplements

Pregnancy and breastfeeding are times when women may need additional nutrients in their diet. Supplement can be prescribed by GP, Midwives, Obstetricians, Pharmacist prescriber, and Dietician.

	Supplement	Dose & MoA
Highly Recommended	Folic Acid (Folate)	<p>Reduces the risk of NTD (Neural Tube Defect/Spina Bifida) <i>800mcg OD for:</i></p> <ul style="list-style-type: none"> • At least 4 weeks before pregnancy and first 12 weeks of pregnancy. • If you are already pregnant and have not started taking any folic acid, start now! <p>5mg OD if:</p> <ul style="list-style-type: none"> • Higher risk of NTD (history of NTD affected pregnancies, family history) • Taking medicines that cause folate deficiency (anti-epileptics, methotrexate) • Diabetes pregnancy (NZSSD) <p>Folic acid protects against the risk of neural tube defects of the brain and spinal cord. It is a naturally occurring vitamin B that the body needs (found in leafy green vegetables, citrus fruit and juices, wholemeal bread, brown rice,, cereals, liver, peas, beans)</p> <p>Note: Funded folic acid tablets contain gluten, therefore in celiac disease, cut the tablet (i.e. quarter the 5mg tablets) so that 1mg will be absorbed (higher than normal) - does not address gluten sensitivity</p>
	Iodine (Potassium Iodate)	<p>For normal brain development & prevention of hypothyroidism <i>150mcg OD (NeuroTabs):</i></p> <ul style="list-style-type: none"> • Throughout pregnancy and breastfeeding.
Recommended	Vitamin D	<p>For efficient absorption of calcium from gut & bone mineralisation (reduces development of rickets) <i>1.25mg (1000IU) monthly</i></p> <ul style="list-style-type: none"> • Only under specific circumstances (e.g. woman with darker skins, indoor places, sunlight deficiency)
Additional (under certain circumstances)	Vitamin K	<p>If cholestasis in late pregnancy Vitamin K deficiency and impaired coagulation in cholestasis result from malabsorption of fat soluble vitamins caused by reduced bile drainage.</p>
	Omega 3	If low dietary levels
	Vitamin B12	<p>Recommended in vegetarians and vegans in pregnancy and lactation. Deficiency may cause neurological sequelae in exclusively breastfed infants</p>
	Iron	<p>May be required as blood volume increases in late pregnancy (i.e. in the final 10 weeks). Also may be a chance of postpartum haemorrhage (bleeding after pregnancy)</p>
	Calcium	<p>May be needed in late pregnancy for bone growth and pre-eclampsia. If low dietary levels (e.g. lactose intolerance)</p>
AVOID	Vitamin A (retinol)	Contraindicated in pregnancy — induces birth defects

Community Support Lines

For New Mums & Newborn Health

COMMUNITY SUPPORT FOR NEW MUMS AND NEWBORN HEALTH		
	Support Line	Description
Pregnancy	LMC	See pregnancy & breastfeeding initial chapter
	Parent helpline	Parent Helpline offers compassionate, friendly, non-judgemental support and advice on all parenting issues: 0800 568 856 from 9am to 9pm seven days a week
	National Women's Health	Povides high-quality health services for women who need maternity, newborn, gynaecology and fertility care.
Breastfeeding	La Leche League ND	Help mothers to breastfeed through mother-to-mother support, education, information, and encouragement and to promote a better understanding of breastfeeding as an important element in the healthy development of the baby and mother.
	New Zealand Breastfeeding Alliance (NZBA)	Protect and support breastfeeding in New Zealand
	New Zealand Lactation Consultants Association (NZLCA)	Foster optimal maternal and child health by protecting, promoting and supporting breastfeeding and the use of human milk for infants
	KellyMom	Breastfeeding and parenting guide
	Te Rito Ora	free community-based service that provides breastfeeding and baby feeding information and support for all mothers and babies who live in South Auckland
	Breastfeeding New Zealand	May be useful for quick help. They regularly run live chat sessions for people to get some instant advice.
Postpartum	Well Child	Free to all children from birth to 5 years (not government funded, fundraising to support). Includes 12 core contacts , as well as GP checks at 6 weeks (linked to the 6 week immunisations).
	Plunket	NZ's largest provider of support services for the development, health, and wellbeing of children under 5 . Free for all families (non-for profit organisation).
	Bellyful	Provides meals for families with newborn babies and families with young children who are struggling with illness.
	Multiples NZ	Is a nationwide parent-led support network supporting families in their journey from expecting to raising multiples.
	Parents Centre	Parent education programmes aim to assist parents with the various ages and stages of their children, giving them the knowledge and skill sets to be effective.

Example: Well Child Tamariki Ora



Common Complaints

Introduction

We will look into common presenting complaints in pregnant and/or breastfeeding women. Some particular issues in breastfeeding include:

1. Engorged breasts: breast too full of milk: cold press (cabbage leaves), pads
2. Latching pain: incorrect technique from the baby which results in:
 - Sore, cracked nipples: lanolin/shields (ok for baby)
 - Blocked ducts and mastitis — refer to GP
 - Inverted or flat nipples: causes milk to leak out
 - Tongue-tie: baby can't stretch tongue — refer to GP/midwife
 - Low milk supply: keep feeding/supplements to increase

Common Symptoms in Pregnancy

Description

Hormonal changes in pregnancy can cause the following:

Symptom	Description	Timing	Non-Pharmacological Treatment	Pharmacological Treatment
Nausea & Vomiting	Common early symptom of early pregnancy - caused by rising levels of hCG, which is produced shortly after implantation.	Begins 1st trimester and resolves usually by 16-20 weeks gestation (commonly by 12 weeks)	<ul style="list-style-type: none"> • Drink small amounts of water/liquids often • Avoid fatty/spicy/salty/harsh foods • Avoid an empty stomach • Dry biscuits can help morning sickness • Acupressure wrist band 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Ginger capsules, B6 capsules • Promethazine, Prochlorperazine, Cyclizine, Metoclopramide • Ondansetron • Doxylamine, Electrolytes
Heartburn	GORD is a normal part of pregnancy - it is due to the baby pushing against the stomach we as well progesterone valve-relaxation	Begins late first trimester/early second trimester and becomes more severe and frequent as gestation progresses	<ul style="list-style-type: none"> • Avoiding salty, spicy foods • Lying down after a big meal • Maintain healthy weight • Eating food slowly and thoroughly 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Antacids • Ranitidine • Omeprazole
Constipation	High levels of progesterone can cause this. It can also be caused by medicines prescribed for N&V, antacids, strong painkillers and supplements (iron, calcium, multivitamins)	Begins 1st trimester - could resolve over time or worsen as the uterus grows.	<ul style="list-style-type: none"> • Increase fluids and fibre • Be physically active • Eat more wholegrain cereals, vegetables and fruit, especially skin • Don't delay bowel motions • Avoid straining! 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Fibre supplements • Osmotic Laxatives (short term) <p>Avoid other types of laxatives as they can cause abdominal cramping.</p>
Haemorrhoids	Occur due to constipation and/or pressure from the enlarged baby/uterus.	Usually around 3rd trimester	<ul style="list-style-type: none"> • See constipation section • Icepack can reduce swelling • Warm bath can reduce pain 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Osmotic laxatives • Paracetamol for soreness • Haemorrhoid creams (first line is anusol, second line is proctosedyl or ultraproct)
Vaginal Thrush	Increased estrogen levels increases the risk of thrush.	Any time	<ul style="list-style-type: none"> • Glucose control in diabetes • Aerating area • No soaps, perfumes, douching • Wipe front to back 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Clotrimazole cream 1% • Miconazole cream 2% • Oral Fluconazole contraindicated
Tender & Swollen Breasts	Hormonal changes can cause this and darken and widen the area around the nipple.	1-2 weeks after conception	<ul style="list-style-type: none"> • Loose fitting clothes • Cold compress • Warm showers 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Paracetamol
Backache	Pregnancy softens body ligaments to prepare you for labour. Additionally, the extra weight of the uterus can also add to the problem.	All trimesters due to different reasons (first - stress, change in hormones; third - baby is big)	<ul style="list-style-type: none"> • Firm mattress • Flat shoes • Sit straight with supported back • Don't stand/sit for long periods • Get enough rest, regular exercise 	<i>For severe symptoms</i> <ul style="list-style-type: none"> • Paracetamol • Topical capsaicin cream • Do not use ibuprofen or voltaren emulgel

Tiredness	Feel a constant need to nap.	Reduces in second trimester and returns in the last trimester.	<ul style="list-style-type: none"> • Just sleep 	N/A
Mood Swings	Changes in hormones can make you feel hungrier, irritable, overwhelmed.	Early gestational days	<ul style="list-style-type: none"> • Get enough rest, eat well, exercise 	N/A
Frequent Weeing	Pressure of baby on the uterus	Worsens as pregnancy progresses	<ul style="list-style-type: none"> • Maternity pads 	N/A
Light spotting & cramping	Fertilised egg attaching to lining of the uterus. May also feel mild cramping.	Initially	N/A	N/A
Cravings	Overwhelming desire to eat a certain type of food (even things you don't normally eat)	Initially (first trimester)	N/A	N/A
Metallic Taste (dysgeusia)	Increased estrogen associated with pregnancy can cause a metallic taste	This sensation usually improves greatly/ends entirely after first trimester.	N/A	N/A

Mastitis

[BPAC Mastitis Management](#)

Description

Mastitis is an inflammatory condition of the breast tissues that may either be *infectious* or *lactational* in nature. Infectious mastitis is accompanied by systemic symptoms and can be bacterial or fungal. Lactational mastitis occurs due to prolonged engorgement of milk ducts due to poor milk drainage (milk stasis) — this may be related to nipple trauma.

It is a common preventable complication during breastfeeding (usually occurs within 3 months). It can often be self-managed; however many breastfeeding women do not get the information or support they need to avoid mastitis or manage it if it does occur.

Risk factors

- Blocked milk duct, cracked skin for bacterial entry
- *Lactational Mastitis*: Milk stasis (baby not latching on properly) and nipple trauma

Symptoms

Breast pain, swelling, warmth, lump, **systemic symptoms** (fever, chills, malaise **in infectious mastitis**)

Non-Pharmacological Treatment

1. Breastfeed frequently (particularly from affected breast) to keep milk flowing, massage, warm or cold compresses, warm shower.
2. Latching methods with Plunket
3. Breastfeed frequently and regularly drain breast
4. Gently massage lumpy area under hot shower or heat
5. Keep feeding! Feed baby first with the affected breast.



Compresses in Mastitis: Cold or Warm?

Cold compress *after* feed and warm compress *before* feed

Pharmacological Treatment

[BPAC Mastitis Antibiotic Guidelines](#)

1. Bacterial Infection:

- Flucloxacillin empiric antibiotic therapy
- Antibiotic crosses milk in very **small** amounts: monitor baby for ADRs (e.g. diarrhoea, rash)

2. Pain relief: Paracetamol or Ibuprofen

OSCE Points

- Flucloxacillin on empty stomach — finish whole course
- Warm shower before, cold compress after feed, gently massage breast
- Keep feeding (with the affected breast first) — flucloxacillin okay for breastfeeding

Low Milk Supply

Description

Some mothers worry they do not have enough milk, however this is in response to a baby feeding more often than normal. Mothers do not have to worry as long as the baby appears healthy and active AND is gaining weight AND having 6 or more wet nappies a day.

Occasionally, a baby may not be getting enough milk due to incorrect latching or sucking. This may require contact with midwife or lactation consultant.

Non Pharmacological Treatment

- Supplements: fennel seeds, pumpkin seeds

Cracked Nipples

Description

A dry, sore, irritated and cracked nipple is often the result of babies latching on improperly.

Signs & Symptoms

Symptoms include soreness, crusting, oozing and bleeding of the nipple tissue.

Non Pharmacological Treatment

- Soothing cream e.g. lanolin
- Proper latching technique e.g. Planet, Lactation Consultant
- Rubbing breast milk onto the nipple
- Breast or nursing pads (contain Manuka honey) — protect the nipple, relieve discomfort and absorb excess milk/any leakage between feeds. After each feed, let your nipples dry before getting dressed – change your breast pads after every feed.
- Please note, nipple shields are not recommended unless the mother has inverted nipples

Pharmacological Treatment

1. *Barrier Creams e.g. lanolin, hydrogen dressing, vaseline*

Purified lanolin or a hydrogel dressing can soothe cracked nipples and help them retain moisture.

2. *Topical Antibiotic*

If nipple becomes infected

Weaning & Infant Formula

Description

Babies should be exclusively breastfeed until they are around 6 months old. After this, mothers should reduce feeding gradually and infant formula may be advised. During this time, the breasts may become engorged with milk, expressing a little milk will make them more comfortable.

A note on Infant Formula

Infant formulas are formulated to contain differing levels of whey and casein depending on the baby's age, as well as the recommended essential vitamins and minerals. Most infant formulas are derived from cow's milk, although goat's milk, soy-based, lactose-free, and hypoallergenic formulas are available. Regular cow's milk must not be used for infants less than one as it contains higher levels of protein and salt and not enough iron and other nutrients for a growing baby.

Formulas are age-based: 0-6 months, 6-12 months, >12 months

- Use within 4 weeks of opening

Nipple Thrush

Description

Thrush in a breastfeeding baby can result in infection of the mother's nipple.

Pharmacological Treatment

Treat the mother and baby simultaneously

1. *Oral antifungal liquid for the baby*

- Nystatin (Nilstat drops)

2. *Topical Antifungals for the mom's nipple*

- Clotrimazole (canesten) or Miconazole (Daktarin)
- Cream should be applied following feeds and excess cream should be removed from the nipple before breastfeeding.

Hypertensive Disorders

Overview & Treatment Summary of Hypertensive Disorders

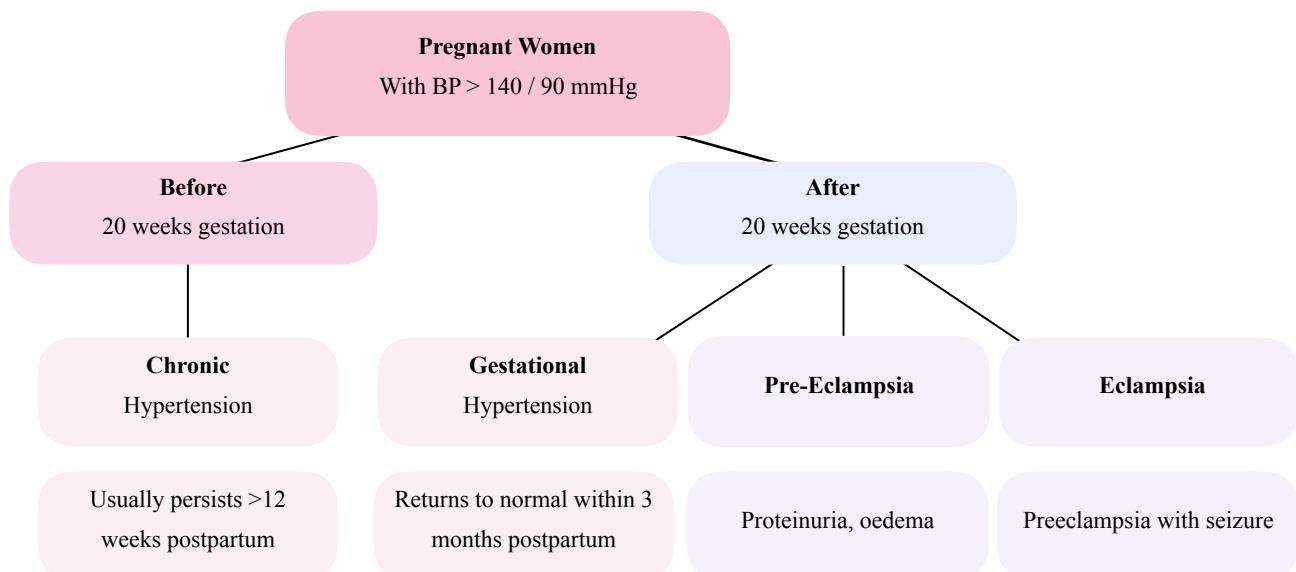
Introduction

[Hypertensive Disorders in Pregnancy Management PDF](#)

Hypertensive disorders are a condition in which vasospasm occurs during pregnancy in both small & large arteries. High blood pressure is generally of concern as the increased blood vessel resistance may hinder blood flow in many different organ systems in the expectant mother including the liver, kidneys, brain, uterus, and placenta and additionally, also may mean the baby isn't getting nutrients it needs.

Normally, blood pressure in pregnancy decreases and increases back to its normal value by mid-second trimester. However certain factors can affect this process and induce hypertensive disorders in the gestational period - for example the amount of blood increases (by as much as 45%!).

We will look into three hypertensive disorders: gestational hypertension, pre-eclampsia and eclampsia. As the latter two are much more severe manifestations, we aim to prevent their progression in pregnant women presenting with chronic or gestational hypertension. Please find an overall summary below:



	When?		Postpartum BP returns to normal?	Abnormalities?
	Before 20 weeks	After 20 weeks		
Chronic HTN	Y	-	N (persists > 12 weeks)	-
Gestational HTN	-	Y		-
Pre-eclampsia	-	Y	Y (within 3 months)	Y
Eclampsia	-	Y		Y?

Pharmacological Treatment Summary

To avoid the risk of complications from elevated blood pressure in pregnancy such as progression to pre-eclampsia - the following should be initiated:

1. *Anti-Hypertensive Therapy e.g. labetalol, nifedipine, methyldopa, hydralazine*
 - Anti-hypertensives of choice differ - this is mainly because of the teratogenic potential some of these medications carry. ACEI and ARBs should generally be avoided in pregnant women for example!

2. *Supplements to prevent progression to pre-eclampsia e.g. aspirin and calcium*
 - Pre-eclampsia is not completely preventable, therefore close monitoring of those at risk (chronic/gestational HTN) is crucial. Women at high risk should be given dietary advice/supplementation (by Midwife or GP) and educated about signs and symptoms of pre-eclampsia:

Treatment of Hypertension in Pregnancy			
	Drug	Mechanism of Action	Side Effects
Chronic or Gestational Hypertension	[PRESCRIPTION] β -Blocker Labetalol (Trandate)	Labetalol non-selectively antagonises β -adrenergic receptors (careful in asthmatics), and selectively antagonises alpha-1-adrenergic receptors	
	[PRESCRIPTION] DHP CCB Nifedipine (Adalat)	Relaxation of blood vessels, induce peripheral vasodilation to decrease blood pressure.	Tachycardia, palpitation, flushing, hypotension, fluid retention, GI disturbances.
	[PRESCRIPTION] Methyldopa	α 2 sympathetic agonist which acts to decrease peripheral resistance and venous constriction.	
	[PRESCRIPTION] Hydralazine	Interferes with calcium transport to relax arteriolar smooth muscle and lower blood pressure.	
Pre-Eclampsia Supplementation	[PRESCRIPTION] Aspirin	100mg at night between 12-16 weeks of pregnancy and continue until the baby is born Low dose aspirin suppresses the production of prostaglandins and thromboxane and inhibiting inflammation and platelet aggregation.	
	[PRESCRIPTION] Calcium	1g elemental Ca daily throughout pregnancy Low Ca may cause high BP, hence calcium will prevent preterm labour and birth + may increase magnesium level	
Seizure Prevention	[PRESCRIPTION] Anticonvulsant IV Magnesium Sulfate (DBL Magnesium Sulfate Concentrated)	The mechanism of action is unclear but it is thought that magnesium acts to increase the seizure threshold by inhibiting NMDA receptors, thereby limiting the effect of glutamate. Will not stop current seizures but will prevent future ones.	Hypermagnesemia, N/V, thirst. Magnesium Sulfate Toxicity [BURP]: • ↓ BP (heart block/collapse of circulatory system) • ↓ Urine output • ↓ Respiratory rate (respiratory paralysis) • Patellar reflex • Death Reversal agent for magnesium toxicity is calcium gluconate .

Chronic Essential Hypertension (Pre-existing HTN)

Description

Chronic Essential Hypertension is high blood pressure that was present before pregnancy (diagnosed before 20 weeks of pregnancy), and usually persists >12 weeks postpartum (3 months).

Signs & Symptoms

- Systolic BP \geq 140 mmHg **and/or**
- Diastolic BP \geq 90 mmHg

Complications: Progression to pre-eclampsia

Pharmacological Treatment

1. Consider labetalol, nifedipine, methyldopa as anti-hypertensive therapy (switch ACEI/ARB to these)
2. Consider aspirin and calcium (for prevention of pre-eclampsia)



Preventing Pre-Eclampsia

Aspirin: 100mg at night between 12-16 weeks of pregnancy and continue until the baby is born

Calcium: 1g elemental Ca daily throughout pregnancy

Monitoring & Management

Target BP: <140/100

What	Antenatal Period	Intrapartum	Postpartum
Anti-hypertensive treatment	<ul style="list-style-type: none">• Change ACEI to first line anti-hypertensives in pregnancy	<ul style="list-style-type: none">• Continue anti-hypertensives	<ul style="list-style-type: none">• If on methyldopa, change to another anti-hypertensive
Mother	<ul style="list-style-type: none">• Monitor BP• Monitor progression to pre-eclampsia	<ul style="list-style-type: none">• Monitor BP hourly	<ul style="list-style-type: none">• Daily BP for first week after birth and then weekly for 6 weeks.
Baby	<ul style="list-style-type: none">• Monitor fetus growth	<ul style="list-style-type: none">• Deliver before 38 weeks if maternal/fetal complications	

Pre-existing/chronic hypertension

(Hypertension confirmed pre-conception or before 20 weeks gestation)

Pre-pregnancy or at first visit

- Change from ACE inhibitors to alternative antihypertensive
- Note increased risk factor for pre-eclampsia
- Initiate calcium
- Initiate aspirin from 12 weeks' gestation
- Refer to obstetric team (see referral codes 1014, 1015)
- Educate about signs and symptoms of pre-eclampsia

- First-line antihypertensives**
- Labetalol
 - Nifedipine
 - Methyldopa

Maternal monitoring

- Begin usual schedule of antenatal visits but monitor blood pressure more closely if blood pressure is unstable
- Aim to control hypertension at pre-pregnancy range or lower

Fetal monitoring

If scanning raises fetal growth concerns:

- conduct USS, AFV, umbilical artery Doppler and CTG if indicated
- follow SGA guidelines for management if diagnosed

Timing of birth

- **Before 37 weeks:** Do not recommend birth unless other maternal or fetal indications support it
- **After 37 weeks:** For women with low risk of adverse outcomes, consider expectant management beyond 37 weeks with increased monitoring

Intrapartum

- At least hourly BP in labour
- Continue antihypertensives

Postpartum

- If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor
- Daily BP to 7 days after birth, then at least weekly to 6 weeks
- Give woman's GP a comprehensive discharge summary

Gestational Hypertension

Description

Pregnancy-induced hypertension develops after 20 weeks gestation in a woman that was normotensive before this. It presents without any of the abnormalities that define pre-eclampsia, and usually returns to normal within 3 months postpartum.

Symptoms

- Systolic BP \geq 140 mmHg **and/or**
- Diastolic BP \geq 90 mmHg

Complications: Progression to pre-eclampsia, placental abruption and impaired fetal growth

Pharmacological Treatment

- Consider labetalol, nifedipine, methyldopa
- If SBP > 160mmHg or DBP > 110 mmHg: Oral Nifedipine, IV labetalol, IV hydralazine
- Consider aspirin and calcium for prevention of pre-eclampsia



Preventing Pre-Eclampsia

Aspirin: 100mg at night between 12-16 weeks of pregnancy and continue until the baby is born

Calcium: 1g elemental Ca daily throughout pregnancy

Monitoring & Management

Target BP: <140/100

What	Antenatal Period	Intrapartum	Postpartum
Anti-hypertensive treatment	• Change ACEI to first line anti-hypertensives in pregnancy	• Continue anti-hypertensives	• If on methyldopa, change to another anti-hypertensive
Mother	• Monitor BP: 1-2 weekly • Monitor progression to pre-eclampsia: weekly proteinuria	• Monitor BP hourly	• Daily BP for first week after birth and then weekly for 6 weeks.
Baby	• Monitor fetus growth	• Deliver before 38 weeks if maternal/fetal complications	
Other HCP	Involve obstetrician and LMC		

Gestational hypertension

New onset of hypertension after 20 weeks' gestation without signs of pre-eclampsia and dBP ≥ 90 OR sBP ≥ 140 mmHg

At diagnosis

- Spot urine protein creatinine ratio (PCR)
- Pre-eclampsia bloods
- Prompt referral to obstetric team (see referral code 4009)
- Assess fetal growth/wellbeing (USS, umbilical artery Doppler assessment and CTG if indicated)
- Consider initiating first-line antihypertensives
- Educate about signs and symptoms of pre-eclampsia

First-line Antihypertensives

- Labetalol
- Nifedipine
- Methyldopa

Maternal monitoring

- The obstetric team makes a management plan for ongoing care and monitoring in discussion with the woman and her LMC
- Carry out BP and urinalysis for protein at least weekly
- If sudden increase in BP or new proteinuria, or other signs of pre-eclampsia, do pre-eclampsia bloods and PCR

Pre-eclampsia bloods

- FBC
- Electrolytes
- Creatinine
- LFT (incl AST, ALT)
- Coagulation if AST ALT abnormal/low platelets

Fetal monitoring

If scanning raises fetal growth concerns:

- conduct USS, AFV, umbilical artery Doppler and CTG if indicated
- follow SGA guidelines for management if diagnosed

Timing of birth

- **Before 37 weeks:** Recommend expectant management. Do not recommend birth unless other maternal or fetal indications support it
- **After 37 and before 40 weeks:** Consider birth. The woman, her LMC and the obstetric team should negotiate the timing together

Signs and symptoms of pre-eclampsia

- Severe headache
- Visual disturbances
- Severe epigastric pain
- Shortness of breath
- Retrosternal pressure/pain
- Nausea, vomiting
- Sudden swelling of face, hands or feet
- Hyperreflexia

Intrapartum

- At least hourly BP in labour
- Continue antihypertensives – adjust if necessary for other factors, eg, neuraxial anaesthesia

Antihypertensives and breastfeeding

- Establish breastfeeding if desired
- Change to compatible antihypertensive, eg, ACE inhibitor
- Very pre-term babies may have an increased risk of adverse effects from antihypertensives

Postpartum

- If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor
- Daily BP to 7 days after birth, then at least weekly to 6 weeks
- Give woman's GP a comprehensive discharge summary

Pre-Eclampsia (Mild & Severe)

NZF Pre-Eclampsia & Eclampsia

Description

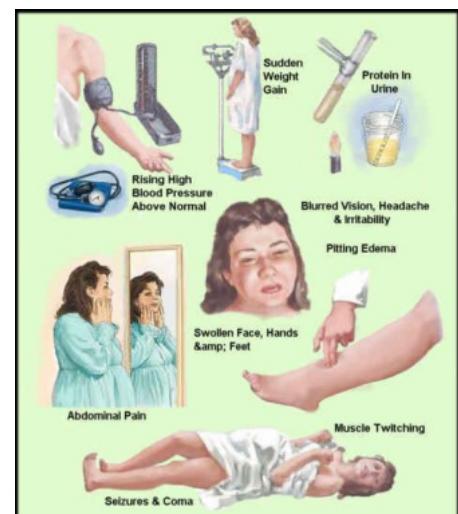
Pre-eclampsia is defined as the new onset or worsening of pre-existing high BP after 20 weeks gestation, with one or more of the following new abnormalities. Urgent referral to an obstetrician is warranted in pre-eclampsia and eclampsia as the women will usually require hospital care.

Pre-eclampsia does not go away even after delivery — the difference is that we can only control it during pregnancy.

Abnormality	Signs	Symptoms
Proteinuria	<ul style="list-style-type: none"> Spot urine protein/creatinine ratio ≥ 30 mg/mmol, or ≥ 2 on dipstick testing confirmed by a protein creatinine ratio test. 	<ul style="list-style-type: none"> Foam in urine
Renal Dysfunction	<ul style="list-style-type: none"> Creatinine $>90 \mu\text{mol/L}$ Urine output of $<80\text{mL/4hr}$ 	<ul style="list-style-type: none"> Sudden swelling of the face, hands and feet Decreased peeing
Liver Involvement	<ul style="list-style-type: none"> Elevated liver transaminases (ALT & AST) – at least twice upper limit of normal 	<ul style="list-style-type: none"> Right upper quadrant or epigastric abdominal pain
Neurological Complications	<ul style="list-style-type: none"> Cerebral or visual disturbances 	<ul style="list-style-type: none"> Frontal headache that doesn't go away with simple painkillers Problems with vision: blurring, flashing lights and dots Heartburn that doesn't go away with antacids General unwellness
Haematological Complications	<ul style="list-style-type: none"> Thrombocytopenia: platelet count $<100 \times 10^9/\text{L}$ Haemolysis 	<ul style="list-style-type: none"> Bruising, feeling unwell
Uteroplacental Dysfunction	<ul style="list-style-type: none"> Reduction in mother's blood supply 	<ul style="list-style-type: none"> Fetal growth restriction, placental abruption

Risk Factors

- Chronic/Gestational Hypertension
- History of eclampsia/pre-eclampsia
- Extremes of age (< 20 or > 40 years)
- Obesity, diabetes
- Renal disease
- Autoimmune disease
- In vitro fertilisation (IVF)
- First pregnancy
- Gap between first and second baby is >10 years
- Multiple partner pregnancies



Signs & Symptoms

- May be **asymptomatic**

Severe Pre-Eclampsia

- Severe hypertension (SBP \geq 160 mmHg OR DBP \geq 110 mmHg)
- Pre-eclampsia abnormalities
- Severe features (worsening haematological or maternal organ)

HELLP Syndrome (Haemolysis, Elevated Liver enzymes, Low Platelet count)

A variant of severe pre-eclampsia, where one or more of the following is present:

- Maternal platelet count of less than $100 \times 10^9/L$
- Liver transaminases twice the upper limit of normal
- Microangiopathic haemolytic anaemia

Pharmacological Treatment

- Labetalol, nifedipine, methyldopa
- If SBP $>$ 160mmHg or DBP $>$ 110 mmHg: Oral Nifedipine, IV labetalol, IV hydralazine
- **For prevention of seizures:** IV Magnesium sulfate (keep going 24 hours postpartum)



Do You See A Pattern?

In Chronic/Gestational Hypertension - we try and prevent pre-eclampsia with Aspirin and Calcium
In Pre-Eclampsia - we try and prevent eclamptic seizures by giving Magnesium!

Monitoring & Management

Target BP: **<140/100mmHg**

Note: Despite the recovery of normal blood pressure, these women remain at higher risk of stroke, cardiovascular, and renal disease and should be given information on the long-term risks of pre-eclampsia (including in future pregnancies) and be followed up accordingly.

What	Antenatal Period	Intrapartum	Postpartum
Immediately	<ul style="list-style-type: none">• Immediately consult obstetrics team/LMC. Blood pressure is primary focus!		
Anti-hypertensive treatment	<ul style="list-style-type: none">• Change ACEI to first line anti-hypertensives in pregnancy	<ul style="list-style-type: none">• Continue anti-hypertensives	<ul style="list-style-type: none">• If on methyldopa, change to another anti-hypertensive
Seizure prevention	<ul style="list-style-type: none">• Initiate IV Magnesium Sulfate	<ul style="list-style-type: none">• Continue Magnesium Sulfate until 24 hours after delivery	

What	Antenatal Period	Intrapartum	Postpartum
Mother	<ul style="list-style-type: none"> Monitor BP: 4-6 hourly (except overnight: q8h) Pre-eclampsia bloods: FBC, Electrolytes, creatinine, LFTs (AST, ALT) Coagulation studies if liver dysfunction or placental disruption 	<ul style="list-style-type: none"> Monitor BP hourly Fluid balance monitoring 	<ul style="list-style-type: none"> Daily BP for first week after birth and then weekly for 6 weeks.
Baby	<ul style="list-style-type: none"> Monitor fetus growth 	<ul style="list-style-type: none"> If uncontrollable and is a term pregnancy: induce labour via vaginal delivery or C-section. May need to administer antenatal corticosteroids depending on gestation. 	
Other HCP	Involve obstetrician and LMC		<ul style="list-style-type: none"> 6 weeks obstetrics review

Pre-eclampsia		Severe/unstable pre-eclampsia	
Hypertension (dBP ≥90 mmHg OR sBP ≥140 mmHg) + other signs and symptoms (refer to definitions)		Uncontrolled severe hypertension (dBP ≥110 mmHg OR sBP ≥160 mmHg) + worsening PE bloods + other signs and symptoms (refer to definitions)	
<p>At diagnosis</p> <ul style="list-style-type: none"> Immediately consult with obstetric team. Transfer of care recommended (referral code 4022) Blood pressure control of primary importance. Start first-line antihypertensive if dBP ≥90 mmHg OR sBP ≥140 mmHg or acute regimen if dBP ≥110 mmHg OR sBP ≥160 mmHg. Aim for target BP 140/100 mmHg or lower Admit to secondary or tertiary facility Spot urine protein: creatinine ratio (PCR) Pre-eclampsia bloods Assess fetal growth/wellbeing (USS, umbilical artery Doppler assessment and CTG if indicated) Educate about signs and symptoms of worsening pre-eclampsia 	<p>First-line antihypertensives</p> <ul style="list-style-type: none"> Labetalol Nifedipine Methyldopa <p>Antihypertensives for acute lowering of BP if dBP ≥110 mmHg OR sBP ≥160 mmHg</p> <p>Nifedipine 10 mg conventional release tablet (oral) Onset: 30–45 minutes Repeat: after 30–45 minutes (if needed) Maximum: 80 mg daily</p> <p>Labetalol Initially 20 mg IV bolus over 2 minutes Onset: 5 minutes Repeat with 40–80 mg Repeat: every 10 minutes (if needed) Maximum: 300 mg</p> <p>Hydralazine 5–10 mg (5 mg if fetal compromise) IV bolus over 3–10 minutes) Onset: 20 minutes Repeat: every 20 minutes (if needed) Maximum: 30 mg (consider IV bolus crystalloid fluid before or when administering first IV hydralazine dose (usually 200–300 mL)</p>	<p>At diagnosis</p> <ul style="list-style-type: none"> Consult immediately with obstetric team. Transfer of care recommended (referral code 4022) BP control of primary importance. Initiate acute antihypertensive care regimen, aim for target BP 140/100 mmHg or lower Also consider magnesium sulphate to prevent a primary seizure Admit to secondary or tertiary facility Spot urine protein: creatinine ratio (PCR) Pre-eclampsia bloods Assess fetal growth (umbilical artery Doppler assessment and CTG, if indicated) 	<p>Antihypertensives for acute lowering of BP</p> <p>Nifedipine 10 mg conventional release tablet (oral) Onset: 30–45 minutes Repeat: after 30–45 minutes (if needed) Maximum: 80 mg daily</p> <p>Labetalol Initially 40 mg IV bolus over 2 minutes Onset: 5 minutes Repeat with 40–80 mg Repeat: every 10 minutes (if needed) Maximum: 300 mg</p> <p>Hydralazine 5–10 mg (5 mg if fetal compromise) IV bolus over 3–10 minutes Onset: 20 minutes Repeat: every 20 minutes (if needed) Maximum: 30 mg (consider IV bolus of crystalloid fluid before or when administering first IV hydralazine dose, usually 200–300 mL)</p>
<p>Maternal monitoring</p> <ul style="list-style-type: none"> The obstetric team makes a management plan for ongoing care and monitoring in discussion with the woman and her LMC BP 4–6 hourly (except overnight when an interval of 8 hours is acceptable) Clinical deterioration can be rapid Twice weekly pre-eclampsia bloods Conduct coagulation studies if liver function tests are abnormal or you have concerns about possible placental abruption <p>Fetal monitoring</p> <ul style="list-style-type: none"> Follow SGA guidelines for management if diagnosed After assessment at the time of diagnosis, do not repeat USS for growth in <2 weeks Daily CTG if inpatient <p>Timing of birth</p> <ul style="list-style-type: none"> Before 37 weeks: (eg, 36+6): Adopt expectant approach. Do not recommend delivery in the absence of other maternal indicators (eg, premature rupture of membranes, preterm labour or vaginal bleeding, deterioration of condition) or fetal indications. Should usually be managed as an inpatient. After 37 weeks: (eg, 37+0): Recommend birth. No appreciable benefit in continuing pregnancy after 37 weeks. The woman, her LMC and the obstetric team should negotiate the timing and method. 	<p>Pre-eclampsia bloods</p> <ul style="list-style-type: none"> FBC Electrolytes Creatinine LFT (incl AST, ALT) Coagulation if AST, ALT abnormal/low platelets <p>Signs and symptoms of pre-eclampsia</p> <ul style="list-style-type: none"> Severe headache Visual disturbances Severe epigastric pain Shortness of breath Retrosternal pressure/pain Nausea, vomiting Sudden swelling of face, hands or feet Hyperreflexia 	<p>Maternal monitoring</p> <ul style="list-style-type: none"> Management plan should include discussions with the obstetric and anaesthetic teams along with the woman and the LMC Hourly BP and respiratory rate Fluid balance chart At least daily pre-eclampsia bloods Conduct coagulation studies if liver function tests are abnormal or you have concerns about possible placental abruption <p>Maternal monitoring – magnesium sulphate</p> <ul style="list-style-type: none"> Blood pressure every 5 minutes during bolus dose, then hourly during maintenance dose Respiratory rate, O₂ saturation, reflexes hourly Urine output (>100 mL over 4 hours) Fluid restriction (replace loss at delivery and then 80–85 mL/hour total fluid) <p>Fetal monitoring</p> <ul style="list-style-type: none"> Follow SGA guidelines for management if diagnosed After assessment at time of diagnosis, do not repeat growth USS in <2 weeks Daily CTG (continuous if magnesium sulphate running) <p>Timing of birth</p> <ul style="list-style-type: none"> Peri-viability and before: Manage in a tertiary setting with maternal fetal medicine involvement if possible, and with careful discussion with the woman Before 34 weeks: Adopt expectant approach in a secondary or tertiary centre with resources for maternal and fetal monitoring and critical care of the mother and the baby. If indication for birth presents, administer corticosteroids for fetal lung maturation and magnesium sulphate for fetal neuroprotection (if <30 weeks). Not required if already on magnesium sulphate. After 34 weeks: Recommend birth after stabilising the woman in a centre with appropriate resources for care of the mother and baby 	<p>Pre-eclampsia bloods</p> <ul style="list-style-type: none"> FBC Electrolytes Creatinine LFT (incl AST, ALT) Coagulation if AST, ALT abnormal/ low platelets <p>Signs and symptoms of pre-eclampsia</p> <ul style="list-style-type: none"> Severe headache Visual disturbances Severe epigastric pain Shortness of breath Retrosternal pressure/pain Nausea, vomiting Sudden swelling of face, hands or feet Hyperreflexia
<p>Intrapartum</p> <ul style="list-style-type: none"> At least hourly BP in labour Continue antihypertensives – adjust if necessary for other factors, eg, neuraxial anaesthesia Fluid balance monitoring <p>Postpartum</p> <ul style="list-style-type: none"> If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor Continue to monitor for disease resolution, titrate antihypertensives as required Advise to stay in secondary/tertiary facility for at least 72 hours (4–6 hourly BP) Daily BP to 7 days after birth, then at least weekly to 6 weeks Give woman's GP a comprehensive discharge summary 6-week obstetric review 	<p>Intrapartum</p> <ul style="list-style-type: none"> At least hourly BP in labour Continue antihypertensives – adjust if necessary for other factors, eg, effect of magnesium sulphate, neuraxial anaesthesia <p>Postpartum</p> <ul style="list-style-type: none"> Continue magnesium sulphate for 24 hours If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor Continue to monitor for disease resolution, titrate antihypertensives as required Advise to stay in secondary/tertiary facility for at least 72 hours (4–6 hourly BP) Daily BP to 7 days after birth, then at least weekly to 6 weeks Give woman's GP a comprehensive discharge summary 6-week obstetric review 	<p>Intrapartum</p> <ul style="list-style-type: none"> At least hourly BP in labour CTG Continue antihypertensives – adjust if necessary for other factors, eg, effect of magnesium sulphate, neuraxial anaesthesia <p>Postpartum</p> <ul style="list-style-type: none"> Continue magnesium sulphate for 24 hours If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor Continue to monitor for disease resolution, titrate antihypertensives as required Advise to stay in secondary/tertiary facility for at least 72 hours (4–6 hourly BP) Daily BP to 7 days after birth, then at least weekly to 6 weeks Give woman's GP a comprehensive discharge summary 6-week obstetric review 	<p>Magnesium sulphate</p> <p>To prevent progression to eclampsia, this anticonvulsant drug may be administered – see protocol</p> <p>Pre-eclampsia bloods</p> <ul style="list-style-type: none"> FBC Electrolytes Creatinine LFT (incl AST, ALT) Coagulation if AST, ALT abnormal/ low platelets <p>Signs and symptoms of pre-eclampsia</p> <ul style="list-style-type: none"> Severe headache Visual disturbances Severe epigastric pain Shortness of breath Retrosternal pressure/pain Nausea, vomiting Sudden swelling of face, hands or feet Hyperreflexia

Eclampsia

NZF Drugs Used in Obstetrics

Description

Eclampsia is a severe manifestation of pre-eclampsia defined as a **new onset of seizures** in association with pre-eclampsia. It can occur before, during or after birth, and can be the presenting feature of pre-eclampsia in some women.



Magnesium Sulfate Administration

Eclamptic seizures are generally short-lived and self-limiting, therefore it is reasonable to *delay* administration of magnesium sulphate until the seizure has stopped. (Only prevents further seizures)

Signs & Symptoms

Abdominal pain, severe headache, vision and mental status changes

Pharmacological Treatment

- Labetalol, nifedipine, methyldopa
- If SBP > 160mmHg or DBP >110 mmHg: Oral Nifedipine, IV labetalol, IV hydralazine
- For prevention of seizures: IV Magnesium sulfate (keep going 24 hours postpartum)

Monitoring & Management

The only cure is **delivery!**

- Vaginal or Cesarean Section delivery depending on severity of hypertension
- May need to administer antenatal *corticosteroids* depending on gestation!

Why is pre-eclampsia/eclampsia a problem?

In the Mum (usually CVD issues)

- Stroke (due to high BP)
- Post-partum haemorrhage
- Seizure
- Pulmonary oedema
- Vessels constricted + leaky
- Heart failure
- Reversible blindness
- Bleeding from the liver

In the baby

The increased blood pressure and narrowing of the blood vessels affects the placenta and can decrease the supply of food and oxygen to the baby. This can result in:

- Reduced fetal growth

- Preterm birth
- Placental abruption (separation of the placenta from the uterine wall)
- Stillbirth if placental abruption leads to heavy bleeding in the mother
- Infant death

Eclampsia

New onset of seizures in association with pre-eclampsia

<p>At diagnosis</p> <ul style="list-style-type: none"> • Immediately consult with obstetric team. Transfer of care (referral code 4006) • Immediate Airway, Breathing, Circulation, Disability, Exposure (ABCDE) management • BP control of primary importance if severe • Admit to secondary/tertiary facility • Pre-eclampsia bloods + coagulation bloods • Assess fetal growth (umbilical artery Doppler assessment and cardiotocography if indicated) 	<p>Antihypertensives for acute lowering of BP</p> <p>Nifedipine 10 mg conventional release tablet (oral) Onset: 30–45 minutes Repeat: after 30–45 minutes (if needed) Maximum: 80 mg daily</p> <p>Labetalol Initially 20 mg IV bolus over 2 minutes Repeat with 40–80 mg Onset: 5 minutes Repeat with 40–80 mg Repeat: every 10 minutes Maximum: 300 mg</p> <p>Hydralazine 5–10 mg (5 mg if fetal compromise) IV bolus over 3–10 minutes Onset: 20 minutes Repeat: every 20 minutes Maximum: 30 mg (consider IV bolus of crystalloid fluid before or when administering first IV hydralazine dose, usually 200–300 mL)</p> <p>Magnesium sulphate To prevent further eclamptic seizures, this anticonvulsant drug should be administered – see protocol</p> <p>Pre-eclampsia bloods</p> <ul style="list-style-type: none"> • FBC • Electrolytes • Creatinine • LFT (incl AST, ALT) • Coagulation if AST, ALT abnormal/ low platelets <p>Signs and symptoms of pre-eclampsia</p> <ul style="list-style-type: none"> • Severe headache • Visual disturbances • Severe epigastric pain • Shortness of breath • Retrosternal pressure/pain • Nausea, vomiting • Sudden swelling of face, hands or feet • Hyperreflexia
<p>Treatment</p> <ul style="list-style-type: none"> • Only conclusive treatment is birth of baby but aim to stabilise and monitor if possible if <37 weeks' gestation • Begin magnesium sulphate – see protocol • If hypertensive, start antihypertensive, aim for a target BP below 140/100 mmHg 	
<p>Maternal monitoring</p> <ul style="list-style-type: none"> • One-to-one midwifery care • Management should include discussion with the anaesthetic and intensive care teams but with obstetric lead • Continuous SpO₂ monitoring • Fluid balance • At least daily pre-eclampsia bloods • Conduct coagulation studies if liver function tests are abnormal or you have concerns about possible placental abruption 	<p>Maternal monitoring – magnesium sulphate</p> <ul style="list-style-type: none"> • Maternal monitoring – magnesium sulphate • Blood pressure every 5 minutes during bolus dose then hourly during maintenance dose • Respiratory rate, reflexes hourly • Urine output (>100 mL over 4 hours) • Fluid restrictions (80–85 mL/hour total fluid)
<p>Fetal monitoring</p> <ul style="list-style-type: none"> • CTG (continuous if magnesium sulphate running) 	
<p>Timing of birth</p> <p>Any gestational age: Recommend birth after stabilising the woman and a course of corticosteroids (if ≤34+6 weeks) and magnesium sulphate for neuroprotection (if <30 weeks) has been completed (if time permits) – not required if already on magnesium sulphate</p>	
<p>Intrapartum</p> <ul style="list-style-type: none"> • Frequent BP monitoring (eg, every 5–15 minutes) in labour. If on magnesium sulphate – follow protocol • Continuous CTG • Continue antihypertensives – adjust if necessary for other factors, eg, effect of magnesium sulphate, neuraxial anaesthesia 	
<p>Postpartum</p> <ul style="list-style-type: none"> • Continue magnesium sulphate for 24 hours • If on methyldopa, consider changing to another antihypertensive, eg, ACE inhibitor • Continue to monitor for disease resolution, titrate antihypertensives as required • Advise to stay in secondary/tertiary facility for at least 72 hours (4–6 hourly BP) • Daily BP to 7 days after birth, then at least weekly to 6 weeks • Give woman's GP a comprehensive discharge summary • 6-week obstetric review 	

Diabetic Disorders

Gestational Diabetes

[NZF Gestational Diabetes](#)

Description

Gestational diabetes is defined as the new onset of diabetes that occurs during pregnancy, causing high glucose levels in the blood due to insufficient insulin production — usually around the 20th to 24th week of pregnancy and resolves after it. However, it can recur in future pregnancies.

Pathophysiology

Hormonal changes during pregnancy increase nutrient requirements and fat deposition. This is because the mother's metabolism shifts, leading to increased liver metabolism and gluconeogenesis to provide for the growing fetus as well as for the development of the uterine lining and breast glandular tissue. Therefore, as the maternal glucose levels increase, a pregnant woman's insulin needs are 2-3x times more than normal.

In pregnancy, the placenta produces certain hormones that may induce insulin resistance, therefore causing less glucose to enter the cells. While in most cases, the body successfully makes enough insulin to bypass the placenta's hormones, in some cases it is unsuccessful — this leads to gestational diabetes.

Risk Factors

Past pregnancies with:

- Gestational diabetes
- Stillbirth or spontaneous miscarriage
- Previous baby with birth defect
- Macrosomia (large baby/birthweight > 4 kg)
- Pregnancy-induced high BP, UTIs or polyhydramnios (excess amniotic fluid)

Current factors:

- Overweight
- Aged > 30-40
- History of PCOS
- Family history of T2DM in a close relative (parents/brothers/sisters)

Complications: Gestational diabetes and pre-eclampsia are risk factors for each other.

Signs & Symptoms

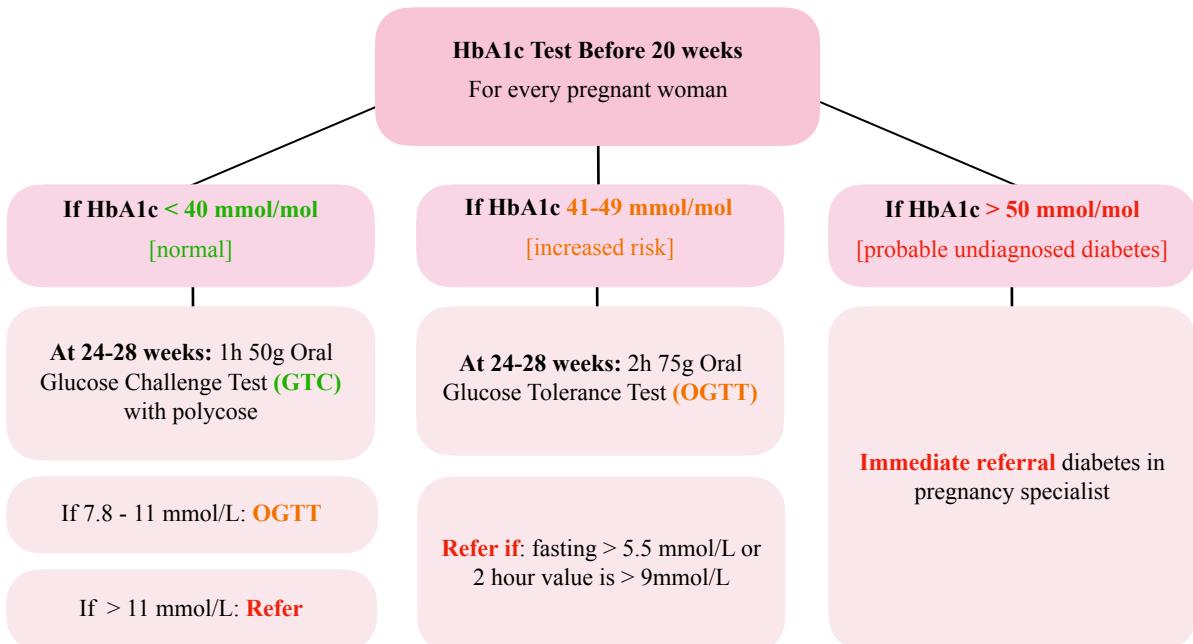
- Usually asymptomatic
- If uncontrolled women may feel more thirsty, tired, recurrent and have prolonged urogenital infections

Diagnosis (Screening)

Diabetes in Pregnancy Ministry of Health Guidelines

This condition is often picked up during screening. Every pregnant woman should be offered glycated haemoglobin (HbA1c), as part of routine antenatal blood tests **before 20 weeks** to identify if:

- Probable undiagnosed diabetes or pre-diabetes
- High risk of developing gestational diabetes



Goal of Treatment

Target Blood Glucose Values

- Fasting and preprandial BG < 5.0 mmol/L
- 1h post-prandial BG < 7.4 mmol/L
- 2h post-prandial BG < 6.7 mmol/L

The aim is to meet target blood glucose goals and weight according to MoH NZ recommendations based on pre-pregnancy BMI interventions to reduce large gestational age (LGA) and the need for C-section.

Pre-Pregnancy BMI (kg/m ²) of mother	RECOMMENDED weight gain range (kg)
Underweight (> 18.5)	12.5 - 18
Healthy weight (18.5-24.9)	11.5 - 16
Overweight (25.0 - 29.9)	7 - 11.5
Obese (> 30.0)	5 - 9

Complications

While GDM resolves after the pregnancy, it can recur in future pregnancies. If left untreated, it can cause health problems for both the mother and the fetus, such as increasing the risk of:

Mum

- Needing a C-Section
- Developing HTN/pre-eclampsia
- UTIs

Baby

- High birthweight (risk factor for serious problems later on in life)
- Shoulder dislocation during birth process (too large to fit through birth canal)
- Seriously low blood glucose level soon after birth (as they are used to having so much glucose from the mom, when they are born, they have adapted and produced more insulin)
- Prolonged new-born jaundice (due to liver activity/gluconeogenesis)
- Low blood calcium levels
- Respiratory distress syndrome

Non-Pharmacological Treatment

In most cases, gestational diabetes is able to be managed by diet and exercise during the pregnancy.

NON-PHARMACOLOGICAL TREATMENT OF GESTATIONAL DIABETES	
Intervention	Description
Diet Interventions	<ul style="list-style-type: none">• Do not skip meals• Minimum of 175 g carbohydrate per day. May add a sandwich in late pregnancy.• Replace high-glycemic index foods with low ones• Reduce intake of saturated fats, consume lean protein
Exercise Interventions	<ul style="list-style-type: none">• 30 minutes of moderate exercise most days (should be able to carry out a conversation but not sing)• Activities should not require much standing/balance (e.g. swimming)• Avoid excessive sweating/increased body temperature: loose light clothing, do not workout in hot weather• Keep up fluid intake before and after workout• Do not do any activities lying on your back in the 2nd or 3rd trimester or those that can hurt your belly• Do not do physical activity while hungry

Pharmacological Treatment

[Screening, Diagnosis and Management of GD in NZ](#), [Up to Date Gestational Diabetes](#)

1. First Line: Insulin

- Alternative (similar perinatal outcomes): Aspart, lispro, glulisine

2. Additions: Metformin or Glibenclamide

- Evidence of less maternal weight gain, less LGA, less neonatal hypoglycaemia
- Women should be informed that it **crosses the placenta**

Monitoring & Management

MONITORING & MANAGEMENT OF WOMEN WITH GESTATIONAL DIABETES	
During Pregnancy	<p>Fetal Surveillance <i>Monitoring</i> Advise women to report any reduction or change in fetal movements from 28 weeks' gestational age onwards</p> <p><i>Management</i> Increased surveillance and thus earlier/later induction should be considered in women poorly controlled and/or with co-morbidities. Offer induction at 38-40 weeks GA to potentially reduce stillbirth and C-section if growth is > 90th percentile at 37 weeks.</p>
Postpartum	<p>1. Encourage Breastfeeding Reduces neonatal hypoglycaemia, childhood obesity & diabetes, AND maternal risk of diabetes & hypertension</p> <p>2. Re-Screen HbA1c 3 months postpartum and annually thereafter. GDM should resolve after the birth of the baby, women with GDM may have an increased risk (50-60%) of developing T2DM in the future</p> <p>3. Lifestyle Keep good lifestyle and exercise and diet. Maintain healthy weight.</p>

Postpartum Conditions

Postpartum Depression

Description

There are three types of depression which can occur after childbirth (can also occur in the dad):

1. *Postnatal or maternity blues* are very common and involve a brief period of the mother feeling down and tearful in the week after her baby is born. This feeling passes after a few days. It's all very normal.
2. *Postpartum depression*, a much more serious condition, is also common. The woman becomes seriously depressed in the first months following the baby's birth.
3. *Postnatal psychosis* (sometimes called postpartum psychosis) is rare and involves symptoms of psychosis (being out of touch with reality) associated with changes in mood – either a depressed or an extremely high mood. It usually begins in the first two weeks after the child is born.

Risk Factors

Risk factors before pregnancy and birth

- Past history of depression or other mental health problem
- Relationship difficulties, especially with the father of the baby or with own mother
- Having little social support
- Onset of depression during pregnancy
- Life stresses or difficulties such as money or housing problems

Risk factors related to the birth

- Birth did not go as planned (complications such as a C-section, birth in hospital instead of a natural birth)
- Birth of a brain-damaged or ill baby

Risk factors after birth

- Persisting postnatal blues
- The baby is fussy, has problems feeding, or has colic or reflux

Signs & Symptoms

- Not wanting to hold the baby or feeling detached, having negative thoughts about the baby.
- Sleep problems, severe mood swings
- Intense irritability and anger, feelings of shame/inadequacy, social isolation, loss of appetite/interest in sex

Diagnosis

- EPDS Questionnaire

Non Pharmacological Treatment

- Enhanced social support and psychological therapy if symptoms are mild

Pharmacological Treatment

- If depression is moderate, sertraline or escitalopram are the preferred options (compatible in breastfeeding)

Postpartum Haemorrhage (PPH)

Description

Postpartum haemorrhage is severe vaginal bleeding that occurs after childbirth, and can be fatal — the most common cause being uterine atony.

Pathophysiology

Causes of postpartum bleeding include:

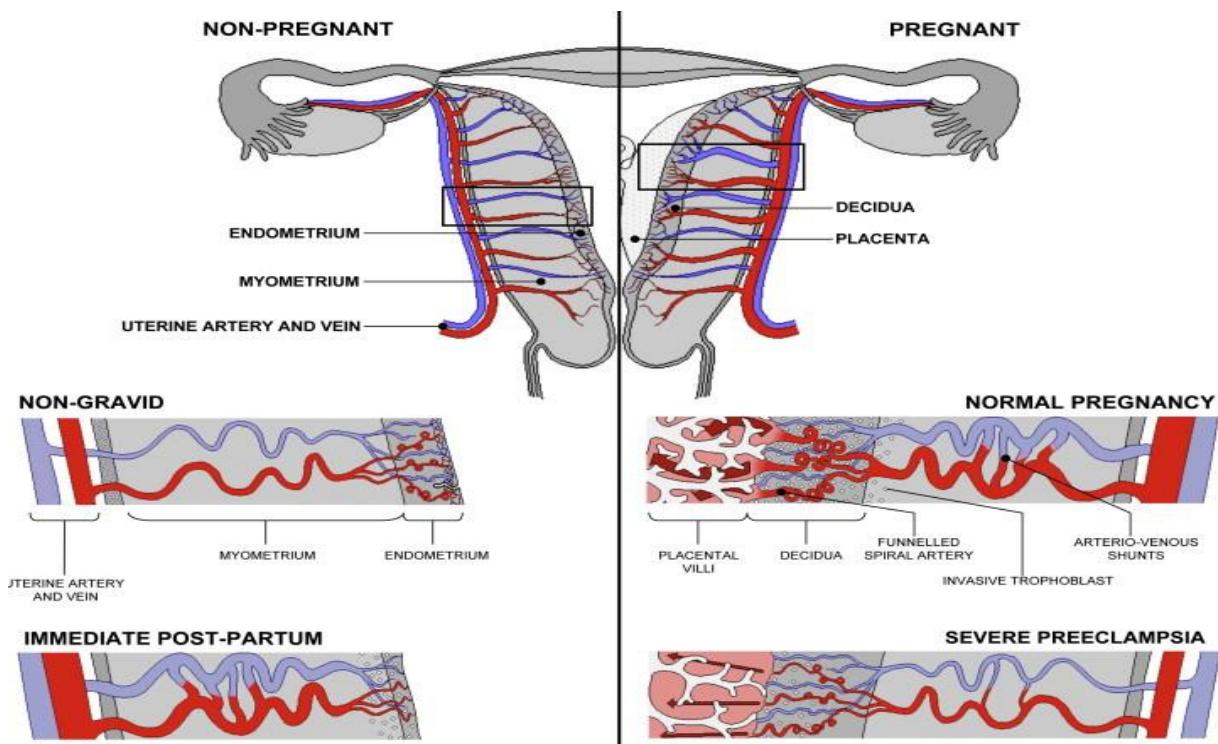
1. *Uterine Atony (loss of tone in the uterine muscles)*: Following the delivery of the placenta, the uterus contracts to compress the bleeding vessels in the area where it was attached. However in uterine atony, the uterus fails to contract enough and the blood vessels subsequently bleed freely.
2. *Bleeding Disorders*
3. *Placenta failing to come out completely or tearing*

Signs & Symptoms

- Dizziness, feeling faint, blurred vision

Pharmacological Treatment

1. *Tranexamic Acid (TXA)*: acts as an anti-fibrinolytic agent to stabilises clots formed at site of tissue/vessel injury/disruption.
2. *Uterine stimulants* (Oxytocin, Prostaglandins, Ergot Alkaloids): used for labour induction, cervical ripening, and postpartum haemorrhage



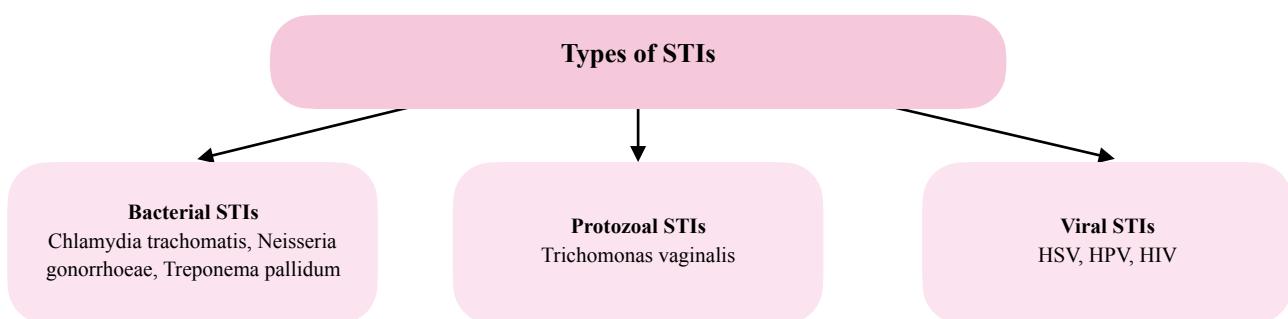
SEXUALLY TRANSMITTED INFECTIONS (STIs)

Overview & Summary

See the [New Zealand Sexual Health Society](#)

Introduction

STIs and infections that are passed on from one person to another through unprotected sexual contact. The bacteria, viruses or parasites that cause sexually transmitted diseases may pass from person to person in blood, semen, or vaginal and other bodily fluids. Sometimes these infections can be transmitted non-sexually, such as from mothers to their infants during pregnancy or childbirth, or through blood transfusions or shared needles.



Risk Factors

- Sexually active young adults
- Infants infected in utero or during delivery
- Alcohol/drug abuse (leading to unsafe/unwanted sexual practises)
- Multiple partners
- Failing to use barrier protections (condoms)
- History or current STI

Prevention

Prevention always outweighs treatment

- Education
- Screening programmes for high risk groups (e.g. pregnant women)
- Using a condom every time you have vaginal, oral or anal sex
- Do not share sex toys

Bacterial Sexually Transmitted Infections (STIs)

Description

We will cover the following bacterial sexually transmitted diseases: *chlamydia, gonorrhoea and syphilis*.

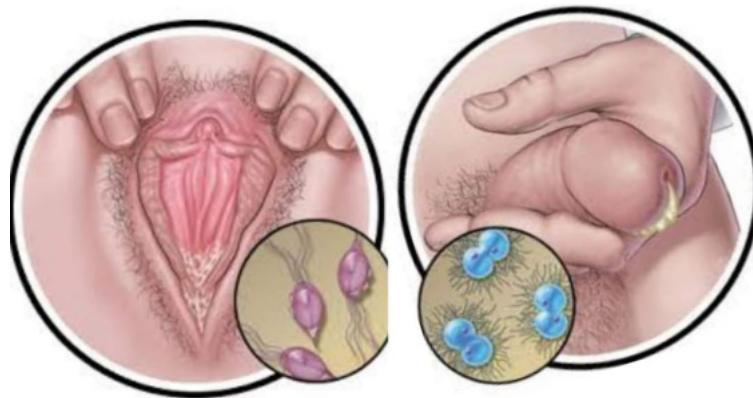
Chlamydia Trachomatis & Neisseria Gonorrhoea (“The Clap”)

[Chlamydia Health Navigator](#), [Gonorrhoea Health Navigator](#) [NZSHS Chlamydia Patient Information](#),
[NZSHS Gonorrhoea Patient Information](#)

Description

Bacterial STIs such as chlamydia and gonorrhoea are the most common STIs in New Zealand. They are a silent epidemic, often found in *young females and MSM populations*.

They are not spread by kissing, hugging, swimming pools, toilet seats or sharing toiletries or utensils. The bacteria cannot survive outside the human body for long, thus its common method of transmission is through sexual contact (e.g. vaginal, oral and anal sex or even mutual masturbation).



Signs & Symptoms

Often asymptomatic. It may take a few weeks following sex with the infected person to appear.

Gonorrhoea infections are limited to mucus membranes lined with columnar epithelium (as they don't shed - urethra, cervix, rectum, pharynx, conjunctiva)

Women

- *Urethritis*: painful urination
- *Cervicitis*: vaginal discharge, vaginal bleeding after sex (or in between periods)
- *Pain*: low tummy pain during sex

Men

- *Epididymitis*: swollen, painful testicles, painful urination, itchy opening of the penis (urethra)
- *Proctitis* (rectal infection): pain, bleeding, discharge

Complications

Untreated infections can cause many long term health consequences:

COMPLICATIONS OF CHLAMYDIA & GONORRHOEA	
In Women	<ul style="list-style-type: none"> <i>Pelvic Inflammatory Disease (PID), which can lead to:</i> <ul style="list-style-type: none"> Chronic pain Infertility Life-threatening ectopic pregnancy
In Utero/Neonates	<i>Spread of the infection from pregnant women to their children during delivery can cause:</i> <ul style="list-style-type: none"> Premature births, miscarriages Ear or eye (conjunctivitis) infections — could lead to blindness with gonorrhoea Pneumonia
In Men	<ul style="list-style-type: none"> Prostate or testicle involvement, causing infertility
Systemic Spread	<ul style="list-style-type: none"> Endocarditis, meningitis

Diagnosis & Routine Screening

Collecting pharyngeal swab tests for chlamydia and gonorrhoea is recommended as a routine part of a sexual health check for men who have sex with men (MSM populations)

Gender Specific Testing

- Females:* Vaginal swab NAAT (for trichomoniasis, gonorrhoea & chlamydia)
- Males:* Urine sample (PCR | NAAT) testing

Other types of tests specific to the type of sexual contact e.g. recommended in MSM

- Anorectal swabs* for suspected rectal infections
- Pharyngeal swabs* for suspected oral infections

Note: while urine tests are more convenient, swabs are more accurate.

Patients should be tested for other STIs

- Patients with chlamydia should be tested for gonorrhoea and vice versa

Non-Pharmacological Treatment

- Condoms:* use condoms to prevent transmission of STIs: use for 7 days after starting treatment and until 7 days after all sexual contacts have been treated. Use is important especially if on COCs & antibiotics — certain antibiotics can affect the reliability of OC's.

Pharmacological Treatment (Chlamydia)

BPAC Treatment Guidelines for Chlamydia, BPAC Chlamydia Antibiotic Guidelines

Any sexual contacts the person has had in **the last 3 months** must be contacted, checked, and treated.

Re-infections are common and often from the rectal area. Therefore, treat as though females with genital chlamydia also have a rectal infection. Can start treatment **without** waiting for test results.

- First Line: Doxycycline (7 day therapy): 100mg bd*

- First line in female genital/rectal/pharyngeal and male urethral/pharyngeal chlamydia as well as empiric treatment of sexual contacts
- Not for pregnancy (teratogenic)**

2. Alternative: Azithromycin (single dose treatment): Ig STAT
 - Alternative due to issues with the developing resistance to other STIs
 - For asymptomatic urogenital infection
 - Safe in pregnancy

Pharmacological Treatment (Gonorrhoea)

[BPAC Treatment Guidelines for Gonorrhoea, BPAC Gonorrhoea Antibiotic Guidelines](#)

Can start treatment **without** waiting for test results.

1. Dual Therapy Antibiotics (genital, rectal, or pharyngeal infections)
 - Ceftriaxone 500mg IM STAT **AND** Azithromycin 1g STAT
 - Both drugs suitable in pregnancy
 - If co-infection with rectal chlamydia: **ADD** doxycycline 100mg po twice daily for 7 days.

Monitoring & Management

[NZHS Management of Chlamydia, NZHS Management of Gonorrhoea](#)

- Follow up (verbal/phone) 1 week following treatment to ensure the above (condoms, treatment tolerability)
- Follow up test in 3-6 months following treatment (to ensure recurrence did not occur)

Prevention

Cross protection with MensB vaccine (similar bacteria which causes meningitis)

Syphilis (T. Pallidum)

[Health Navigator Syphillis](#) [NZHS Syphillis Patient Information](#), [Dermnet Syphillis Photos](#)

Description

A bacterial infection caused by *Treponema pallidum* that is usually spread by sexual contact (oral, vaginal, anal).



Risk Factors

- MSM (men who have sex with men)
- Change in sexual partners

Signs & Symptoms

Symptoms are very non-specific and often are not present (asymptomatic)

PATHOPHYSIOLOGY & SYMPTOMS OF SYPHILLIS			
Stage		Description	How far back to trace contacts
Infectious	Primary Stage	Primary Syphilis — Painless Ulcerative Sore The first sign of this infection is one or more ulcerative sores on the genitals, cervix, rectum or mouth that heals spontaneously within 3-6 weeks. At these sites are hidden and the sore is painless, it will often go unnoticed. It will in fact disappear on its own within a few weeks.	3 months + duration of symptoms
	Secondary Stage	Secondary Syphilis — Rash The most common symptom presents as a skin rash with brown sores on the palms of hands, soles of feet alongside mild fever, aches. If untreated, the symptoms of primary and secondary syphilis disappear, but you can remain infectious for up to 2 years.	6 months + duration of symptoms
	Early Latent Stage	Early Latent Syphilis — No clinical symptoms but infectious Early Latent Syphilis is defined as less than 2 years duration. The person is still infectious in this stage but does not develop any more symptoms.	12 months
Non-infectious	Late Latent Stage	Late Latent Syphilis — No clinical symptoms and no longer infectious Late Latent Syphilis is defined as beyond 2 years of duration. Although it causes no further symptoms and the person is no longer infectious, it leads to the tertiary stage!	Current/last sexual contacts. and/or Serologic evaluation of children (for women)
	Tertiary Stage	Tertiary Syphilis — Complications If untreated, a small number of people will progress to this stage. This stage will cause, via systemic spread, damage to the heart, brain, nerves, blood vessels, liver, bones and joints many years later, resulting in mental illness, blindness or even death	



Sexual Contacts of Syphilis

All sexual contacts within the intervals above should be clinically and serologically evaluated.

Complications

- Increased risk of HIV infection
- Can be spread from mother to baby during pregnancy: miscarriages, still-births, infections of the newborn

Diagnosis

Syphilis is usually diagnosed by blood tests for antibodies to the syphilis bacterium. It can take up to 3 months to develop antibodies. It can take up to 90 days for a test to become positive after infection therefore contacts of infectious syphilis should be treated empirically regardless of test results. If you have symptoms, you may also need to have samples taken from the sores or body rash.

1. *Blood Test (particularly if you have a genital sore/rash):*
 - Syphilis is one of the routine blood tests in pregnant women
2. *Direct microscopy or specific antibodies (ELISA)*
3. *Also test for exclusion of HIV*

Non-Pharmacological Treatment

- Refrain from any sexual activity until assessed and treated and until any rashes or lesions have healed.

Pharmacological Treatment

BPAC Syphillis

Any **sexual contacts** the person has had must be contacted, checked, and treated — refer to notification intervals listed above. **Do not use/prescribe** any topical agents or oral antibiotics for genital ulcers (insufficient)

1. IM penicillin: 1.8g **long-acting** Bicillin (benzathine penicillin)
 - If *infectious* (primary, secondary & early latent): STAT
 - If *non-infectious* (late latent): weekly for 3 weeks

Monitoring

NZSHS Management of Syphilis

Infectious Syphilis (Primary, Secondary & Early Latent or of Unknown Duration)

- Repeat serology at 3, 6, 12 months

Non-Infectious Syphilis (Late Latent & Tertiary)

- Repeat serology at 6, 12 months to ensure remains serofast

Protozoal STIs

Trichomonas Vaginalis (TV)

[Health Navigator Trichomoniasis](#), [NZHS Trichomoniasis Patient Information](#)

Description

Trichomoniasis is a sexually transmitted infection (STI) caused by the parasite *Trichomonas vaginalis* — it spreads via sexual contact (e.g. genital fluids, sex toys).

Signs & Symptoms

Symptoms are very non-specific and often are not present (asymptomatic).

Women

- Yellow-green discharge that is thin and frothy
- Foul odour
- Severe vaginitis (red swollen vulva that is itchy)
- Bleeding following intercourse
- Cervical haemorrhage
- Low abdominal pain

Neonates

- Some female infants born to infected mothers can develop self-limiting and asymptomatic vaginal infections. These will resolve when maternal hormones of the baby develop.
- Other: pre-term delivery, low birth weight

Men

- Asymptomatic, self-limiting infection
- Thin yellow-green discharge
- Urethritis, pain on urination

Diagnosis

Gender Specific Testing

- *Females:* Vaginal swab NAAT (for trichomoniasis, gonorrhoea & chlamydia)
- *Males:* Urine sample (PCR | NAAT) testing

Non-Pharmacological Treatment

1. *Condoms:* Avoid sex for 7 days after you and your partner(s) have been treated so you don't pass the infection on, or use condoms if this is not possible.

Complications

If untreated:

- Co-infection with other STIs is common (e.g. HIV, bacterial vaginosis)
- *Women*: PID, Infertility (severe disease can spread to fallopian tubes), vaginal discharge (**yellow frothy**), irritation, dysuria, offensive odour, pain or bleeding associated with sex and lower abdominal pain
- *Men*: Prostatitis, dysuria, urethral irritation or discharge.
- *In Utero/Neonates*: Pre-term deliveries, low birthweight

Pharmacological Treatment

[NZHS Trichomoniasis Management](#), [BPAC Trichomoniasis Antibiotic Guidelines](#)

Any sexual contacts the person has had in **the last 3 months** must be contacted, checked, and treated.

1. *Metronidazole (oral): 2g STAT or 400mg BD for 7 days*

- Resistance in 4-10% of cases
- **Avoid alcohol**
- Ok in pregnancy

2. *Ornidazole: 1.5g STAT or 500mg BD for 5 days*

- Not recommended in pregnancy



Did You Know?

Metronidazole is the only antibiotic you must avoid alcohol with - it causes something called a disulfiram-like reaction.

Monitoring & Management

[NZHS Trichomoniasis Management](#)

- Follow up after 1 week to ensure symptoms resolution, give results, check compliance, sexual contacts...
- Recommend sexual health check in 3 months to test for re-infection

Viral STIs

Genital Warts | HPV

[Health Navigator Genital Warts](#), [NZHS Genital Warts Patient Information](#). [Dermnet Genital Wart Photos](#)

Description

Genital warts are a common virus in sexually active people — they spread through skin-to-skin and sexual contact. They are highly infectious when the warts are present but may still be infectious when virus is latent.



Signs & Symptoms

Warts can vary in size and appearance (flat, cauliflower-like, dome shaped, crust), often appear in clusters.

- *Females*: they can appear on the vulva, in and around the vagina/anus, cervix, groin or thighs.
- *Males*: they can appear on the penis, scrotum, around the anus, or on the groin and thighs.

Complications

Co-infection with different HPV strains is common. HPV 16 & 18 are associated with an increased risk of cervical cancer.

Diagnosis

- Visual examination — no test exists for the virus so it is impossible to check if the person carries the virus.
- Women with genital warts are not at greater risk of cancer, but they should have routine cervical smears.

Non-Pharmacological Treatment

While condoms are the best form of protection, they don't offer full protection from HPV as they only cover the penis, not the rest of the genital skin.

Pharmacological Treatment — **Wart Removal**

1. *Women or Perianal Wart*
 - Imiquimod cream 5% for warts not responsive to podophyllotoxin or in areas not easily visualised e.g. vulva, perianal
2. *Men only*
 - Podophyllotoxin

3. External warts only

- Trichloroacetic acid, liquid nitrogen, laser therapy, surgery

Drug	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Imiquimod Cream 5%</i> Perrigo	Immune Modulator <i>OD 3x week for up to 16 weeks</i> In genital warts it is thought to stimulate immune cell-mediated viral cell lysis.	<ul style="list-style-type: none"> • May damage latex condoms and diaphragms. • Avoid normal or broken skin, and open wounds, not suitable for internal genital warts 	Local reactions such as itching, burning, erythema, erosion, oedema, scabbing
[PRESCRIPTION] <i>Podophyllotoxin Solution 0.5%</i> Condylone	Antimitotic. For men only <i>BD daily for 3 consecutive days per week for 5 weeks</i> Prevents viral warts from dividing and multiplying. Eventually all the warts die and new healthy cells grow in their place	<ul style="list-style-type: none"> • Wash and dry the affected area before use and wash hands thoroughly after application. • Allow the preparation to dry thoroughly on your skin to avoid inadvertent spreading. 	Local irritation

Prevention

Gardasil HPV vaccine (most effective — all eligible patients should get this)

Genital Herpes | HSV-2

[Health Navigator Genital Herpes](#), [Dermnet Genital Herpes Photos](#)

Description

Genital herpes is a common viral infection that spreads through sexual contact and is caused by a virus known as the herpes simplex virus (HSV).

HSV-1 usually causes oral/cold sores and HSV-2 usually causes genital lesions. Transmission is via contact of broken skin with person having an outbreak. The virus is non-curable as it remains latent in nerve endings.



Symptoms

On average, symptoms of genital herpes are likely to recur 4–5 times in the first 2 years after being infected with HSV. However, over time the virus tends to become active less often and each time you get symptoms they are less severe.

Symptoms can vary from mild irritation to painful blisters/sores and malaise. Sores can be found on the vulva and entrance to the vagina, cervix, anus, buttocks, and top of thighs.

Adults

Often asymptomatic.

1. *Primary infection (lasts 3 weeks)*: systemic symptoms (fever, headache, malaise) + local symptoms (pain, itching, discharge, pustular or ulcerative lesions that burst and gradually heal without scarring)
2. *Subsequent outbreaks*: no or local symptoms only, outbreak frequency decreases with time

Neonates

- If infected at delivery, there is a greater risk if primary infection (50%, < 5% for outbreak)
- Mortality rate of 65% from disseminated disease

Diagnosis

Sexual Health Check Up

- Physical examination (ulcers, blisters)
- Lab Test Swab to confirm genital herpes (HSV Type involved)

- Both types can produce similar looking infections and thus can only be told apart from lab testing.
- Co-Infection with other STI

Complications

- Disseminated infection, CNS complications (meningitis)

Non-Pharmacological Treatment

- Condoms can reduce risk of passing on the virus by about 50%, but does not remove it completely.
- Wear loose underclothes, ice through flannel/cloth (otherwise can burn sores), vaseline
- Drink plenty of fluids as this dilutes your pee and may help reduce stinging.
- Salt baths

Pharmacological Treatment

[NZ Herpes Simplex Foundation - Summary of the Treatment Guidelines](#)

Notifying sexual contacts is **not** necessary

1. Systemic antivirals (7 days): aciclovir, valaciclovir.
 - a. *Episodic treatment*: take as soon as symptoms appear to fasten resolution and reduce severity of disease. However, it has no impact on risk/severity of recurrences
 - b. *Prevention*: take continuously for **suppressive therapy** to prevent recurrent episodes and spread of virus to other sexual partners.
2. Pain relief: paracetamol, ibuprofen
3. Local anaesthetic: lignocaine cream



Note

Antiviral creams are not recommended as treatment for a first episode or recurrent genital herpes

Acquired Immune Deficiency Syndrome (AIDS) | HIV

[Health Navigator AIDS & HIV](#)

Description

Human immunodeficiency virus (HIV) is a retrovirus that attacks the body's immune system and interferes with the body's ability to fight infections. If HIV is left untreated, it can lead to AIDS which causes severe deficiency of the immune system, thereby increasing risk of severe and opportunistic infections. There is currently no cure for the virus but treatment can control HIV.

Pathophysiology

Immunosuppression occurs in HIV due to a depletion of CD4 lymphocytes. HIV enters the host by interacting with those lymphocytes and is converted from RNA to DNA inside of them using a reverse transcriptase enzyme. The virus has primarily three methods of transmission:

1. *Sexual Transmission (most common)*: blood, semen, pre-seminal fluids
2. *Parenteral Transmission*: IVDU, occupational exposure, blood products/organ transplants
3. *Mother to Child Transmission*: childbirth, breastfeeding

The virus can be transmitted through contact with infected fluids (e.g. blood, needles, semen, or vaginal fluids). You can't become infected through ordinary day-to-day contact such as kissing, hugging, shaking hands or from sharing personal objects, food or water.

There are three stages to an HIV infection:

Stage 1 – Primary Infection Phase

- Signs of a systemic infection appear here, onset is 1-6 weeks following exposure and can last 1-3 weeks.

Stage 2 – Clinical latency

- HIV begins to weaken the immune system, no other symptoms are exhibited during this stage.

Stage 3 – AIDS

- Opportunistic infections begin here

Risk Factors

- Injecting drugs, needle use (e.g. sharing)
- Occupational hazard: blood products, organ transplant
- Sex with a HIV infected partner
- People being treated for other STI
- Sex workers
- MSM/Bisexual Male populations

Signs & Symptoms

HIV infection

- Flu-like symptoms (fever, sore throat, fatigue, swollen glands).
- Other: diarrhoea, N&V, headache, rash, muscle aches
- May be asymptomatic until it progresses to AIDS.

AIDS

- Weight loss, fever or night sweats, fatigue, recurrent infections

Screening

- Routine, voluntary screening for all aged 13-54 years old
- High risk groups: IVDU, multiple sexual partners, MSM

Diagnosis

1. Antigen/Antibody Testing:

- Usually positive within 2 weeks from primary infection

2. Antibody Testing

- Look for HIV antibodies in blood or saliva - rapid tests and self-tests
- Can take 3 to 12 weeks after you are exposed to become positive

3. Nucleic Acid Tests (NATs)

- Viral load tests
- First test to be positive after exposure

Pharmacological Treatment — ART

Health Navigator - Antiviral Treatment

All HIV infected patients, regardless of CD4 count should be treated. No cure exists for AIDS, but strict adherence to anti-retroviral regimens (ART) can dramatically slow the disease progress as well as prevent secondary infections and complications.

ART is usually a combination of two or more medications from several different drug classes. There are many ART options that combine multiple HIV medications into one pill, taken once daily. Treatment regimen depends on many factors e.g. patient, pregnancy, adherence, ADRs, interactions, availability, resistance etc.

First Line Options

- 2x Nucleoside Reverse Transcriptase Inhibitors (NRTIs), **AND either**
- Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), **OR**
- Integrase Strand Transfer Inhibitors (INSTIs), **OR**
- Protease Inhibitors (ritonavir) +/- boosted regimens (cobicistat)

Drug Class	Mechanism of Action	Examples	Side Effects
Nucleoside reverse transcriptase inhibitors (NRTIs)	Nucleoside analogues that inhibit viral replication by being incorporated into viral DNA by reverse transcriptase.	1. Emtricitabine 2. Tenofovir disoproxil 3. Abacavir 4. Lamivudine 5. Didanosine? 6. Zidovudine	GI disturbances (including nausea, vomiting, abdominal pain, flatulence, diarrhoea, constipation), abnormal dreams, insomnia, rash, fever. Associated with life-threatening lactic acidosis
Non-Nucleoside reverse transcriptase inhibitors (NNRTIs)	Noncompetitively inhibit HIV-1 reverse transcriptase impairing DNA polymerase activity and inhibiting HIV-1 viral replication. These drugs may interact with a number of drugs metabolised in the liver.	1. Efavirenz 2. Etravirine 3. Nevirapine 4. Rilpivirine	
HIV integrase inhibitors	Block the strand transfer step of retroviral DNA integration which is essential for HIV replication.	1. Dolutegravir 2. Elvitegravir 3. Raltegravir	
Pharmacokinetic enhancer	Boosts the concentrations of other antiretrovirals, but it has no antiretroviral activity itself.	1. Cobicistat	
Protease Inhibitors	Interfere with viral replication by binding to the site of HIV protease activity, preventing cleavage of viral precursor polyproteins. The protease inhibitors are metabolised by cytochrome P450 enzyme systems and therefore have a significant potential for drug interactions.	1. Atazanavir 2. Darunavir 3. Indinavir? 4. Lopinavir 5. Ritonavir	

Monitoring & Management

- Plasma lipids and blood glucose should be measured before starting antiretroviral therapy, after 3–6 months of treatment, and then annually.

Prevention

- PrEP (pre-exposure prophylaxis) for risk individuals e.g. MSM: **Emtricitabine + Tenofovir disoproxil**
- PEP (post-exposure prophylaxis): prompt antiretroviral therapy required

Goals of Therapy

- Prevent complications e.g. mortality, AIDS defining illnesses, minimise ADRs,
- Normalise symptoms
- Reduce transmission and viral load (undetectable)
- Increase CD4+ count
- Improve quality of life

REPRODUCTIVE TRACT INFECTIONS (RTIs)

Description

We will look into three RTIs: vulvovaginitis, CMV and PID. Please note, many infections which occur in pregnancy can translate to congenital infections. The most critical include: *TORCH*

- Toxoplasma Gondii
- Other: Listeria monocytogenes, Treponema pallidum, VZV, HIV, enteroviruses, parvovirus B19
- Rubella virus
- Cytomegalovirus (CMV)
- HSV-1 and HSV-2

Vulvovaginitis

[Health Navigator Vulvovaginitis](#), [Dermnet Candida Vulvovaginitis Photos](#)

Description

Vulvovaginitis describes the inflammation of the vagina that can result in discharge, itching and pain. There are two types:

1. Thrush (caused by a fungal infection) and
2. Vaginosis (caused by a bacterial infection)



Pathophysiology

The vagina has a normal microflora—with *lactobacilli* being the most commonly occurring organism in the reproductive tract. Other bacteria & *Candida* may also be present as commensals. Vulvovaginitis occurs when the normal balance of yeast and bacteria in the vulva/vagina is disturbed e.g. a shift from lactobacillus to abnormal mixed microflora. It is the most frequent reproductive tract infection in women and there are many things that can cause it:

Risk Factors

- Recent antibiotic use (broad-spectrum)
- Pregnant
- Smoking
- Diabetes

- Immunosuppression
- HRT, OC use with estrogen (replace with progesterone only if recurrent infections)

CAUSES/RISK FACTORS FOR VULVOVAGINITIS	
Cause	Description
Infections	<p>There are 3 common infections that cause vulvovaginitis: Bacterial, Fungi or STIs:</p> <ol style="list-style-type: none"> 1. Vaginal Thrush – candida overgrowth can cause this — see vaginal thrush. 2. Bacterial Vaginosis – proliferation of harmful bacteria — see bacterial vaginosis 3. Trichomoniasis – <i>trichomonas vaginalis</i> is transmitted via sexual contact — see trichomoniasis
Medical Condition	<ol style="list-style-type: none"> 1. Diabetes: uncontrolled blood sugar can enable proliferation of harmful micro-organisms
Hormonal Changes	<ol style="list-style-type: none"> 1. Post-menopause: reduced estrogen levels after menopause (genitourinary syndrome of menopause; vaginal atrophy) 2. Pregnancy: hormonal changes can dampen the mother's acquired immune system, predisposing her to infections. This is of concern because it can vertically transmitted to the newborn - particularly during delivery.
Medicines	<ol style="list-style-type: none"> 1. Recent antibiotic treatment: can disrupt the normal microflora. 2. HRT, OC: estrogen exposure
Irritation	<ol style="list-style-type: none"> 1. Urine or faeces that is not wiped away after toileting 2. Soaps, lubricants or bubble baths 3. Tight-fitting clothing 4. Scratchy toilet paper 5. Douching
Other	<ol style="list-style-type: none"> 1. Age

Signs & Symptoms

Symptoms are usually noticed in the area in or around your vagina and include — depending on the cause

- Redness and inflammation
- Itchiness
- Burning sensation
- Pain when peeing or during intercourse
- Abnormal vaginal discharge and odour
- Light vaginal bleeding or spotting

TYPICAL FEATURES OF VAGINITIS vs OTHER STIs				
Symptom	Bacterial Vaginosis	Vaginal Thrush (Yeast Infection)	Trichomoniasis	Chlamydia & Gonorrhoea
Causative Agent	Gardnerella Vaginalis	Candida albicans	Trichomonas Vaginalis	Chlamydia Trachomatis & Neisseria Gonorrhoea
Discharge	Off-white or green watery discharge that is heavier than usual	Thick white, clumpy discharge that resembles cottage cheese.	Greenish-yellow or white sometimes frothy discharge.	Scant to absent
Itching	±	++++	+	None
Odour	Strong fishy odour	None	Mild odour	None
Other	External dysuria	Dysuria, erythema, associated genital skin rash	External dysuria	Internal dysuria, painful sex
Sexually Transmitted?	Atypically	Atypically	+	+
Precipitating factors	Frequent sexual activity, change in sexual partners (upsets normal balance) pregnancy, OCs, diabetes, recent antimicrobial treatment, menopause, corticosteroid use		None	Sexual activity with new partner

Red Flags (Fungal Thrush)

- Patients should seek medical advice if symptoms return within 2 months or they have had 3 or more fungal infections within the past 6 months.
- Refer to GP if age <16 years or >60 years



Differential Diagnosis

It can sometimes be difficult to distinguish STIs from vaginitis as both share the same risk factors - especially changes in sexual partners. The only sure way to tell is to get tested - encourage patients to do this, especially if you suspect that they may have contracted one.

Complications

- If occurs in first trimester, it can increase in childbirth difficulties (pre-term birth, miscarriage, lower neonatal birthweight)
- GBS Infections in Neonatal (vertical transmission during delivery)

Non Pharmacological Treatment & Prevention

- Wearing loose-fitting breathable clothing that doesn't hold moisture in e.g. loose cotton undies
- Not using perfumed soaps or sprays on or near your vagina
- Avoiding washing inside your vagina
- Using a condom during sex
- Avoiding tampons
- Wipe front to back
- While passing urine, use toilet paper as a blotter instead of wiping

Pharmacological Treatment

- Bacterial Vaginosis:* Metronidazole, Clindamycin (see [BPAC Bacterial Vaginosis Treatment Guidelines](#))
- Candida Vulvovaginitis:* Miconazole (creams), Clotrimazole (creams/pessaries), Fluconazole (tablet)
- Trichomoniasis:* Metronidazole or Ornidazole

TREATMENT OF VAGINAL CANDIDIASIS [PHARMACIST ONLY MEDICATIONS]				
Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Fluconazole 150mg one-dose capsule	<ul style="list-style-type: none"> One off dose capsule. Must be sold in manufacturer's OP containing 150mg or less as a single dose for the treatment of vaginal candidiasis 	Pregnancy: Contraindicated Breastfeeding: Okay	<ul style="list-style-type: none"> Relief of symptoms is quicker with oral options Take with food and water Check for allergies Should work within a day Causes N&V 	<ul style="list-style-type: none"> If symptoms do not resolve after 1-3 days or get worse e.g. fever, patient becomes systemically unwell Allergic reaction develops e.g. itching, rash, swelling
Miconazole + Hydrocortisone <i>Micreme H</i> Topical Cream	<p><i>Note:</i> if product contains hydrocortisone (e.g. Micreme H, Canesten Plus) - it is for external symptoms of thrush (do not use vaginally)</p>			
Miconazole <i>Micreme</i> Vaginal Cream (2%) with Applicator	<ul style="list-style-type: none"> 1 applicatorful for 7 days before bed (regardless of whether symptoms disappear) 	Cautions <ul style="list-style-type: none"> For vaginal use only Cream reduce effectiveness of latex condoms 	<ul style="list-style-type: none"> Wash hands and insert one applicator filled with cream into the vagina while lying on your back as far as it will comfortably go. Slowly press the plunger of the applicator in to apply the cream. Wash applicator thoroughly before reusing Symptoms resolve within a week 	<ul style="list-style-type: none"> If symptoms worsen or persist. Treatment longer than 7 days may be required - refer to doctor
Nystatin <i>Nilstat</i> Vaginal Cream (100,000 IU/5g)	<ul style="list-style-type: none"> 1 applicatorful, TWICE daily for 14 days 		<ul style="list-style-type: none"> Wash hands before use. Similar to Miconazole, fill the applicator up with cream (5g) and insert high into the vagina ONCE or TWICE daily. Applicator can be reused. Wash thoroughly before reusing. 	<ul style="list-style-type: none"> If symptoms worsen or persist after 3 days Treatment longer than 14 days might be required - refer to doctor
Clotrimazole <i>Canesten, Clomazol</i> <ul style="list-style-type: none"> Vaginal Cream (1%); 6 Days Vaginal Cream (2%); 3 Days Vaginal Cream (10%); 1 Day - Canesten 	Depends		<ul style="list-style-type: none"> Wash hands and insert one applicator filled with cream into the vagina while lying on your back as far as it will comfortably go. Slowly press the plunger of the applicator in to apply the cream. DISPOSE applicator after use. 	<ul style="list-style-type: none"> If symptoms worsen or persist after 4 days Longer treatment may be needed.

Clotrimazole Treatment Options for Vaginal Thrush					
Type Formulation	Formulation	Convenient oral treatment	Suitable in Pregnancy	Helps soothe vaginal dryness	Immediate relief from external itching and soreness
Oral	Oral Canesten	✓			
	Canesten Duo (+ Fluconazole)	✓			✓
Creams	1 day cream		✓	✓	
	3 day cream		✓	✓	
	6 day cream		✓	✓	

Pessaries	1 day pessary + Cream		✓		✓
	Once Pessary		✓		
	6 day Pessary		✓		

OSCE Points

- *Differential diagnosis:* itch, discharge, odour
- *Precipitating factors:* antibiotics, pregnancy/menopause, change in sexual partners, diabetes
- *Potential contraindications to medicines:* pregnancy/breastfeeding
- *Red flags:* recurrent episodes, child, <16 or > 60
- Options:
 - Antifungal vaginal cream
 - Fluconazole (pharmacist only) with food — contraindicated in pregnancy

Cytomegalovirus (CMV)

[NHS Cytomegalovirus \(CMV\)](#), [Cytomegalovirus \(CMV\) and pregnancy](#)

Description

Cytomegalovirus (CMV) is a common virus that is passed on through close contact with another person. When a pregnant women passes an active CMV infection to her unborn baby, this is known as congenital CMV.

Pathophysiology

CMV spreads from person to person through close contact, body fluids, such as blood, saliva, urine, semen and breast milk. It is to be noted this virus can only be passed on when ‘active’ which:

- If it’s your first time e.g. young children
- Re-activation through a weakened immune system e.g. pregnancy, chemotherapy
- Re-infection with a different strain (type) of CMV



Note

Once you have CMV, **it stays in your body for the rest of your life.**

Risk Factors

Pregnant women who work closely with children or have a young family are more at risk of catching CMV

Signs & Symptoms

- Most people are asymptomatic: a healthy immune system usually keeps the virus from causing illness
- Flu-like symptoms are common: high temperature of $\geq 38^{\circ}\text{C}$, aching muscles, tiredness, feeling sick, sore throat, swollen glands
- People with weakened immune systems can experience more serious symptoms: affecting the eyes, lungs, liver, oesophagus, stomach, and intestines
- Babies born with congenital CMV are usually healthy and grow up with normal health, however some develop hearing problems later on. Some may be born sick at birth e.g. premature, LBW, jaundice, poor liver function, rashes, microencephaly, pneumonia, still birth — these babies develop severe long-term health problems later on in life

Non-Pharmacological Treatment

Decrease infection risk with good hygiene practices, especially after touching children e.g. nappy changes

Pharmacological Treatment

There is no cure, but there are medications that can help treat the symptoms.

- *Generally:* most people don't need treatment for CMV, but antiviral medicine can be used to treat people with a weakened immune system and babies.
- *In Pregnancy:* no treatment for CMV in pregnancy — in most cases, the virus doesn't cause problems for your baby.

Prevention

There's currently no vaccine for CMV

Pelvic Inflammatory Disease (PID)

Description

Pelvic Inflammatory Disease is an infection of the female upper reproductive organs in the pelvis (uterus, fallopian tubes, ovaries). It is a common complication of STIs such as Chlamydia & Gonorrhoea, however other bacteria from your vagina and cervix to the uterus and fallopian tubes can also cause PID.

Risk Factors

- Age < 30 years
- Unprotected sex, STIs (may refer for STI check), new sexual partners
- IUD insertion
- Termination of pregnancy/miscarriage/childbirth

Signs & Symptoms

- Lower abdominal pain
- Abnormal vaginal bleeding or discharge, pain during sex
- Fever, N/V

Red Flags: Severe tummy pain, fever and chills, repeated episodes of vomiting, generally unwell, heavy vaginal bleeding

Complications: Chronic or long term lower abdominal pain, scarring of the fallopian tube which can cause infertility or ectopic pregnancy, abscess in/around fallopian tube or ovary

Non-Pharmacological Treatment

- Use condoms
- Regular sexual health check for STIs: advise sexual partners to get tested and treated
- Avoid sex or use condoms for 2 weeks after starting treatment

Pharmacological Treatment

[BPAC Pelvic Inflammatory Disease Antibiotic Guidelines](#) [NZSHS PID](#) [The Pink Book: PID](#)

- *Antibiotics:* Ceftriaxone, doxycycline, metronidazole, azithromycin
- *Pain relief:* Paracetamol

Monitoring — [NZSHS PID](#)

- Advise to abstain from sex until abdominal pain has settled and to use condoms for 14 days from the start of treatment and until 1 week after all sexual contacts have been treated.
- Advise all partners from the past 3 months to get a sexual health check.
- Follow up with GP post-treatment

Resources

- [Bloke's Book & Men's Health Trust NZ](#)

Description

Men's health constitutes an important part of pharmacy practice, mainly due to the fact they have different health needs and different priorities. Between the ages of 50 and 75, the overall number of deaths for men is 30% higher and earlier than for women — the top killers in younger years being suicides and accidents and later on life being cancers, heart disease, COPD and strokes.

Pharmacists hold an important role in encouraging healthy habits and healthy living:

1. Healthy Diet
2. Physical Activity (30 minutes of moderate to vigorous activity)
3. Healthy Body Weight (BMI 18.5 - 24.9)
4. Smoking Cessation
5. Moderate Alcohol Intake

Six Signs Men Shouldn't Ignore:

1. Chest Pain
2. Big Belly ('Beer gut')
3. Erectile Dysfunction
4. Constipation
5. Frequent Urination
6. Mental Health

Factors affecting male fertility

- Smoking tobacco, alcohol, marijuana, anabolic steroids use
- Overweight
- Having certain past or present infections
- Being exposed to toxins
- Overheating the testicles or trauma to the testicles
- Certain prescription medicines can affect sperm health (e.g. CCB)

To optimise fertility:

- Maintain a normal BMI and normal exercise
- Avoid smoking, medicines that affect sperm health
- To optimise chance of fertility, give 2-3 days between ejaculations
- Minimise workplace exposure to chemicals (solvents, industrial chemicals, etc...)
- **Menevit:** male fertility supplement to support sperm health

Erectile Dysfunction (ED)

NZF Erectile Dysfunction

Description

Erectile Dysfunction (ED) is the consistent or recurrent inability to obtain and/or maintain an erection sufficient for satisfactory sexual activity. It affects 52% of men aged 40 to 70 years old. It is important to note that erectile dysfunction itself is not a disease but a symptom of a physical and/or psychological problem. ED shares many risk factors for heart disease and warrants a **cardiac risk assessment** in most patients.



Cardiac Risk Assessment - Why Do We Need It?

Having ‘trouble getting it up’ can often be the first presenting symptom of cardiovascular disease - it is thus crucial to investigate the patient’s heart health before proceeding.

Pathophysiology

Normal Erection

An erection is the result of an increased influx of blood and a decreased efflux. The vascular spaces of the 2 erection cylinders of the penis (corpora cavernosum) fill with blood resulting in the swelling of the organ. Relaxation of smooth muscles allow for a high blood flow. Following ejaculation, the influx of blood decreases and the efflux increases, resulting in its deflation (flaccid). This is allowed by the contraction of smooth muscles resulting in a low blood flow.

Erections in ED

While ED stems from multiple causes, anything that can cause issues with the flow of blood in or out (e.g. damage to nerves) can make it difficult for an erection to occur.

Risk Factors

CAUSES OF ERECTILE DYSFUNCTION	
Cause	Description
Vascular	Arterial (HLP, T1/2DM, HTN, Trauma/Surgery e.g. prostate cancer)
Neurogenic	Trauma/Surgery, MS, T1/T2DM
Psychologic	Depression, Anxiety, Substance Abuse
Hormonal	Low Testosterone, Low Thyroid, Low Prolactin
Anatomical	Peyrone's disease, phimosis
Medications	anti-HTN, anti-depressants (SSRIs), anti-histamines, anti-psychotics, digoxin
Chronic Conditions	COPD, Alzheimer's, Renal/Liver complications
Other	Smoking, Drinking, Reduced Quality of Life, Emotional Stress, Damaged relationship between partners

Signs & Symptoms

Inability to get or keep an erection firm enough for sexual intercourse.

Non-Pharmacological Treatment

1. Smoking cessation, limit alcohol intake
2. Diet & Exercise
3. Control underlying conditions

Pharmacological Treatment

1. Phosphodiesterase type-5 inhibitors (PDE5i)
2. Hormonal treatment
3. Intracavernosal injection (ICI) therapy: Alprostadil
4. Pumps
5. Implants

[PHARMACIST-ACCREDITED MEDICINE] <i>PDE5 Inhibitors</i> Sildenafil (Vedafil, Viagra), Tadalafil, Vardenafil	
Mechanism of Action	In summary, PDE5i relax smooth muscles and increase blood flow to encourage an erection <u>in response to sexual stimulation</u> . Nitric oxide passes into the smooth muscle cells of the blood vessel wall and produces cGMP, which decreases Ca levels, resulting in muscle relaxation. PDE5i allow this process to occur by inhibiting PDE5. <ul style="list-style-type: none">• PDE5 is an enzyme that breaks down cGMP, increasing Ca levels and causing muscle contractions (creating a low blood flow and thus no erection)
Patient Counselling	<ul style="list-style-type: none">• Take 1 hour before sexual activity.• Food can delay onset of effect (high fatty foods). Avoid grapefruit and its juice• No more than 1 dose in 24 hours <ul style="list-style-type: none">• Sexual and mental stimulation is required — anxiety can counteract effects!• This medicine will not work if ED is related to nerve-damage.• ED may be an early warning sign of CV disease <ul style="list-style-type: none">• If you anticipate sexual activity at least twice weekly, 5mg Tadalafil OD can be taken• Efficacy of the 3 drugs vary! Must have at least 4 attempts with 2 different PDE5i in the absence of contraindications before declaring failure.
Side Effects	Headaches, dyspepsia, rhinitis, flushing of the face/skin, abnormal vision (sildenafil), dizziness, myalgia (tadalafil)
Contraindications	Nitrates, Hypotension, Recent stroke or MI, unstable angina
Interactions	Metabolised predominantly by CYP450, 3A4 and 2C9 (e.g. cimetidine, erythromycin (inhibitor), rifampicin (inducer))
Pharmacist Supply	<p>Sildenafil accredited pharmacist supply</p> <ul style="list-style-type: none">• Maximum 12 dosage units (tablets containing ≤ 100mg) in manufacturer's original pack• For the treatment of ED in males aged 35-70 years• No underlying CV problems (HTN, diabetes), not smoking <ul style="list-style-type: none">• Accreditation required• Pharmacist must record the sale, give verbal and written advice• Take BP and HR on initial consultation and then yearly thereafter <ul style="list-style-type: none">• Outside of these criteria, a GP must be consulted.• Needs to have an assessment completed before any resupply.

A note on Alprostadil (Intracavernosal injection):

- MoA: Prostaglandin E1 which binds to G proteins coupled to PGE1 receptors on the surface of smooth muscle cells, activating cyclic adenosine monophosphate (cAMP) pathway and thus inducing vascular smooth muscle relaxation and erection.

- Note: If **priapism** (persistent and painful erection) occurs, intracavernosal injection with **adrenaline** should not be delayed more than 6h.

OSCE Points

If new supply

- Vedafil form: Check age (35-70), CV health, **LIFESTYLE**, penile deformity/serious eye disorders, smoking
- 1 tablet 1 hour before sexual activity on an empty stomach
- Need sexual stimulation
- Maximum 1 dose in 24 hours
- Avoid grapefruit and its juices
- Side effects: low BP, headaches, flushing, dizziness
- Do not take with any other erectile dysfunction medications or poppers (sexual enhancement drugs)
- Red flags: prolonged or painful erection (priapism)

Resupply

- Changes in any factors: medical conditions, medicines, lifestyle (mental health, smoking, recreational drugs, alcohol)
- Check adherence
- Increase dose? (Maximum dose is 100mg)
- Failure can be declared after **4 attempts with 2 different PDE5i** in the absence of contraindications

Heart and Diabetes Check Guidance

- Regular heart and diabetes checks are recommended by the [Ministry of Health](#) starting at different ages for different population subgroups. Starting ages and other details can be found in the ["Cardiovascular Disease Risk Assessment and Management for Primary Care"](#) document on the Ministry of Health website.
- The sildenafil assessment forms include a question asking whether a man has had a recent heart and diabetes check. **Erectile dysfunction (ED)** may be an early warning sign of cardiovascular risk and/or diabetes so this question provides an important opportunity to educate men about the need to have regular risk assessments (i.e. a heart and diabetes check via general practice).
- The ongoing frequency of heart and diabetes checks is determined by the results of the initial assessment. Once a man is connected with his general practice, he should receive recalls for reassessments at the appropriate intervals. The key emphasis for pharmacists is helping to ensure men presenting in the pharmacy with ED are engaged in this system.

In practice, any man presenting with ED who has never had a heart and diabetes check should be advised to have one. Advice regarding the need for reassessment (i.e. another check through general practice) in men who have previously had a heart and diabetes check will depend on how long ago the check was, whether he is engaged with his GP, and the overall clinical picture.

Accredited pharmacists can supply sildenafil at the initial consultation to a man who has not had a heart and diabetes check if he fits all of the other eligibility criteria. However, such men must have this check **before** sildenafil may be supplied to him again.

If you are referring a man for a heart and diabetes check, add a comment in the resupply section of the assessment form (or on his computer record depending on the system used in your pharmacy) to highlight that he must have had a heart and diabetes check **before any resupply**.

If a man needing a heart and diabetes check **has not** had one before he returns for resupply, do not resupply and refer him again for this check recording your action on the assessment form.

If a man needing a heart and diabetes check **has** had it when he returns for a resupply, document this on the form and resupply if he still fits the other criteria.

Pharmacists can accept the man's word that he has had a check but discussion about the results is needed to ensure he still meets the other criteria on the assessment form.

If you have concerns about a man's cardiovascular/diabetes risk at any stage, you may make a professional decision to refer rather than supply.

This document was prepared by Dr Natalie Gauld (sponsored by Douglas Pharmaceuticals Ltd) in collaboration with the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and Green Cross Health Limited. For further detail refer to approved training content, associated assessment forms, and relevant data sheet. **June 2020**

Core Requirements for Pharmacist Supply of Sildenafil

This document outlines the core requirements for the non-prescription supply of sildenafil by pharmacists in New Zealand. It has been created to support pharmacists in areas highlighted for improvement by Medicines Control Pharmacy Quality Audits. It is based on the sildenafil classification statement and reflects the [Pharmacy Council Protocol for the Sale and Supply of Pharmacist Only Medicines for Chronic Conditions](#) and the model provided to the Medicines Classification Committee.

SILDENAFIL CLASSIFICATION STATEMENT: Prescription Medicine, EXCEPT in medicines for oral use containing 100 milligrams or less per dose unit when sold in the manufacturer's original pack containing not more than 12 solid dosage units for the treatment of erectile dysfunction in males aged 35-70 years by a registered pharmacist who has successfully completed a training programme endorsed by the Pharmaceutical Society of New Zealand.

1. Pharmacists must successfully complete a sildenafil training course approved by the Pharmaceutical Society to supply non-prescription sildenafil, even resupplies.
2. Complete every question on the assessment form for all men on their first presentation to your pharmacy for non-prescription sildenafil and retain the form in the pharmacy. For guidance on the heart and diabetes checks please see the next page.
3. Repeat the full assessment form every 12 months and record answers to all questions.
4. Resupplies: Complete the resupply section on the assessment form, review any health or medication changes as they may affect eligibility for resupply. Reconsider any concerns from previous visits.
5. Do not supply outside the criteria detailed on the assessment form, e.g. do not supply to a smoker, a diabetic, or if BP, pulse or age is out of range – always refer these men to their GP.
6. Supply unopened manufacturers' packs of sildenafil only, e.g. 4 or 12 tablets. Do not repack or add/remove tablets to the pack.
7. Provide a maximum of 12 tablets of sildenafil at a time.
8. Process all supplies of non-prescription sildenafil (initial and resupplies) through your dispensary software (include dosing instructions and pharmacist name as prescriber). Resupplies must be processed as a new dispensing, not as repeats.
9. Provide supporting written information and verbal advice at every initial consultation. Reoffer written information at the 12-monthly assessment or as appropriate to the individual needs of the man.
10. Inform the man's GP of the supply unless the man opts out.

For any questions please contact the professional support team most appropriate to you:

Pharmaceutical Society
practice@pznz.org.nz
04 802 0030 ext. 3

Pharmacy Guild
audit@pznz.org.nz
04 802 8200 ext. 1

Green Cross Health
calthy.martin@gxh.co.nz
09 371 9084

This document was prepared by Dr Natalie Gauld (sponsored by Douglas Pharmaceuticals Ltd) in collaboration with the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and Green Cross Health Limited. For further detail refer to approved training content, associated assessment forms, and relevant data sheet. **June 2020**

Date: 21/07/20 15:26 NHI: Pharmacy Name: School of Pharmacy Phone: 03 479 7280

Vedafil		Patient Assessment	Page 1 Screening																															
Age between 35 & 70 yrs old	<input type="checkbox"/>	Age:	DOB:	If <35 yrs or >70 yrs REFER>																														
Has erectile dysfunction (ED)?	<input type="checkbox"/>	Discuss the patient's concerns and consider possible causes (e.g. relationship problems, anxiety, depression). Record details:																																
Used ED medication before? Did it work? Any adverse effects?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	If previous use of ED medication has not been effective or if significant adverse events occurred. REFER>																																
Medical History (please tick) <table border="0"> <tr> <td>Diabetes</td> <td><input type="checkbox"/></td> <td>Unable to walk briskly for 5mins or walk uphill without becoming breathless or getting chest pain; OR advised by Doctor to avoid exercise including sexual activity.</td> <td><input type="checkbox"/></td> </tr> <tr> <td>High cholesterol (uncontrolled or untreated)</td> <td><input type="checkbox"/></td> <td>Previous heart attack/stroke/TIA</td> <td><input type="checkbox"/></td> </tr> <tr> <td>Current smoker</td> <td><input type="checkbox"/></td> <td>History of angina</td> <td><input type="checkbox"/></td> </tr> <tr> <td>Severe liver dysfunction</td> <td><input type="checkbox"/></td> <td>Previous coronary intervention (e.g. angioplasty, bypass surgery, valve replacement)</td> <td><input type="checkbox"/></td> </tr> <tr> <td>Severe kidney dysfunction</td> <td><input type="checkbox"/></td> <td>Personal or family history of serious eye disorders, excluding glaucoma and cataracts (e.g. Retinitis pigmentosa)</td> <td><input type="checkbox"/></td> </tr> <tr> <td>Blood disorders (sickle cell disease, leukemia, multiple myeloma)</td> <td><input type="checkbox"/></td> <td colspan="3"></td> </tr> <tr> <td>Any deformity of the penis (e.g. Peyronie's disease)</td> <td><input type="checkbox"/></td> <td colspan="3"></td> </tr> </table>					Diabetes	<input type="checkbox"/>	Unable to walk briskly for 5mins or walk uphill without becoming breathless or getting chest pain; OR advised by Doctor to avoid exercise including sexual activity.	<input type="checkbox"/>	High cholesterol (uncontrolled or untreated)	<input type="checkbox"/>	Previous heart attack/stroke/TIA	<input type="checkbox"/>	Current smoker	<input type="checkbox"/>	History of angina	<input type="checkbox"/>	Severe liver dysfunction	<input type="checkbox"/>	Previous coronary intervention (e.g. angioplasty, bypass surgery, valve replacement)	<input type="checkbox"/>	Severe kidney dysfunction	<input type="checkbox"/>	Personal or family history of serious eye disorders, excluding glaucoma and cataracts (e.g. Retinitis pigmentosa)	<input type="checkbox"/>	Blood disorders (sickle cell disease, leukemia, multiple myeloma)	<input type="checkbox"/>				Any deformity of the penis (e.g. Peyronie's disease)	<input type="checkbox"/>			
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Blood disorders (sickle cell disease, leukemia, multiple myeloma)	<input type="checkbox"/>																																	
Any deformity of the penis (e.g. Peyronie's disease)	<input type="checkbox"/>																																	
Blood Pressure mmHg / mmHg	Restarting heart rate bpm	If <110/70 or >160/95 If <50bpm or >100bpm REFER>																																
Other medicines, either prescribed or purchased?		If any of the following are being taken: REFER>																																
Details:		Nitrates, e.g. glycerol trinitrate, isosorbide salts, amyl nitrates Pulmonary arterial hypertension (PAH) treatments ED medications including other PDE5 inhibitors Ritonavir or saquinavir Two or more antihypertensives.																																
Any other health concerns or comments?		If any of the following are being taken a REDUCED DOSE is required. Alpha blockers, erythromycin, ketoconazole, itraconazole <input type="checkbox"/>																																
Vedafil is a suitable treatment for your patient. You can proceed with supplying Vedafil																																		

Patient Assessment	Page 2 Supply	21/07/20 15:31
Patient: NHI: DOB: Pharmacy Details: Name: School of Pharmacy Address: 18 Frederick Street Phone: 03 479 7280 Fax: 03 479 7034		
To enable your pharmacist to correctly assess whether Vedafil® is suitable for you, please tick to confirm that the information you have provided during this assessment is correct and complete		
To ensure your GP is aware of your health, we would like to contact your GP to advise of this assessment and supply of Vedafil®. If you do not want your GP to be contacted please tick here:		
GP Name:	Phone: Fax:	
Facility Name:		
Patient Signature:		
Product Selection <ul style="list-style-type: none"> - A starting dose of 25mg is required for patients <ul style="list-style-type: none"> o Over 65 years of age o Taking Alpha-blockers (e.g. doxazosin) o Taking erythromycin ketoconazole or itraconazole and titrate according to response/tolerability. - For all other eligible patients, a starting dose of 50mg is recommended, and 100mg can be offered to established patients requiring a higher dose. - A pack size of 4 tablets is recommended for patients using Vedafil for the first time. Larger pack sizes may be recommended for patients who previously have used Vedafil® successfully. - Supply is restricted to maximum of 12 tablets at any one time. 		
Counselling Tips <ul style="list-style-type: none"> - How to take Vedafil® - What to expect with Vedafil® - When to seek further medical assistance - Adverse Effects - General advice -e.g. lifestyle changes, offer Self-care cards - Recommend to visit the GP for heart health and diabetes check - Provide Vedafil® CMI for Pharmacist-Supply 		
Vedafil® to be supplied: <p><input type="checkbox"/> 25mg <input type="checkbox"/> 50mg <input type="checkbox"/> 100mg</p>		
Consulting Pharmacist	Signature _____	
Date of consultation	/ /	
Date next full assessment due	/ /	
Re-Supply (please tick)		
Changes in health?	Changes in medication?	Vedafil® working with no adverse effects?
Comments: A full assessment is required every 12 month or sooner if clinical status of the patient has changed since last assessment.		
Consulting Pharmacist	Signature _____	
Date of consultation	/ /	
Date next full assessment due	/ /	



CHAPTER 13

PAEDIATRICS



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Chapter 13

Paediatrics

Paediatrics Overview

Chapter Resources

See [Starship Hospital Guidelines](#) for Antibiotics in Paediatrics

Introduction

Stage	Description
Conceptional/Fetal Age	Age from the date of conception/fertilisation
Gestational Age	Age from the first day of the last menstrual period
Postnatal Age	Age from the day of birth
Viable Fetus	From ~ 28 weeks gestation
Preterm Newborn	< 38 weeks gestational age
Term Newborn	\geq 38 weeks gestational age
Full-Term	40 weeks gestational age
Neonatal	0 - 30 days of postnatal age
Infant	1 month - 2 years
Young Child	2 - 6 years
Adolescent	12 - 18 years

GENERAL COMPLAINTS

Introduction

We will look into: feeding, sleeping, skin issues, nappy rash, jaundice, colic, blocked tear ducts and teething!

Newborn Feeding & Sleeping

Ministry of Health Baby Sleep & Settling

Description

Sleep

Generally, newborns sleep about 8 to 9 hours in the daytime and about 8 hours at night. However getting sleep as a new Mum is thus often not easy — it is recommended that the Mom tries to get rest when the baby does.

Eating

Newborns and young infants have a small stomach and must wake every few hours (3-4h) to eat.

The Ministry recommends exclusive breastfeeding to around 6 months of age. From around 6 months, babies start to need food and continued breastfeeding to at least one year, or beyond. Non-breastfed infants should be given a commercial infant formula until the baby is 12 months old.

The following indicate that the baby is getting enough to eat:

1. Eats every 1-3 hours and sleeps no more than 3hrs between feedings during day
2. Has 5-6 wet nappies
3. Has 2-4 loose grainy mustard coloured stools a day
4. Is audibly swallowing
5. The baby is satisfied at the end of each feeding and generally content in-between feeds

New Born Skin (Acne, Dryness, ETN & CC)

Description

A newborn's skin will gradually adjust to their new environment in the first six to 12 weeks. A range of conditions may be seen, however, it is usually best to leave the affected areas alone to heal.

Condition	Description	Recommendation
New Born Acne	Very common condition, they appear as red bumps on a baby's cheeks, nose and forehead two to four weeks after birth.	The best way to treat it is to do nothing. Don't treat, pick or scrub them.
Dry & Peeling Skin	Natural process of dead skin shedding.	Lotions will not speed up this process
Erythema Toxicum Neonatorum	Rash appears as red marks on the skin and affects 50% of babies.	It is harmless and requires no treatment
Cradle Cap	Scaly rash that commonly affects the scalp of babies. Possible causes include overactive oil producing glands, mum's hormones and yeasts that live on the skin.	<i>See Chapter 1 - Seborrheic Dermatitis</i> Baking soda and water work quite well.

Nappy Rash

Description

Nappy rash is a type of Irritant Contact Dermatitis (ICD) also known as *Ammoniacal Dermatitis*. It is characterised by inflammatory eruptions in the nappy area caused by urine and faeces sitting close to the skin for extended periods of time. Almost all babies or toddlers will have nappy rash at some stage.

Causes

- Frequent bowel motions due to malabsorption e.g. diarrhoea
- Residual nappy detergent
- Changes in nappy brand
- Zinc deficiency
- Infections
- Antibiotic use (either in mom or baby)
- Teething
- Diet changes e.g. recent changes in milk



Teething & Nappy Rash

Nappy rash can occur or worsen when your baby is teething. It's unclear why teething can lead to nappy rash, although it's thought it could be due to your baby producing more saliva. This changes the nature of their stool, making it more likely to cause a reaction when it touches their skin.

When to Refer?

- If there is no improvement after 4 days
- Broken skin is **not** always a trigger for referral

Differential Diagnosis

Fungal vs Contact Nappy Rash

Fungal Nappy Rash tends to accumulate in groin creases due to the moist environment, has bumps, and is a much brighter shade of red while contact nappy rash is just generally widespread around the nappy area.

Note that fungal nappy rash is often associated with oral thrush - which can affect the mother's nipple

Nappy Rash vs Seborrhoeic Dermatitis/Eczema

Rashes in the nappy area may also be caused by SD or eczema - in those cases, you will see rashes elsewhere in the body.

Non-Pharmacological Treatment

1. Frequent nappy changes as soon as they have been soiled (this can mean up to 12 times a day)



Poo or Pee?

- If nappies only contain pee - simply pat your baby's skin dry and reapply barrier cream.
- If nappies contain poo - wash area with warm water, a soft cloth and a soap substitute. Do not over wash and stay clear of soaps and fragrance containing products e.g. baby wipes, bubble baths, lotions, plastic pants, talcum powder.

2. Bottom must be pat (not rubbed) dry before putting on a new nappy.
3. Expose buttocks to gentle sunlight, with nappy-free period each day for as long as possible!
4. Encourage/support breastfeeding throughout infancy.
5. Disposable nappies are recommended over cloth ones. However, if using the latter, nappies should be washed and rinsed thoroughly to ensure they do not contain residues of soap and detergent.
6. **Do not use vaseline** as it will cause discomfort/irritation

Pharmacological Treatment — [Starship Hospital Nappy Dermatitis Guidelines](#)

Uncomplicated Nappy Rash

1. *Barrier creams*: lanolin or zinc & castor oil cream (apply following nappy changes/bathings)
2. *Soap-free substitute*: sorbolene cream with glycerine

Complicated Nappy Rash

Usually develop within 72 hours of the initial presentation. Use the above + treat secondary infection:

1. *Topical Anti-fungals* if candida infection: miconazole +/- hydrocortisone
2. *Oral Antibiotics* if staph infection (do not use antibiotic ointments as they increase of contact dermatitis)



Counselling Point

When using both a barrier cream and a topical antifungal - recommend application of the topical antifungal first, then wait **15-30 minutes** for absorption and then apply the barrier cream.

Category	Ingredients	Mechanism of Action	Counselling	Side Effects	
Barrier Creams	[GENERAL SALE] <i>Zinc Oxide Cream</i> Sudocrem	Rehydrates and soothes the skin. Creates barrier between skin and diaper, may have additional antiseptic properties.	Apply to affected and surrounding areas to rehydrate and soothe the skin following nappy changes (to prevent contact between excretions and skin)	N/A	
	[GENERAL SALE] <i>Zinc & Castor Oil Ointment</i> Zinc Oxide & Castor Oil				
	[GENERAL SALE] <i>Lanolin</i> Lanolin				
	[GENERAL SALE] <i>White soft paraffin ointment</i>	Rehydrates and soothes the skin.			
	[GENERAL SALE] <i>Dexpanthenol Pro Vitamin B5</i> Bepanthen nappy rash ointment				
Topical Antifungal (+/- Corticosteroid)	[PHARMACY ONLY] <i>Miconazole 2%</i> Daktarin, Resolve	Antifungal + Anti-inflammatory	Apply twice daily continuing for 10 days after lesions have healed	Local irritation and hypersensitivity reactions	
	[PHARMACIST ONLY] <i>Miconazole 2% + Hydrocortisone</i> Micreme H		Apply to affected areas 1–2 times daily until inflammatory symptoms resolve (usually within 7 days) Follow with miconazole alone until complete disappearance of the lesion (usually 2–5 weeks) Steroid may be useful in severe inflammation or concurrent dermatitis	Local irritation, hypersensitivity reactions, thinning of the skin	

Jaundice

Description

Babies are born with an excess of red blood cells due to a need for reserves in the birthing process. Over time, these extra blood cells break down into a chemical called bilirubin.

As the liver is not yet fully functional, it cannot yet break down the excess bilirubin, it thus gets stored in the skin until then, giving it an orange hue within the first week following birth. This is known as jaundice.

Non-Pharmacological Treatment

Jaundice is sometimes treated by putting the baby under special lights which help the body break down the bilirubin more easily.

Complications: Too much bilirubin can cause permanent brain damage.

Colic

Description

Colic is when a baby cries and fusses for hours at a time usually without an obvious cause, and may be difficult to console. It begins around **2 weeks** of age but more babies grow out of it by **16 weeks**. While it does resolve on its own with time, steps can be taken to reduce the severity of colic and lessen parental stress.

Pathophysiology

The cause of colic is unknown but it is not considered to be harmful. Some theories are that the baby's gut hasn't fully developed (inadequate amounts of lactobacilli) or that the gut bacteria is out of balance, but these theories have not been proven. Sometimes other conditions such as reflux, lactose intolerance or cow's milk allergy may be involved, but with colic, the baby is otherwise healthy. Attacks usually more common in the evening (*6pm colic*)

Signs & Symptoms

Excessive and inconsolable crying, facial flushing, drawing up of the legs, pain, restlessness.

Diagnosis

Rule of 3s: infant cries for > 3 hours a day, for > 3 days a week, and for > 3 weeks.

Non-Pharmacological Treatment

Reassure that the child's symptoms will subside over time.

- Encourage passing of a bowel motion or gas, or the baby may simply cry him or herself to sleep.
- Hold baby upright during feeds and burp them afterwards, or raise cot bedhead
- If baby is breastfed and seems worse after Mum has eaten certain foods, or if family history of food allergies: consider avoiding these foods for a couple of weeks to see if the colic improves
- If baby is bottle-fed, consider changing the type of bottle or formula
- Hold baby during crying episodes. Play soothing music or white noise and keep the lights dimmed
- Babies like movement: try gentle swaying or pushing them in a pram, or use a front pack or sling to carry the baby
- A warm bath or a gentle stomach rub might comfort the baby

Pharmacological Treatment

- Simeticone (De-Gas)
- Lactase enzymes
- Low-lactose milk formulas



Note

Before recommending a product, **review** the feeding technique. Underfeeding the baby can cause excessive sucking result in air being swallowed (causing colic like symptoms). Additionally check teat size of bottle in bottle feeding. When turned upside down, the

Blocked Tear Ducts

Description

Blocked tear ducts occur when tears cannot move from the corners of the eyelids into the ducts lining your nose. It is experienced by almost a third of babies and usually resolves itself by the first birthday.

Signs & Symptoms

- Watery teary eyes in the absence of the child crying.
- Pus in the eyes
- Crusting eyelids/eyelashes
- Redness in the inner corner of the eye

Non-Pharmacological Treatment

- Gentle cleaning and massage

Red Flags — signs of an infection

- Inflammation, redness, itching, pain
- Discharge that is yellow or green in colour
- Changes in eye or eyelid structure
- Sensitivity to light

Teething

Description

Many babies start teething around 6 months to 1 year of age and often with no problems. However in some babies, the gums swell and become sore as the teeth break through.

Signs & Symptoms

- Crying, slight fever, red cheeks, drool
- Not eat or sleep well
- Want to bite something hard

Non-Pharmacological Treatment

- Gently rub their gums with a clean finger or the back of a cold spoon. Can also wrap an ice pack in a wash cloth and place it on the baby's cheek
- Give baby something to chew on, such as a clean teething ring

Pharmacological Treatment

- Bonjela (Teething Gel)

Red Flags

- Blue lips
- Blue, yellow or pale skin
- Yellow eyes
- A red, pusy, or smelly umbilical cord
- An extreme temperature or fever
- <6 wet nappies a day
- Frequent bowel movements, especially with liquid or mucous
- Repeated vomiting
- Several refusals to feed in a row
- Excessive sleepiness or any other drastic behaviour change

SERIOUS COMPLAINTS

Introduction

We will look into GBS, SBS, SIDs, FAS, NAS, arrhythmia, thyroid problems, lung problems, cerebral palsy, CAH and CNLD.

Neonatal GBS Infection

[Auckland DHB Neonatal GBS Infection](#)

Description

Group B strep is the most common cause of serious infections in newborns - they are of worry as they can lead to meningitis, pneumonia or sepsis. It is also an infection that the mother can catch during pregnancy and pass onto the fetus at birth.

Risk factors

- Maternal colonisation
- Prolonged membrane rupture
- Fever in labour
- Preterm delivery

Signs & Symptoms

- Newborns: fever, trouble feeding and lethargy

Complications

Group B streptococcus can cause neonatal sepsis, pneumonia, meningitis.

Pharmacological Treatment

1. Penicillin prophylaxis

Shaken Baby Syndrome (SBS)

Description

Shaken Baby Syndrome (SBS) is a serious brain injury resulting from forcefully shaking an infant or toddler — it destroys a child's brain cells and prevents their brain from getting enough oxygen. It is often the result of a parent going crazy due to the baby's uncontrollable crying. It is a form of child abuse that can result in permanent brain damage or death.

Recommendations

1. Put your baby somewhere safe (in a cot or pram) and walk away
2. Take a deep breath and count to 10
3. Ask someone else to come and take over
4. Do not pick up the baby again until you've calmed down

Sudden Infant Death Syndrome (SIDs)

[Mayo Clinic SIDs](#)

Description

Sudden infant death syndrome (SIDS) is the unexplained death, usually during sleep, of a seemingly healthy baby less than a year old — however many of these deaths are avoidable.

Pathophysiology

A combination of physical and sleep environmental factors can make an infant more vulnerable to SIDS. These factors vary from child to child.

Prevention

Perhaps the most important is placing your baby on his or her back to sleep. There's no guaranteed way to prevent SIDS, however these can decrease the risk:

1. Back for sleeping: for the first year of life, places the baby on their back to sleep
2. Keep crib as bare and firm as possible
3. Don't overheat baby, don't cover their head
4. Have baby sleep in your room (but not in adult beds, e.g. use pepi-pods)
5. Breastfeed: breastfeeding for at least 6 months lowers the risk of SIDs
6. Don't use baby monitors or devices that claim to reduce the risk of SIDs (safety issues)
7. Offer a pacifier at nap time
8. Immunise the baby

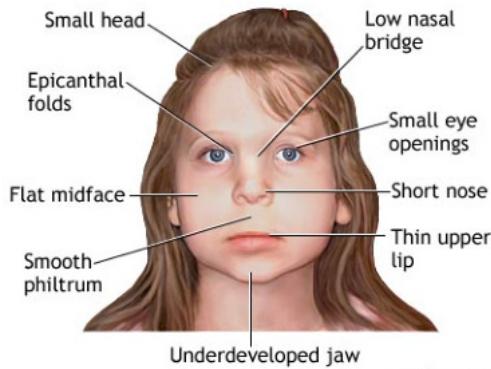
Risk Factors

Factors	Description
Physical	Physical Factors 1. <i>Brain Defects</i> : sometimes the part of the brain that controls breathing and arousal from sleep hasn't matured enough 2. <i>Low birth weight</i> : premature birth/being part of a multiple birth increases the risk of a premature brain 3. <i>Respiratory infection</i> : May contribute to breathing problems
Sleep / Environmental	Sleep/Environmental Factors The items in a baby's crib and his or her sleeping position can combine with a baby's physical problems to increase the risk of SIDS. Examples include: <ul style="list-style-type: none">• Sleeping on the stomach or side (difficulty breathing)• Sleeping on a soft/fluffy surface (can block an infant's airway)• Sharing a bed: While the risk of SIDS is lowered if an infant sleeps in the same room as his or her parents, the risk increases if the baby sleeps in the same bed with parents, siblings or pets.• Overheating: Being too warm while sleeping can increase a baby's risk of SIDS
Biological	Biological Factors 1. <i>Sex</i> : Boys are slightly more likely to die of SIDS. 2. <i>Age</i> : Infants are most vulnerable between the second and fourth months of life. 3. <i>Race</i> : Non-white infants are more likely to develop SIDS. 4. <i>Family history</i> : Babies who've had siblings or cousins die of SIDS are at higher risk of SIDS. 5. <i>Secondhand smoke</i>
Maternal	Maternal Factors During pregnancy, the mother also affects her baby's risk of SIDS, especially if she: <ul style="list-style-type: none">• <i>Age</i>: < 20• <i>Social history</i>: Smokes cigarettes, drugs or alcohol use• <i>Has inadequate prenatal care</i>

Fetal Alcohol Syndrome (FAS)

Description

Fetal alcohol syndrome is a condition in a child that results from alcohol exposure during the mother's pregnancy. Symptoms vary from child to child but they usually involve brain damage, growth problems and are **not reversible**.



Neonatal Abstinence Syndrome (NAS)

Description

Mothers taking opioids/opiates during pregnancy can cause signs of withdrawal in the baby - this is known as Neonatal Abstinence Syndrome (NAS).

Signs & Symptoms

These can be very disturbing to look at in a small baby:

- Tremor, irritability
- Hypertonicity and Hyperactivity (eg. frantic sucking of fists)
- Vomiting
- High-pitched cry
- Sneezing, respiratory distress
- Fever, sweating, diarrhoea
- Rarely convulsions

Diagnosis

Scoring of withdrawal: [Neonatal Scoring Chart CR5664](#) (treatment indicated if several scores >8)

Pharmacological Treatment

Starship Guidelines

1. *Morphine (1mg/mL) solution: 0.5mg/kg/day in 4 divided doses by syringe*

- Titrate following stabilisation (50% will require treatment for 10-20 days, and 1/3 will require treatment up to 49 days after birth)

Fetal Arrhythmia

Description

Abnormal or irregular heartbeats that happen to babies still in the womb

Pharmacological Treatment

Digoxin or β -blocker administered to the **mother**

Monitoring

Levels of digoxin are monitored to avoid maternal toxicity. Fetal rate will usually be controlled before an adult therapeutic level is achieved.

Fetal Thyrotoxicosis & Goitre

Description

Fetal hyperthyroidism. Can cause complications such as breathing problems with the baby.

Pharmacological Treatment

- *Propylthiouracil* (PTU) or *Methimazole* (MMI) administered to the **mother**
- If the mother is herself **euthyroid**, she is administered *thyroxine* so that she doesn't become hypothyroid.

Monitoring

Fetal cord blood can be sampled to monitor fetal thyroid function

Fetal Lung Maturity Acceleration

Description

Corticosteroids can accelerate lung formation and maturation of blood vessels in the brain of pre-term deliveries (<34 weeks gestation), therefore reducing the incidence of intra-ventricular haemorrhage and reduce the risk of respiratory distress syndrome. They stimulate the synthesis and release of surfactants, which lubricates the lungs, allowing the air sacs to slide against one another without sticking when the infant breathes.

Pharmacological Treatment

- *Betamethasone*: 12 mg IM administered in two doses 12-24 hours apart
- *Dexamethasone*

Cerebral Palsy

Description

Cerebral Palsy is a physical disability that occurs due to abnormal brain development during gestation.

Pharmacological Treatment

1. *Magnesium sulphate*: administered to patients delivering at <30 weeks gestation to reduce risk of cerebral palsy.

Congenital Adrenal Hyperplasia (CAH)

Description

Congenital adrenal hyperplasia can cause ambiguous genitalia in girls and an enlarged penis in boys.

Pathophysiology

It is an *autosomal recessive* genetic deficiency in enzymes involved in steroid synthesis. Usually is a *21-hydroxylase deficiency* which shunts (expedites) 17-OH pregnenolone to androgen production. This will virile (masculinize) an affected female fetus.

Pharmacological Treatment

1. Maternal administration of *dexamethasone* in early pregnancy: suppresses fetal adrenal glands

Monitoring

- After administration of dexamethasone, the fetus is then tested for gender and for the enzyme deficiency
 - *If male or unaffected* = treatment discontinued
 - *If female and affected* = treatment continued

Chronic Neonatal Lung Disease (CNLD) / Bronchopulmonary Disease (BPD)

[CHOP - Infant Chronic Lung Disease](#)

Description

Chronic neonatal lung disease (CNLD) is a general term for persisting and long term respiratory problems in premature babies. Most commonly, sustained ventilator support required by infants born <30 weeks gestational age due to their underdeveloped lungs causes pressure and excess oxygen intake to injure the lungs.

Pathophysiology

Damage or injury to immature lungs trigger a pathway that includes:

- Release of pro-inflammatory and anti-inflammatory cytokines
- Imbalance in cytokine mediators that leads to activation of cell death pathways in lungs

Risk Factors

1. Prematurity (underdeveloped air sacs): < 30 weeks white male babies are at the greatest risk
2. Infant respiratory distress: disease that causes low surfactant amounts (surfactant keeps alveoli open)
3. Oxygen pressure from ventilation
4. Low birthweight (<1kg)
5. Pulmonary Interstitial emphysema (PIE) - air leaks out of airways.
6. Maternal womb infection (during or after birth)
7. Family history of asthma

Signs & Symptoms

- Inflammation and scaring of the lungs, increased RR
- Baby not thriving, powerful sucking of the chest when inhaling
- Exposing ribs under skin
- May be associated with pulmonary hypertension

Diagnosis

- Imaging (x-ray, CT): underinflated/overinflated areas of the lungs would be visible on the scans
- Blood gases
- Blood cultures and WBC to rule out infection

Non-Pharmacological Treatment

Supportive care

- O₂ supply → home oxygen
- Mechanical ventilation
- Surfactant replacement therapy
- Avoiding fluid overload
- **Continuous positive airway pressure (CPAP):** Prevention of Respiratory Distress Syndrome

Pharmacological Treatment

1. *Diuretics* (furosemide, **spironolactone & hydrochlorothiazide**): reduce fluid build-up in the lungs
2. *Bronchodilators* (to help open the airways): Aminophylline used within 2 weeks may reduce risk of CLD
3. *Steroids* (for inflammation): Hydrocortisone, betamethasone, dexamethasone **only use if life-saving**
4. *Vasodilators* (decrease BP in lungs): Hydrochlorothiazide
5. *Antibiotics* (for infection)



CHAPTER 14

GERIATRICS



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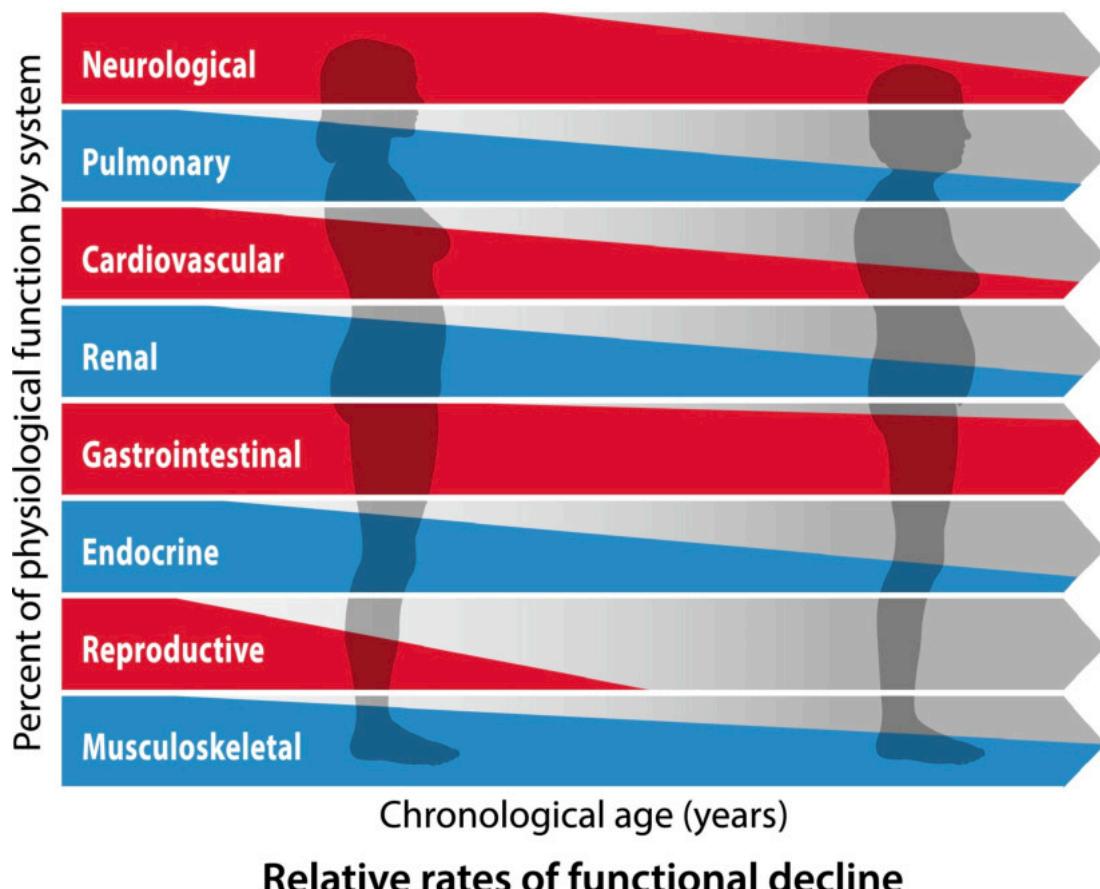
Chapter 14

Geriatrics

Understanding Ageing

Introduction

The world's population is gradually ageing due to people having fewer children and living longer. The human body reaches a peak physiological performance in its 20s and 30s - in the later years (after 35), there is a gradual, hardly perceptible decline in physiological function (skeletal muscle mass, bone mineral density, impaired digestive system).



DEFINITIONS	
Geriatric Syndrome	Geriatric Syndrome describes that complex health states that tend to occur only later in life and do not fall into discrete disease categories. They are often a consequence of multiple underlying factors and dysfunction in multiple organ systems. This includes: <ul style="list-style-type: none">• anorexia of ageing, cognitive impairment, frailty, incontinence, immobility• impaired memory (dementia and delirium), instability (falls), sarcopenia (loss of muscle mass)
Polypharmacy	Polypharmacy refers to the taking of multiple long-term medicines by a person - "many medicines" <ul style="list-style-type: none">• Commonly, taking 5 or more medicines is used as a marker of polypharmacy.• It can be beneficial ('appropriate polypharmacy') or harmful ('problematic polypharmacy').
Prescribing Cascade	The situation in which a first drug administered to a patient causes an adverse effect, that is misinterpreted as a new condition, resulting in a new medicine being prescribed. The cascade may have multiple steps and differ in complexity and severity.
Deprescribing	Deprescribing is the systematic process of identifying and discontinuing medicines when: <ul style="list-style-type: none">• Existing or potential harms outweigh existing or potential benefits within the context of an individual patient's goals or current level of functioning.• When life expectancy is shorter than the time that medicine would take to achieve significant effect.
Senescence	Refers to biological ageing and is an inevitable biological process. The term can be used to describe the ageing of cells or the organism as a whole. When applied to a cell, senescence can be defined as a state in which, despite a growth stimulus, the cell is unable to divide.
Frailty	This is a medical syndrome with multiple causes and contributors that is characterised by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death. Frailty is NOT based on the age of a person but on their physical and functional ability. It is a marker of vulnerability and signifies the need for extra care.

Reduced Homeostatic Capacity

Homeostasis	
<i>Factors that affect homeostasis</i>	
1. Disease	
2. Age: homeostatic mechanisms take longer to return to normal in elderly (reduced homeostatic capacity)	
Mechanism: Controlled in a feedback loop	
Negative (damping, reducing oscillations)	E.g. Glucose, oxygen, water, electrolyte regulation, pH, blood pressure
Positive (amplifying)	E.g. Coagulation, immune system, child birth
<i>Components of a homeostatic system</i>	
1. Stimulus	E.g. Standing up
2. Sensor: a detector that determines whether the system is high or low	E.g. Baroreceptors
3. Control centre: determines what will happen	E.g. ANS
4. Effector: one or more body functions/organs that act in response to a perturbation)	E.g. Sympathetic system increases tone
<i>Systems that show homeostasis</i>	
Temperature	Neurotransmission
Glucose	Neuroendocrine (e.g. gonadal, adrenal, thyroid axes)
Most electrolytes / water (most renal systems)	Haemodynamics (BP)
Blood gases / pH	

PK & PD of Medicines in the Elderly

The Drug & The Body

As the homeostatic capacity of elderly people is reduced - this often means a different response to drugs. Thus, there are a few considerations we need to take into account surrounding medications in the elderly.

PHARMACOKINETICS OF MEDICINES IN THE ELDERLY <i>How the body affects the drug</i>	
Factor	Description
Absorption	<p>No significant effect unless a GI pathology is present. Slower absorption, increased time to peak concentration</p>
Distribution	<p>Increase (or decrease) half life Due to changes in body composition with age (e.g. increased fat mass), some drugs (e.g. lipophilic drugs) have a prolonged duration of effect due to prolonged redistribution from fat sites.</p> <p><i>Example:</i> benzodiazepines may have longer sedative effects in an older person compared to a younger people.</p> <p><i>Note:</i> Age does not always increase the 'effectiveness' of a drug. PK differences can also decrease it (e.g. loop diuretics have a decreased effect with decreasing renal function as a result of age)</p>
Elimination	<p>Increased half life due to decreased clearance Age affects both renal (1% GFR reduction per year after age of 20) and hepatic clearance (15-50% clearance reduction) — with no differences in their function between fit and frail elderly. The decrease in clearance consequently prolongs the half life of the drug. Since most drugs are dosed chronically then start low and go slow is the most important message.</p>
PHARMACODYNAMICS OF MEDICINES IN THE ELDERLY <i>How the drug affects the body</i>	
Factor	Description
Receptor Sensitivity	<p>Ageing causes a change in receptor sensitivity This leads to the same concentration of a drug producing a greater or lesser physiological response.</p> <ol style="list-style-type: none"> 1. Vit K dependent clotting factors are more sensitive to warfarin (warfarin dose reduction needed) 2. CCBs have a greater sensitivity to HR and BP changes 3. β-blocker receptors are generally less sensitive due to reduced second messenger activity (salbutamol has a reduced bronchodilator response, propranolol has impaired effects) 4. α-receptors function is maintained with age 5. Muscarinic receptor function in CNS is decreased (leading to increased effects of anti-muscarinics) 6. GABA receptor function is increased in the CNS (leading to increased sedation with benzos) <p>Changes in receptor function are often the result of changes in homeostatic mechanisms (this is a more important change). Therefore it is not always possible to determine whether changed receptor pharmacology actually exists.</p> <p><i>A note on anti-muscarinics:</i> Older adults are particularly sensitive to anticholinergic drug effects. Many drugs (eg, tricyclic antidepressants, sedating antihistamines) can thus cause older adults to more easily become confused, drowsy, constipated, have urinary retention, dry mouth, etc.. In general, older adults should avoid drugs with anticholinergic effects when possible.</p>
Homeostasis	<p>Ageing & Disease break homeostasis Homeostasis is not as effective in older people</p> <ol style="list-style-type: none"> 1. Stimulus: becomes less sensitive to change with age 2. Sensor: Affected by underlying pathology. Not usually affected by age, but pathologies tend to cumulate in older people 3. Control centre: Depends on consciousness 4. Effector: Usually affected by pathology <p><i>Example: Blood Pressure</i> With age, arteries stiffen resulting in the reduced effectiveness of baroreceptors (the arteries are not flexible enough to detect the change). This results in failure to maintain blood pressure upon standing, the person becomes hypotensive and falls.</p>

Drugs break homeostasis

Drugs work because they temporarily overcome and break homeostasis. As homeostasis is impaired in elderly, it takes longer for the system to return to set point, therefore drugs tend to have a longer effect after cessation e.g. there will be a very slow return of blood pressure back to 'normal' after stopping an antihypertensive.

Even in the absence of a homeostatic pathology (e.g. postural hypotension), any drug that reduces vascular tone (e.g. anti-hypertensives) will reduce the body's ability to respond to positional change, leading to a falls risk.

Crushing, Chewing or Splitting Medicines

Modifying Formulations

Patients with dysphagia may need their medicines modified into a form that is easier to take. Be careful of what medicines can be crushed/split. Please see [SafeRx Crushing Table](#) for a guide.

Tapering, De-Prescribing & Gradual Dose Reduction (GDR) Guidelines

Important Resources

[Health Quality & Safety Commission NZ](#) — All links

[Deprescribing Long Term Opioid \(>3 Months\) In Older Adults](#)

[BPAC - Deprescribing](#)

[Tapering MD - Tapering, Dose Reduction & Deprescribing Guidelines for Specific Medicines](#)

[Desprescribing.org - Guidelines & Algorithms](#)

Introduction

Stopping medicines can be as important as starting medicines. Medications review is particularly important in elderly due to changes in organ function, co-morbidities, presence of frailty, and so forth. Questions as to whether the medication is still indicated, is the medicine providing appropriate management, can regimens be simplified, is the dose appropriate need to be determined.

Medicines can be grouped as:

1. Those that keep the patient well and improve day-to-day quality of life e.g. analgesics, thyroxine, or anti-anginals. In some cases, if these medicines are stopped, the patient may become ill or unable to function. However, some drugs may be able to be stepped-down, stopped, or used on an as required basis (prn) e.g. a protein pump inhibitor (PPI).
2. Those that are used for the prevention of illness in the future e.g. statins, aspirin, warfarin or bisphosphonates. A decision about whether to stop medicines such as these should include consideration of the risks and benefits of treatment for that particular patient, the length of time required for benefit and the life expectancy of the patient.

What are the likely outcomes of stopping medicines?

Stopping medicines may result in one or more of the following outcomes:

1. No adverse consequence for the patient

2. Withdrawal events/symptoms that have a pharmacological or physiological basis, including rebound symptoms e.g. rebound hypertension after discontinuing therapy with a β-blocker
3. Signs or symptoms of the pre-existing disease may re-appear e.g. increased blood pressure after stopping an antihypertensive.

Take a stepwise approach to stopping medicines. A four step process can be used when stopping medicines.

- Recognise the need to stop
- Reduce or stop one medicine at a time
- Consider if the medicine can be stopped abruptly or should be tapered
- Check for benefit or harm after each medicine has been stopped

Below are the commonly prescribed medicines in elderly which may possess a higher risk to benefit ratio.

Table 1: Commonly prescribed medicines associated with changes in the balance of benefits and risks in older adults.^{2, 11}

Medicine class	Potential harms, particularly in older patients
Anticholinergic medicines	Increased risk of falls, delirium, cognitive impairment and urinary retention
Antihypertensive medicines	Increased risk of hypotension and falls
Antipsychotics	Increased risk of mortality in patients with dementia, increased risk of falls and postural hypotension when used as sedatives or hypnotics, e.g. quetiapine
Aspirin	Increased risk of gastrointestinal bleeding, limited evidence of benefit for CVD prevention ¹²
Benzodiazepines or zopiclone	Increased risk of falls, cognitive impairment and possible association with Alzheimer's disease
Bisphosphonates	Increased risk of atypical fractures with prolonged treatment.
Diabetes medicines	Intensive glucose lowering is unlikely to benefit older patients; risk of hypoglycaemia with some medicines
Hypnotics	Cognitive effects the following day, increased risk of falls, possible increased risk of Alzheimer's disease
NSAIDs	Greater increase in absolute risk of bleeding than in younger patients, acute kidney injury
Opioids	Constipation, delirium, sedation, increased risk of falls or unintentional overdose ¹³
Proton pump inhibitors (PPIs)	Increased risk of fractures, <i>Clostridium difficile</i> infection and renal adverse effects such as interstitial nephritis
Statins	Risk of adverse effects, e.g. myalgia, new onset diabetes mellitus, limited evidence of benefit for CVD prevention ¹⁴
Tricyclic antidepressants	Cognitive impairment, urinary retention, postural hypotension, increased risk of falls

Tapering, Dose Reduction & Deprescribing Guidelines for Specific Medicines (Tapering MD Link)			
Medicine	Tapering/Deprescribing Guideline	Withdrawal Symptoms	Potential Harms From Prescribing in Older Patients
Anti-Cholinergics	<p>TaperMD - Anticholinergics</p> <p>If used daily for more than 3-4 weeks</p> <ul style="list-style-type: none"> Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose. 	<p>Usually for 48-72 hours</p> <p>Jitteriness, nervousness, nausea, dizziness, insomnia, and nightmares.</p>	Increased risk of falls, delirium, cognitive impairment and urinary retention
Anti-Convulsants	<p>TaperMD - Anticonvulsants</p> <p>Epilepsy</p> <ul style="list-style-type: none"> Reduce dose by 10-25% every month If seizure activity occurs, go back to approximately 75% of the previously tolerated dose <p>Mood stabilisation, Pain relief, Migraine, Anxiety</p> <ul style="list-style-type: none"> If used daily for a month: reduce dose by a maximum of 25% every week initially or every month if need be. If any problem or if used for longer than a month: consider tapering more gradually and ideally with the help of a liquid. 	<p>Initial: Agitation, activation, insomnia, rebound psychosis, withdrawal-emergent abnormal movements, nausea, feeling of discomfort, sweating, vomiting, insomnia, sexual dysfunction</p> <p>Protracted: Agitation, pain, dysgeusia, parosmia, food intolerance, insomnia.</p> <p><i>In epilepsy</i> Minimised by switching to a drug from a different group.</p> <p>GABAergic drugs (gabapentin and pregabalin) tend to cause more problems.</p>	
Anti-Depressants	<p>TaperMD - Antidepressants</p> <p>Tapering rate should be guided by the patient's symptoms - do not stop abruptly if they have been taken for more than</p> <ul style="list-style-type: none"> Starting with a taper amount, such as a 10% dose reduction If patients do not experience withdrawal or other distressing symptoms, and have not had previous problems, dropping the dose initially in a 25% step could be an appropriate suggestion. 	<p>Symptoms decrease after one to two weeks of a dose reduction.</p> <p><i>Abrupt cessation carries a higher risk of discontinuation symptoms</i></p> <p>Initial: Nausea, diarrhea, abdominal pains, sweating, headache, dizziness, cold and flu-like symptoms, anxiety, irritability, trouble sleeping, electric shock-like feelings, visual after images, sounds and light sensitivity, muscle aches and pains, chills, confusion, pounding heart (palpitations), sexual dysfunction, twitching or other unusual movements, depression, agitation, and suicidal ideation.</p> <p>Protracted: After the initial withdrawal features wear off, there may be enduring food intolerance, altered taste or smell sensations, cardiac disturbances, pain or burning or other stranger sensory sensations, stress intolerance, temperature dysregulation, anxiety and depression, enduring sexual dysfunction.</p> <p>Antidepressant Discontinuation Syndrome (FINISH) - appear within 1 week</p> <ul style="list-style-type: none"> Flu like symptoms Insomnia Nausea Imbalance Sensory Disturbances Hyperarousal (anxiety/agitation) 	<i>Tricyclic Antidepressants</i> Cognitive impairment, urinary retention, postural hypotension, increased risk of falls
Anti-Hypertensives	<p>TaperMD - Antihypertensives</p> <ul style="list-style-type: none"> Reduce the dose by 25-50% every 1 to 2 weeks. At 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose 	<p>Monitor:</p> <ul style="list-style-type: none"> Diuretic drugs: weight gain, swelling, shortness of breath β-blockers and other antihypertensives: emergent chest pain (masked angina), pounding heart, heart rate, anxiety, tremor BP: monitor for up to 6 months to ensure no rebound 	Increased risk of hypotension and falls

Tapering, Dose Reduction & Deprescribing Guidelines for Specific Medicines (Tapering MD Link)			
Medicine	Tapering/Deprescribing Guideline	Withdrawal Symptoms	Potential Harms From Prescribing in Older Patients
Anti-Psychotics	<p>TaperMD - Antipsychotics</p> <p>If used daily for a month:</p> <ul style="list-style-type: none"> Reduce dose by a maximum of 25% every week initially or every month if need be. If any problems while tapering, or if used for longer than a month: consider tapering more gradually and ideally with the help of a liquid. For some drugs such as quetiapine and olanzapine: a combination of benzodiazepine and an anticholinergic may help 	<p>Based on the effect of missing doses while on treatment, people will often know before starting to withdraw whether there is likely to be a problem. Acute withdrawal responds to the original treatment whereas protracted withdrawal is less likely to – although tardive dyskinesia can be managed to some extent with the original agent.</p> <p>Initial: Agitation, activation, insomnia, rebound psychosis, withdrawal-emergent abnormal movements, nausea, feeling of discomfort, sweating, vomiting, insomnia, sexual dysfunction</p> <p>Protracted: Tardive dyskinesia, tardive akathisia, tardive dysthymia, stress intolerance, temperature dysregulation, sensory disturbances, food intolerance, enduring sexual dysfunction.</p>	<p>Increased risk of mortality in patients with dementia, increased risk of falls and postural hypotension when used as sedatives or hypnotics e.g. quetiapine</p>
Benzo Diazepines	<p>TaperMD - Benzodiazepines</p> <p>Rate of discontinuation needs to be controlled by the person taking the medication and their discontinuation symptoms.</p> <ul style="list-style-type: none"> Reduce dose by a maximum of 25% every week initially and this can be extended if needed If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient. Dose reduction may need to slow down as one gets to smaller doses (i.e., 25% of the original dose <p>Note: If there were no problems when withdrawing the first time, tapering is not required the second time — if the drug is a short acting agent from the same class.</p>	<p>Acute: rebound insomnia, electrical zaps, tremor, anxiety, depression, nausea, vomiting, dizziness, seizures.</p> <p>Protracted: Depression, anxiety, stress intolerance, food intolerance, pain syndrome, dysgeusia, parosmia</p>	<p>Benzodiazepines & Zopiclone Increased risk of falls, cognitive impairment and possible association with Alzheimer's Disease</p> <p>Hypnotics Cognitive effects the following day, increased risk of falls, possible increased risk of Alzheimer's disease</p>
Cortico Steroids	<p>TaperMD - Corticosteroids</p> <p>If used for longer than 3-4 weeks</p> <ul style="list-style-type: none"> Reduce dose by prednisone equivalent of 5mg/week until 10 mg/day prednisone equivalent is reached. Subsequent doses should be decreased by 2.5mg/ week until the medication is stopped If withdrawal symptoms occur, increase the dosage and taper at 1mg/week 	<p>Symptoms of HPA Axis suppression Disease exacerbation, loss of appetite, nausea, vomiting, lack of energy, headache, dizziness, joint pain, low blood pressure, elevated temperature</p>	
Dopamine Agonists & Stimulants	<p>TaperMD - Dopamine Agonists & Stimulants</p> <p>Rate of discontinuation needs to be controlled by the person taking the medication and their discontinuation symptoms.</p> <ul style="list-style-type: none"> Reduce dose by 20-25% every week. Depending on response, this can be extended or decreased (10% dose reductions) if needed. If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient. Dose reduction may need to slow down as one gets to smaller doses (i.e. when 25% of the original dose is reached). 	<p>Initial: Flu-like symptoms, yawning, insomnia, anxiety, panic attacks, dysphoria, depression, agitation, irritability, suicidal ideation, fatigue, orthostatic hypotension, nausea, vomiting, diaphoresis, generalized pain, and drug cravings.</p> <p>Protracted: primarily feature dysthymia, complaints of depression, anxiety, and stress intolerance, anxiety, panic attacks, irritability</p>	

Tapering, Dose Reduction & Deprescribing Guidelines for Specific Medicines (Tapering MD Link)			
Medicine	Tapering/Deprescribing Guideline	Withdrawal Symptoms	Potential Harms From Prescribing in Older Patients
Estrogens	<p>TaperMD - Estrogens Overall, the rate of discontinuation needs to be controlled by the person taking the medication</p> <p>If used daily for more than 1-2 months</p> <ul style="list-style-type: none"> Reduce dose by a maximum of 25% every week initially and this can be extended if needed If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient Dose reduction may need to slow down as one gets to smaller doses (i.e. 25% of the original dose) 	Hot flashes, weight gain, insomnia, anxiety	
Opioids	<p>TaperMD - Opioids</p> <ul style="list-style-type: none"> A gradual dose reduction of 5-10% of the morphine equivalent dose every 2-4 weeks, adjusting as tolerated, with frequent follow up is a reasonable rate to commence opioid tapering. Switching the patient from immediate release to controlled release opioids on a fixed dosing schedule may assist some patients in adhering to the withdrawal plan. 	<p>Initial: Restlessness, runny nose, goose flesh, sweating, muscle cramps, insomnia, nausea, diarrhea, pain, dilation of the pupils</p> <p>Protracted: depression, anxiety, craving</p>	Constipation, delirium, sedation, increased risk of falls or unintentional overdose
PPIs	<p>TaperMD - Proton pump inhibitors (PPIs)</p> <p>If used daily for more than 3-4 weeks</p> <ul style="list-style-type: none"> Reduce dose by 50% every 1-2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen - stop the drug If any withdrawal symptoms occur - go back to approximately 75% of the previously tolerated dose 	Return of symptoms, heartburn, reflux <p>Monitoring at 4 and 12 weeks: PPI Desprescribing Algorithm</p> <ul style="list-style-type: none"> Heartburn, dyspepsia, regurgitation, epigastric pain Loss of appetite, weight loss, agitation 	Increased risk of fractures, C.difficile infection and renal ADRs such as interstitial nephritis.
ACh Inhibitor	<p>TaperMD - Acetylcholinesterase-inhibitors</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	
Allergy & Anaphylaxis Drugs	<p>TaperMD - Allergy and Anaphylaxis Drugs</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	
Anti-Gout	<p>TaperMD - Antigout (Allopurinol/ Antihyperuricemics)</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	
Anti-Hyper glycaemics	<p>TaperMD - Antihyperglycemics</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	<i>Diabetes Medications</i> Intensive glucose lowering is unlikely to benefit older patients, there is a risk of hypoglycaemia in some medicines.
Biphosphonates	<p>TaperMD - Bisphosphonates</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	Increased risk of atypical fractures with prolonged treatment
Glaucoma Eye Drops	<p>TaperMD - Glaucoma-eye-drops</p> <p>Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	

Tapering, Dose Reduction & Deprescribing Guidelines for Specific Medicines (Tapering MD Link)			
Medicine	Tapering/Deprescribing Guideline	Withdrawal Symptoms	Potential Harms From Prescribing in Older Patients
Aspirin	<p>TaperMD - Aspirin Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	<i>Aspirin</i> - increased risk of GI bleeding, limited evidence for CVD prevention
NSAIDs	<p>TaperMD - NSAIDs (Non Selective & COX-2) Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	Greater increase in absolute risk of bleeding than in young patients, risk of AKI
Statins	<p>TaperMD - Statins Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	Risk of ADRs e.g. myalgia, new onset of diabetes mellitus, limited evidence for CVD prevention benefit
Vitamin D & Calcium	<p>TaperMD - Vitamin D & Calcium Deprescribing Guidelines</p> <p>This is a de-prescribing guideline that provide a risk-benefit analysis between continuing the medication or deprescribing it.</p>	-	Cessation may be required if fracture/falls risk is low and thus no longer needed - causes increased falls and hypercalcaemia.

GERIATRIC CONDITIONS

Introduction

For this chapter, we will look into only falls.

Falls

Resources - [Appropriate Prescribing Toolkit](#)

Resources particularly focus on assessing medicine appropriateness in older persons to prevent falls.

1. [The Beers List Pocket Guide - Medications To Avoid in the Elderly](#)
2. [STOPP/START Screening Tool - Medications To Avoid and Appropriate Replacements](#)
3. [GERI-Rxfiles - Assessing Medication Use in Older Adults](#)
4. [Topic 10 - Falls in Older People](#)
5. [STEADI-Rx: Older Adult Fall Prevention](#)
6. [Australian Prescribing Indicators Tool](#)
7. [ASCP-NCOA Falls Risk Reduction Toolkit](#)
8. [Cumulative toxicity tool and adverse drug reactions, NHS Scotland](#)
9. [Anticholinergic Burden Calculator](#)

Description

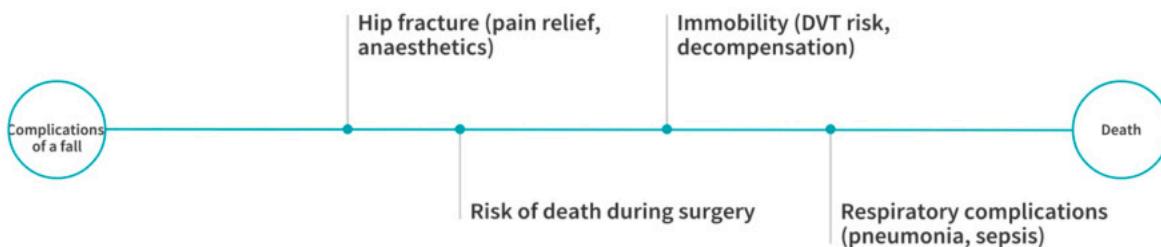
Falls are a common event of the elderly and is associated with increased morbidity and mortality. With age, our homeostatic capacity decreases, and risks by drugs with/without homeostatic pathology (postural hypotension) increase our risk of falls.



Did You Know?

1 in 3 people over 65 years old experience a fall each year and half of these result in injury. **Most falls happen in the community!**

With reason, both older people and healthcare professionals view falls as a threat to an older person's identity and independence. Many consequences also follow its complications.



COMPLICATIONS OF FALLS	
Physical	Mental & Social Wellbeing
Fracture	Reduced confidence (social isolation)
Surgery (risk of death)	Reduced self care
Immobility (DVT risk, decompensation)	Fear of falling & avoidance of activities that could lead to falls
Respiratory Complications (pneumonia, sepsis)	Depression
Bruising, Haematomas	Loss of autonomy
Lacerations	Isolation
Scratches & other superficial wounds	

Pathophysiology

1. *Age*: decrease in homeostatic capacity
2. *Underlying pathology*: postural hypotension
3. *A disturbance* (e.g. drug) in the following body systems:
 - Cardiovascular/Respiratory: low blood pressure, hypoxia
 - Peripheral Nervous System
 - Muscular
 - Neuromuscular
 - Endocrine (hypoglycaemia)
 - Temperature (hyperthermia)
 - CNS Function (Visual, Cerebral, Vestibular (vertigo), Basal Ganglia, Cerebellar (ataxia))

Risk Factors

1. **Fear of falling** (leads to avoiding activities that may cause falling, can lead to muscle weakness)
2. History of previous falls
3. **Polypharmacy** (when at least one established fall risk-increasing drug is in the daily regimen)
4. Drugs associated with increased risk of falls (see below)
5. Medical conditions (e.g. hypotension, depression, delirium, dementia, arthritis, Parkinson's, sensory impairments, CV disease, chronic diseases)

See [Topic 10](#) for more information (particularly Topic 8)

MEDICINE SUMMARY RISK OF FALLING VS RISK FROM FALLING			
Drug Class	Risk of Fall	Risk From Fall	System Affected
Anti Depressants (especially TCAs)	Depression & Weak Bones [OR = 1.68] Both depression and anti-depressants can cause falls (e.g. orthostatic hypotension, decreased bone mass, sedation)	Fractures (osteoporosis) Serotonin has a role in bone metabolism and increases risk of fractures (higher with higher doses)	Affects Cerebral, cerebellar, visual, basal ganglia, CV
Neuroleptics & Antipsychotics	Dementia & Sedation [OR = 1.59] Both dementia and anti-psychotics can cause falls (e.g. hypotension, sedation, and gait abnormalities)	Fractures (osteoporosis) Antipsychotics increase risk of osteoporosis	Affects Cerebral, cerebellar, visual, basal ganglia
Sedatives & Hypnotics	Cognitive Impairment & Sedation [OR = 1.47] Both anxiety, insomnia and benzodiazepines increase risk of falls (e.g. sedation)		Cerebral, cerebellar, visual

Antihypertensive agents & Diuretics	Hypotension [OR = 1.24] Low blood pressure	Fractures (osteoporosis) Hip fractures	Cardiovascular System (vascular tone more than cardiac cycle)
β-blockers	Hypotension & dizziness [OR = 1.01] Non-selective or β_1 -selective β-blockers induce bradycardia, reducing cardiac output and inducing hypotension and dizziness		Cardiovascular System (vascular tone more than cardiac cycle)
Anticholinergics	Anticholinergic Burden Blurry vision, cognitive impairment, delirium, postural hypotension, sedation		Visual
Anti-epileptics	Dizziness, ataxia, unsteady gait Increase the risk of falls by causing dizziness, ataxia, and unsteady gait. Epilepsy also contributes to the increased falls risk.	Fractures (osteoporosis) Anti-epileptics alter bone metabolism and reduce bone mineral density. This risk increases with enzyme-inducing anti-epileptics, multiple anti-epileptics and duration of use.	
Opioids	Postural hypotension, sedation & dizziness [OR = 0.96] Opioids can induce postural hypotension, sedation and dizziness.	Fractures (osteoporosis) Reduces bone density	Cerebral, visual
NSAIDs	?	?	?
Anticoagulants		Bleeding Anticoagulants increase the risk of bleeding in falls-related injuries. However, it is to be noted that the benefits of prescribing warfarin can outweigh the potential risks of falls-related bleeding.	Other drugs increasing risk of bleeding: antithrombotics, aspirin
PPIs		Fracture (osteoporosis) PPIs increased stomach pH which results in a decrease in calcium absorption, and therefore increases the risk of fracture.	Other drugs increasing risk of fracture: glucocorticoids, Medroxyprogesterone, aromatase inhibitors, GnRH agonists, thiazolidinediones

A Note on the Anticholinergic Burden

Anticholinergic burden is referred to the cumulative effect of taking one or more medicines with anticholinergic activity. In older adults, it has been correlated with cognitive decline, delirium, dizziness and confusion, **falls** and hospitalisations.



A Trick to Remember Anticholinergic Side Effects: Spit, See, Shit

Spit (dry mouth), See (blurry vision), Shit (constipation)

Consult the [ACB Calculator](#) and [Table 3B Reducing Anticholinergic Exposure](#) to assess your patient's anticholinergic burden and options.

Treatment Steps (STEADI-Rx)

1. Screen for falls risk

- Risk medications, history of falls, gait/balance problems
- Falls Physical Assessment:
 - a) Timed Up and Go (TUG) test: assesses mobility
 - b) 30 second chair stand test: assessed leg strength and endurance
 - c) 4 stage balance test: assess balance

2. *Assess modifiable risk factors (conduct a medicines review)*
 - STOP, SWITCH, REDUCE
 - Efficacy/safety of medicine, PK change (CrCl, hepatic function), PD change (opiates, infection)
3. *Assess for postural hypotension*
 - Drop in SBP by ≥ 20 mmHg or DBP by ≥ 10 mmHg, signs & symptoms
4. *Recommend effective prevention strategies*
 - Vitamin D, Bisphosphonates, physiotherapy (muscle strengthening)
5. *Intervene*
 - Consult with prescriber, education

STOPP	START	Dr M Hamilton																																	
<p>Cardiovascular</p> <ul style="list-style-type: none"> <input type="checkbox"/> CHF No digoxin with normal Sys function [no benefit] <input type="checkbox"/> CHF No verapamil or diltiazem with Class 3-4 [worsens failure] <input type="checkbox"/> CHF No sildenaflil if systolic BP<90mmHg or with nitrates [collapse] <input type="checkbox"/> BB: avoid with verapamil [heart block] <input type="checkbox"/> BB: avoid with brady or heart block type 2 or complete [CHB/ asystole] <input type="checkbox"/> Loop diuretics: not first line for HTN or for HTN with incontinence <input type="checkbox"/> Loop diuretics: Not for pedal oedema without CHF or liver/renal failure [stocking + elevation] <input type="checkbox"/> Thiazide: avoid with gout or low K, Na, Ca [ppt attack] <input type="checkbox"/> Electrolytes: No ACE/ARB with high K <input type="checkbox"/> ALDO with ACE/ARB- check K every 6 months or more freq if unstable <input type="checkbox"/> Avoid centrally acting anti-HTN (clonidine, methyldopa) [poorer tolerance] <input type="checkbox"/> Avoid amiodarone for SVT- (trial BB/ dig/verapamil/diltiazem) [more ADRs] 	<p>Cardiovascular</p> <ul style="list-style-type: none"> <input type="checkbox"/> Chronic AF- start anticoagulant (Dabigatran, other NOAC or warfarin) <input type="checkbox"/> Hx of ischaemic event- start antiplatelet and statin (unless >85 or end of life) <input type="checkbox"/> HTN >160 / >90 or >140 / >90 if DM: start antihypertensives <input type="checkbox"/> CHF/CAD: start ARB <input type="checkbox"/> IHD: start BB <p>Respiratory</p> <ul style="list-style-type: none"> <input type="checkbox"/> COPD: mild-moderate: start regular SABA/SAMA <input type="checkbox"/> COPD: mod-severe, FEV1<50% + repeat exacerbations: start ICS <input type="checkbox"/> Hypoxaemia: pO2 <60mmHg or sats <89%: start longterm O2 <p>Gastrointestinal</p> <ul style="list-style-type: none"> <input type="checkbox"/> GORD- severe, or peptic stricture or Barrett's: start PPI <input type="checkbox"/> Diverticulosis with constipation: start fibre supplement <p>Musculoskeletal</p> <ul style="list-style-type: none"> <input type="checkbox"/> RhA: start DMARD <input type="checkbox"/> oral steroids: start bisphosphonates, VitD and Ca <input type="checkbox"/> osteoporosis: T-score>-2.5 or prev fragility fracture: start bisphosphonates, Vit D and Ca <input type="checkbox"/> osteopenia: T score -1.0 to -2.5 or housebound or recurrent falls or acquired dorsal kyphosis: start Vit D (+/- calcium) <input type="checkbox"/> Gout- recurrent: start allopurinol <p>Endocrine</p> <ul style="list-style-type: none"> <input type="checkbox"/> DM or proteinuria: start ACEI/ARB <p>Urogenital</p> <ul style="list-style-type: none"> <input type="checkbox"/> Prostatism: start alphablockers <input type="checkbox"/> Atrophic vaginitis: topical oestrogen <p>Analgesia</p> <ul style="list-style-type: none"> <input type="checkbox"/> High potency opioids: use where others not appropriate (always use laxative) <p>Vaccines</p> <ul style="list-style-type: none"> <input type="checkbox"/> Seasonal influenza vaccine annually <input type="checkbox"/> Pneumococcal vaccine at least once over 65 <p>Eyes</p> <ul style="list-style-type: none"> <input type="checkbox"/> Glaucoma: open-angle: topical prostaglandin (latanoprost) or betablocker 																																		
<p>Antiplatelet / anticoagulant</p> <ul style="list-style-type: none"> <input type="checkbox"/> Aspirin LT > 160mg per day <input type="checkbox"/> Aspirin with PUD without PPI/H2 <input type="checkbox"/> Any with uncontrolled HTN or sig Bleeding Hx <input type="checkbox"/> Aspirin + clopidogrel (unless stent <12m or carotid stenosis) <input type="checkbox"/> Chronic AF: don't add Aspirin to warfarin/dabigatran/other [no benefit] <input type="checkbox"/> Prev stroke/IHD/PVD: don't add antiplatelet to anticoagulant [no benefit] <input type="checkbox"/> Anticoagulate <6m first DVT, <12m first PE (check provoking factors-thrombophilia/ ca..) <input type="checkbox"/> NSAID + anticoagulant <input type="checkbox"/> NSAID + antiplatelet without PPI <p>Respiratory</p> <ul style="list-style-type: none"> <input type="checkbox"/> COPD: no theophylline monotherapy, no maintenance oral steroids <input type="checkbox"/> antimuscarinics- not with narrow angle glaucoma or bladder outflow obstruction [worsens] <input type="checkbox"/> Asthma- if for BB use bisoprolol (no non-selective) <input type="checkbox"/> Benzos: not in respiratory failure- acute or chronic <p>Gastrointestinal</p> <ul style="list-style-type: none"> <input type="checkbox"/> Parkinsonism: no prochlorperazine or metoclopramide <input type="checkbox"/> PPI for PUD >8weeks at full dose (trial reduction) <input type="checkbox"/> Chronic constipation: oral iron, opioids, verapamil, Al antacids <input type="checkbox"/> Oral iron: 200mg/day only [not absorbed above this] <p>Musculoskeletal</p> <ul style="list-style-type: none"> <input type="checkbox"/> NSAIDs: if PUD use COX2 and or PPI/H2 <input type="checkbox"/> NSAIDs: not in severe HTN or CHF [worsens] <input type="checkbox"/> NSAIDs: not >3 months <input type="checkbox"/> NSAIDs: with oral steroids- not without PPI <input type="checkbox"/> Oral steroids: not as monotherapy for RhA not for OA <input type="checkbox"/> Gout: use allopurinol (avoid NSAIDs and colchicine as much as possible) <input type="checkbox"/> COX2 NSAIDs: not with CVD [risk stroke or MI] <input type="checkbox"/> Bisphosphonates with upper GI disease / bleed [re bleed] <p>Renal</p> <ul style="list-style-type: none"> <input type="checkbox"/> Digoxin >125ug/day if eGFR<30 [toxicity] <input type="checkbox"/> Dabigatran if eGFR<30 [bleeding] <input type="checkbox"/> Rivaroxaban in eGFR <15 [bleeding] <input type="checkbox"/> NSAIDs if EGFR <50- AKI <input type="checkbox"/> Colchicine if eGFR <10[toxicity] <input type="checkbox"/> Metformin in eGFR <30 [lactic acidosis] <p>Urogenital</p> <ul style="list-style-type: none"> <input type="checkbox"/> Antimuscarinics: not with dementia, NA glaucoma, chronic prostatism <input type="checkbox"/> Alpha blockers: watch BP. Avoid if orthostatic or micturition syncope <p>Endocrine</p> <ul style="list-style-type: none"> <input type="checkbox"/> DM2: avoid LA sulphonylureas (glibenclamide) [prolonged hypos] <input type="checkbox"/> DM2: pioglitazone: avoid with CHF or prev MI [CHF exacerbation] <input type="checkbox"/> DM2: avoid BB if frequent hypos [suppress hypo symptoms] <input type="checkbox"/> Oestrogens: avoid with Hx breast Ca or VTE [recurrence] <input type="checkbox"/> Oestrogens: not without progestagen with intact uterus <p>Falls Risk</p> <ul style="list-style-type: none"> <input type="checkbox"/> Benzo [impaired balance, reduced sensorium] <input type="checkbox"/> Hypnotics: zopiclone [daytime sedation, ataxia] <input type="checkbox"/> Neuroleptics [gait dyspraxia, Parkinsonism] <input type="checkbox"/> Postural drop<20mmHg: alphablockers, CaChB, nitrates, ACE/ARBs <p>Analgesia</p> <ul style="list-style-type: none"> <input type="checkbox"/> Opiates: use with laxative <input type="checkbox"/> Opiates: if using LA always use SA for breakthrough <p>Antimuscarinics</p> <ul style="list-style-type: none"> <input type="checkbox"/> Use only 1: bladder/ intestinal antispasmodics, TCA, antihistamine 1st 	<p>CNS and Psych</p> <p>STOPP</p> <ul style="list-style-type: none"> <input type="checkbox"/> TCA not first line and not with dementia, narrow angle glaucoma, cardiac condition, prostatism, urinary retention Hx <input type="checkbox"/> Neuroleptics with prostatism or prev urinary retention <input type="checkbox"/> SSRI with low Na <130 <input type="checkbox"/> Benzos always <4 weeks <input type="checkbox"/> Antipsychotics with Parkinson's or LB dementia <input type="checkbox"/> Neuroleptic extra-pyramidal ADRs - don't treat with antimuscarinics [toxicity] <input type="checkbox"/> antimuscarinics with delirium or dementia <input type="checkbox"/> neuroleptics with dementia- unless severe resistant [stroke risk] <input type="checkbox"/> neuroleptics as hypnotics <input type="checkbox"/> prochlorperazine- n/v/vertigo, chlorpromazine- intractable hiccoughs [toxicity] <input type="checkbox"/> benign essential tremor- no levodopa or dopamine agonists <input type="checkbox"/> antihistamines- no 1st generation <p>START</p> <ul style="list-style-type: none"> <input type="checkbox"/> Parkinson's with functional impairment: L-DOPA or dopamine agonist <input type="checkbox"/> Alzheimer's or LBD, mid-mod: start acetylcholinesterase inhibitor (donepezil or rivastigmine) <input type="checkbox"/> Depression: persistent- start SSRI <input type="checkbox"/> Anxiety, persistent and function affected: start SSRI <input type="checkbox"/> Restless legs Syndrome: consider dopamine agonist (ropinirole), rule out iron deficiency and renal failure <p>Anticholinergic Burden Scale: Score >3 is significant</p> <table border="1"> <thead> <tr> <th>Score 1</th> <th>Score 2</th> <th>Score 3</th> </tr> </thead> <tbody> <tr> <td>Alverine</td> <td>Amantadine</td> <td>Amitriptyline & most TCAs</td> </tr> <tr> <td>Atenolol & most beta-blockers</td> <td>Belladonna alkaloids not otherwise listed</td> <td>Atropine</td> </tr> <tr> <td>Bupropion</td> <td>Carbamazepine</td> <td>Chlorphenamine and sedating antihistamines</td> </tr> <tr> <td>Chlorthalidone</td> <td>Cyproheptadine</td> <td>Dicyclomine</td> </tr> <tr> <td>Cimetidine & H2RAs</td> <td>Methotriptane (Levomepromazine)</td> <td>Doxepin and others related to TCAs</td> </tr> <tr> <td>Codeine & other opiates</td> <td>Oxcarbazepine</td> <td>Hyoscine (scopolamine)</td> </tr> <tr> <td>Diazepam & BZDs</td> <td>Pethidine</td> <td>Olanzapine and most atypicals</td> </tr> <tr> <td>Digoxin</td> <td>Pimozide</td> <td>Orphenadrine</td> </tr> <tr> <td>Furosemide & other diuretics</td> <td>Cetirizine & non-sedating antihistamines*</td> <td>Oxybutynin and most incontinence drugs</td> </tr> <tr> <td>Haloperidol</td> <td>Loperamide*</td> <td>Paroxetine and most SSRIs</td> </tr> </tbody> </table>	Score 1	Score 2	Score 3	Alverine	Amantadine	Amitriptyline & most TCAs	Atenolol & most beta-blockers	Belladonna alkaloids not otherwise listed	Atropine	Bupropion	Carbamazepine	Chlorphenamine and sedating antihistamines	Chlorthalidone	Cyproheptadine	Dicyclomine	Cimetidine & H2RAs	Methotriptane (Levomepromazine)	Doxepin and others related to TCAs	Codeine & other opiates	Oxcarbazepine	Hyoscine (scopolamine)	Diazepam & BZDs	Pethidine	Olanzapine and most atypicals	Digoxin	Pimozide	Orphenadrine	Furosemide & other diuretics	Cetirizine & non-sedating antihistamines*	Oxybutynin and most incontinence drugs	Haloperidol	Loperamide*	Paroxetine and most SSRIs	
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CHAPTER 15

PALLIATIVE CARE



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Chapter 15

Palliative Care

The Role Of Palliative Care

Chapter Resources

[The Palliative Care Handbook](#) is an excellent resource to use for this chapter.

Introduction

As the New Zealand population ages and increases, the number of people requiring palliative care will grow. Hospices are traditionally viewed as the institutions that deliver end-of-life care to terminally ill patients, however, most deaths in New Zealand occur in hospitals, residential care facilities, and private residences. Primary care clinicians are therefore frequently and increasingly involved in treating patients with terminal illness in community settings, often alongside palliative care teams.

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life threatening illness, through the prevention and relief of suffering by means of early intervention and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. It:

- Affirms death is a normal process
- Improves quality of life
- Prevents and relieves suffering e.g. pain
- Neither hastens or postpones death

Goal of Treatment: A Good Death

Aim of palliative care is to provide a good death. This was helped by the modern hospice which provided the shift of medical vision to caring for the patient.



Priorities in Palliative Care

Because our aim is to ensure patients are able to peacefully pass away - priorities in palliative care thus won't concern certain aspects of medication use e.g. unusually strong doses or combinations will often be seen.

CONDITIONS

Introduction

We will look into pain, breathlessness, death rattle, N/V, hyperglycaemia, constipation & overflow diarrhoea and nutrition.

Palliative Pain

Please visit *Chapter 20 - Fever, Pain & Infection* for more information on Pain and switching opioids.

Description

Pain is estimated to be the most prevalent symptom preceding all deaths occurring in a palliative care setting in New Zealand.

Non Pharmacological Treatment

Note that incident pain also includes the pain of a pathological fracture, which is best managed by mechanical immobilisation (e.g. plaster, traction, operative intervention). When immobilisation cannot be achieved, pain management is very challenging and consultation with a palliative care service should be made.

Pharmacological Treatment

WHO Analgesic Ladder in Palliative Care:

1. Simple Analgesics e.g. Paracetamol or NSAIDs
2. ~~Weak Opioids~~ (general skipped as they are not sufficient)
3. Strong Opioids e.g. morphine (first line)



Morphine in Palliative Care

Traditionally, **morphine** is used in palliative care as it is a ‘gold standard’ strong opioid analgesic for pain scores of > 7 /10. However, when prescribing morphine, always consider prescribing laxatives and antiemetics.

In New Zealand the following strong opioids are available: (in general)

1. *Morphine*: oral solutions, immediate-release tablets, modified-release tablets and capsules, injections
2. *Oxycodone*: oral solution, immediate-release capsules, modified-release tablets and injection.
3. *Oxycodone + naloxone*: modified release tablets are also available but are not subsidised.
4. *Fentanyl*: transdermal patches (applied every 72 hours), injection
5. *Methadone*: oral solutions, immediate-release tablet, injection
6. *Buprenorphine*: injection and transdermal patches are available but neither are subsidised
7. *Pethidine*: tablets and injection are available but **not** appropriate for use in palliative care

A Note on Syringe Drivers

A syringe driver is a small, battery-powered pump that delivers medication from a syringe at a constant rate throughout the day and night. It can be useful for delivering pain medications or anti-emetics when nausea/vomiting threatens the oral route.

Syringe driver compatibility table

Syringe Driver Compatibility Table

Compatibility of drugs for use in syringe drivers over 24 hours of subcutaneous infusions	clonazepam	cyclizine	dexamethasone	fentanyl	glycopyrrolate	haloperidol	hydromorphone
clonazepam	-	SI	Y	?	Y	Y	?
cyclizine	SI	-	SI	SI	Y	Y	?
dexamethasone	Y	SI	-	?	?	SI	?
fentanyl	?	SI	?	-	Y	Y	-
glycopyrrolate	Y	Y	?	Y	-	Y	Y
haloperidol	Y	Y	SI	Y	Y	-	Y
hydromorphone	?	?	?	-	Y	Y	-
hyoscine butyl bromide (Buscopan™)	Y	SI	Y	Y	?	Y	Y
hyoscine hydrobromide	Y	Y	Y	NA	Y	Y	
ketamine	Y	?	Y	Y	Y	Y	?
methotrimeprazine/levomepromazine (Nozinan™)	Y	Y	SI	Y	Y	Y	Y
methadone	Y	?	Y	?	Y	Y	?
metoclopramide	Y	Y	Y	Y	Y	Y	
midazolam	Y	SI	SI	Y	Y	Y	Y
morphine sulphate (normal strengths)	Y	Y	Y	?	Y	Y	-
morphine tartrate (high strengths)	Y	Y	Y	?	?	SI	-
octreotide	Y	SI	SI	Y	Y	Y	?
ondansetron	?	Y	Y	Y	Y	Y	?
oxycodeone	Y	SI	Y	?	Y	Y	-
phenobarbitone	?	?	?	Y	N	?	?

Combinations that have been used

Y = compatible	morphine+clonazepam+cyclizine (morphine sulphate and tartrate)
N = incompatible	morphine+clonazepam+dexamethasone (morphine sulphate and tartrate)
SI = sometimes incompatible (usually at higher concentrations)	morphine+clonazepam+haloperidol (morphine sulphate and tartrate)
NA = not usually used together	morphine+clonazepam+ketamine (morphine sulphate and tartrate)
? = unknown	morphine+clonazepam+metoclopramide (morphine sulphate Y, tartrate SI)

Info from:

- 1) The Palliative Care Handbook 7TH Edition 2014 – 24 hour syringe driver compatibility for subcutaneous administration table.
- 2) Palliative Medicine Handbook on line at <http://book.palicare.info/index.php>
- 3) Compatibility of syringe driver admixtures for continuous subcutaneous infusions, Department of Pharmacy.

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Diluent: water is recommended for all infusions except ketamine, octreotide, ondansetron and levomepromazine where sodium chloride 0.9% should be used although in combinations consider water.

hyoscine butyl bromide(Buscopan™)	hyoscine hydrobromide	ketamine	methotrimeprazine/levomepromazine (Nozinan™)	methadone	metoclopramide	midazolam	morphine sulphate (normal strengths)	morphine tartrate (high strengths)	octreotide	ondansetron	oxycodeone	phenobarbitone
Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	SI Y ? Y ? Y SI Y Y SI Y SI ?	Y Y Y Y SI Y Y SI Y Y SI Y Y ?	Y Y Y Y ? Y Y ? ? Y Y ? Y Y ?	NA Y Y Y Y Y Y Y Y ? Y Y Y N	Y Y Y Y Y Y Y Y Y Y SI Y Y Y Y ?	Y Y Y Y ? Y Y - Y Y - - ? ? - ?	NA Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y - Y Y Y Y Y Y SI Y Y Y ?	Y Y ? Y - Y Y ? ? ? ? ? ? N	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?
Y Y ? Y ? Y Y Y ?	Y Y ? Y ? Y Y Y ?	Y Y ? Y ? Y Y Y ?	Y Y ? Y ? Y Y Y ?	NA Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?
Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	NA - Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?	Y Y ? Y Y Y Y Y Y Y Y ? Y Y Y ?
Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?	Y Y Y Y Y Y Y Y Y Y Y Y ?

morphine+clonazepam+dexamethasone (morphine sulphate and tartrate)	morphine+dexamethasone+haloperidol (morphine sulphate and tartrate)
morphine+cyclizine+haloperidol (morphine sulphate and tartrate)	morphine+dexamethasone+hyoscine hydrobromide (morphine sulphate and tartrate)
morphine+cyclizine+hyoscine butyl bromide (morphine sulphate, tartrate SI)	morphine+dexamethasone+metoclopramide (morphine sulphate and tartrate)
morphine+cyclizine+metoclopramide (morphine sulphate and tartrate)	morphine+dexamethasone+midazolam (morphine sulphate SI, tartrate SI)
morphine+cyclizine+midazolam (morphine sulphate and tartrate)	morphine+dexamethasone+haloperidol (morphine sulphate and tartrate)

Auckland District Health Board 2002 4) Palliative Care Formulary on line at www.palliativedrugs.co.uk
5) Gardiner P R. Compatibility of an injectable oxycodeone formulation with typical diluents, syringes, tubings, infusion bags and drugs for potential co-administration. Hospital Pharmacist 2003; 10: 354-61

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Breakthrough Pain

[Breakthrough Pain NZF](#) [Waitemata DHB - Morphine in Palliative Care](#)

Description

Breakthrough (episodic) pain is a predictable *or* unpredictable transient increase in pain that occurs on a background of adequately controlled pain.

It can be predictable such as ‘incident’ pain associated with weight-bearing, coughing, investigations, or interventions. But it can also be unpredictable e.g. due to colic, nerve pain, disease-related intra-lesional haemorrhage, or liver capsule stretch. IV in general is not used in Hospices

Pharmacological Treatment

Breakthrough analgesics are mainly immediate release (short-acting) opioids such as morphine.

- Dosing guideline: 1/6th or 10% of total daily dose to be used every 2 - 4 hours *or* every 1 hour if pain is severe **as required**.

Please note that some patients may elect not to take breakthrough medication especially if the pain is predictable, mild and of short duration. Please also note that the regular dose of opioid should be reviewed and titrated if breakthrough analgesic doses are consistently required twice daily or more.

Also prescribe PRN short-acting morphine for breakthrough pain:

Use $\frac{1}{6}$ (17%) of total daily morphine dose; in some patients 10% of the total daily dose will be adequate

Example 20mg m-Eslon^{*} every 12h = 40mg/24h

One sixth = 6.6mg

Prescribe: 5-7.5mg RA Morph^{*} or Sevredol[†] PRN up to every 4h (can use every hour if closely monitored)
Do not use SR morphine for breakthrough pain (it takes too long to work)

4.3 Oral Morphine - Converting to Sustained Release Morphine

To change to a sustained release oral morphine preparation (e.g. m-Eslon SR[®]):

- Calculate the total amount of morphine the patient has required over the past 24 hours and then divide by 2 to get the equivalent dose of sustained release morphine²

E.g. 20mg oral immediate release morphine over 24 hours = **10 mg BD** sustained release oral morphine

- m-Eslon SR[®] should be charted as a BD dose (q12 hourly),
 - a three times daily (q8 hourly) dosing schedule may be required in patients who experience consistent breakthrough pain towards the end of the 12 hour period
- Chart PRN doses when charting sustained release morphine
 - PRN doses should be around **1/6th** of the total daily dose and charted q 1 hourly²

Drug	Mechanism of Action	Side Effects
<i>First Line Morphine</i>	<p>Starting Dose - Rapid Acting Analgesia</p> <ul style="list-style-type: none"> • 2.5 to 5mg PO PRN q4h • Oral liquid is used to allow small doses <p>When a stable regimen has been achieved, generally after two to three days, the patient can be converted to long-acting morphine,</p> <p>Long Acting Dose - Baseline Analgesia</p> <ul style="list-style-type: none"> • Usually dosed twice daily, approximately every 12 hours • Smallest dose is 10mg bd <p>Rapid Acting - Top Up Analgesia</p> <ul style="list-style-type: none"> • If the patient is regularly requiring breakthrough analgesia, all doses taken over the previous 24 hours can be added together to calculate a new 24 hour regimen and a new breakthrough dose calculated at one-sixth of the total 24 hour requirement. • If PRN use is escalating - increase baseline analgesia and thus PRN dose. 	
<i>Alternative Fentanyl Patches</i>	<p>Safer option in patients with (eGFR) < 30 mL/min/1.73 m²</p> <p>Fentanyl may also be considered for patients with problems such as recurrent bowel obstruction, difficulty swallowing, e.g. head or neck cancer, or resistant constipation.</p> <p>However:</p> <ul style="list-style-type: none"> • Prn dose of breakthrough pain doesn't apply for fentanyl patches • Should always be 50-100 mcg. 	<p>Side Effects</p> <ul style="list-style-type: none"> • Laxsol for constipation
<i>Alternative Methadone</i>	<p>Excellent for neuropathic pain and patients who cannot tolerate other opioids</p> <p>However it is a tricky painkiller to use due to its strange half life. Close monitoring is required as it takes 7 days to realise an overdose/under-dose has occurred.</p>	
<i>Alternative Oxycodone</i>		
<i>Midazolam Nasal Spray</i>	For anxiety/distress	
<i>Hyoscine Butylbromide</i>	For visceral colic	
<i>Inflammatory or Mass Effect</i>	Dexamethasone	<p>Do not use long term!!!</p> <ul style="list-style-type: none"> • Anxiety, agitation, restlessness, depression • Uncomfortable hyperglycaemia • Thrush/candidiasis, herpetic infections • Muscle weakness

Breathlessness

[Managing Breathlessness in Palliative Care BPAC](#)

Description

Breathlessness is a complex and subjective symptom that is commonly experienced by people who are nearing the end of life.

Non-Pharmacological Treatment

1. Fear induces SoB: *Counselling*

Pharmacological Treatment

1. First Line: *Morphine*
2. SoB induces fear: *Benzodiazepines*

Optimise management of underlying respiratory problems:

4. *Inhalers* (+ technique), steroids, antibiotics...
5. *Oxygen* has risks to be balanced against benefits as it can cause psychical, psychological, financial and social harm.

Respiratory Secretions (Death Rattle)

Description

Also known as the ‘death rattle’ — sputum retention occurs when patients are unable to clear secretions from their respiratory tract by themselves or with assistance. It affects almost 50% of patients at the end of life.

Signs & Symptoms

Wet audible breathing pattern

Non-Pharmacological Treatment

Reposition the patient

Pharmacological Treatment

Pharmacological treatment is not often used as adverse effects generally outweigh benefits. It doesn’t bother the patient, sounds like ‘snoring’ but when awake, mostly bothers family because it sounds so strange — just counsel them.

Anticholinergics

1. Hyoscine butyl bromide (Buscopan)
2. Glycopyrronium
3. Hyoscine hydrobromide

Nausea & Vomiting

Please revisit *Chapter 4 - The Gastrointestinal System* for more information for Nausea & Vomiting.

Description

Nausea and vomiting in palliative care are commonly experienced symptoms, and the aetiology is often multifactorial. The most common causes are:

1. Impaired gastric emptying
2. Chemical causes (eg. medication)
3. Visceral causes (eg. constipation)

Pharmacological Treatment

Antiemetics are usually better taken regularly (pre-emptively) rather than PRN and should be matched to the underlying problem.

Causes of N&V	Description	Antiemetic Recommended
Intracranial Causes	<ul style="list-style-type: none">• Raised ICP• Head Radiotherapy• Brain Tumours	<ul style="list-style-type: none">• Cyclizine• Dexamethasone (unapproved indication)
Chemical Causes	<ul style="list-style-type: none">• Medications e.g. opioid• Biochemical causes e.g. hypercalcemia, uraemia, circulating toxins	<ul style="list-style-type: none">• Haloperidol• Metoclopramide
Anxiety	<ul style="list-style-type: none">• Anticipatory Nausea	<ul style="list-style-type: none">• Benzodiazepines e.g. midazolam (unapproved indication) or oxazepam
Vestibular Causes	<ul style="list-style-type: none">• Motion sickness• Vestibular Disease	<ul style="list-style-type: none">• Cyclizine• Transdermal hyoscine Hydrobromide• Buccal Prochlorperazine
Gastro Intestinal Causes	<ul style="list-style-type: none">• Gastritis• Gastric Stasis	<p><i>Not for use in malignant bowel obstruction with colic</i></p> <ul style="list-style-type: none">• Domperidone• Cyclizine• PPI if gastritis
Bowel Obstruction		<ul style="list-style-type: none">• Cyclizine• Dexamethasone (unapproved indication)• Haloperidol• Hyoscine Butyl-bromide• Levomepromazine• Octreotide
Chemotherapy & Radiotherapy		<ul style="list-style-type: none">• Dexamethasone (unapproved indication)• 5-HT Antagonist e.g. ondansetron
Multifactorial Cause or other Antiemetics are insufficient		<ul style="list-style-type: none">• Levomepromazine

Syringe Driver & Vomiting

As we've seen, vomiting threatens the oral route. Syringe drivers are useful tools to get nausea under control before transferring back to oral regular antiemetics - please find the Syringe Driver Compatibility Table under 'Palliative Pain'

Hyperglycaemia

Description

Treatment for symptomatic patients can be considered to improve patient comfort. Asymptomatic hyperglycaemia can be ignored

Pharmacological Treatment

- Symptomatic hyperglycaemia can cause discomfort, which may be worth using insulin for - especially if it means the patient can enjoy their ice cream!

Constipation & Overflow Diarrhoea

Description

Palliative care patients are at a high risk of constipation, and while general principles of prevention should be followed, pharmacological treatment is often necessary.

Overflow diarrhoea: One of the most typical symptoms of constipation is overflow diarrhoea, it occurs when the faeces become so hard that they cannot be expelled and fecal fluid will flow around the block.

Pharmacological Treatment

The combination of a softener and stimulant laxative is generally recommended, and the choice of laxatives should be made on an individual basis.

- *Oral*: stool softeners and/or stimulants
- *Rectal*: suppositories or enemas
- *Injectable*: methylnaltrexone

Nutrition

Description

The aim of nutrition in palliative care differs drastically from what it normally is — the emphasis is on pleasure and comfort; turn the food pyramid upside down.

One of the reasons behind this aim is because many people during palliative stages will not meet their full dietary needs due to many symptoms that may make intake challenging, for example;

- Anorexia (poor appetite), nausea & vomiting
- Sore mouth or throat, taste changes, dry mouth
- Constipation or diarrhoea, pain, fatigue

The shift in focus from meeting energy needs to spending meal times with loved ones and eating enjoyable/easy foods helps increase the quality of life during that time. The benefit of associating food with pleasure is that it allows a decrease in the severity of the inevitable weight loss. Patients who can maintain their weight have more energy and fewer side effects. This means that restrictive diets for diabetes, kidney or heart disease may even no longer apply.

Non-Pharmacological Treatment

Tips to maintain weight and improve energy levels:

- Aim for six smaller meals per day, rather than three big meals
- Eat when you are feeling your best
- Choose your favourite foods
- Have lots of snacks and ready prepared convenience foods available (frozen meals, tinned items)
- Focus on high protein and energy foods such as dairy desserts, milky drinks, cheese, eggs, cream, extra butter or margarine, honey, sugar
- Enjoy desserts such as trifle, panna cotta, puddings, ice-cream, custard or yoghurt
- Eat with friends or loved ones

Hydration

- Oral or subcutaneous fluids
- Nasogastric tube feeding

Tube feeding may be required if:

- Poor oral intake
- Severe dysphagia
- Head/neck cancer
- GI fistula or oesophageal stricture
- Living wills (may refuse artificial nutrition)

Please note, parenteral nutrition is rarely used at the end of life

Fatigue & Breathlessness

- Avoid dry/crumby foods if very breathless
- Soft and moist foods may work better
- COPD and other respiratory illness have higher nutrient requirements

Pharmacological Treatment

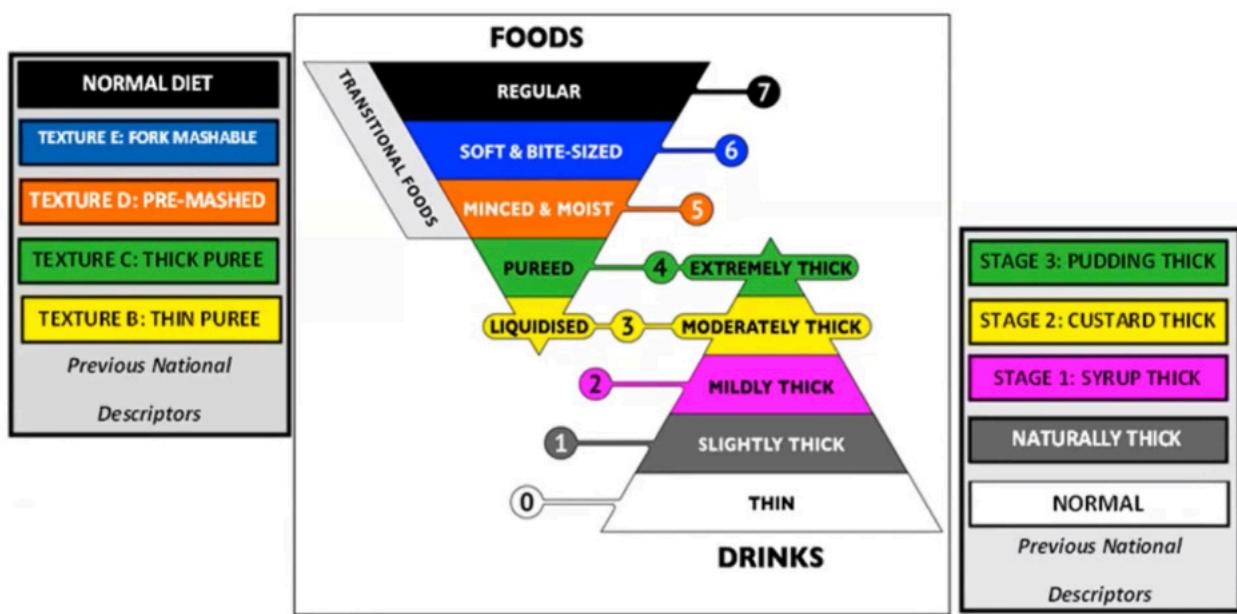
Nourishing drinks and oral nutrition supplements can help provide energy when eating is hard

Standard Supplements

- Ensure Plus, Fortisip, Sustagen

Modules

- Carbohydrates: Polycal
- Carbohydrate + Fat: Duocal
- Fat: Calogen
- Protein: Protifar, Promod, Resource Beneprotein
- Energy, Protein, Calcium: Enprocal



Disease Specific Supplements

- COPD: Pulmocare
- Diabetes: Diasorin, Glucerna, Diasip, Resource Diabetic
- Renal: Nipro, Novosource renal, Renilon, Suplena

Monitoring

Keep an eye on weight and hydration status e.g. urine output, mental state and blood pressure



CHAPTER 16

THE NEUROLOGIC SYSTEM



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Chapter 16

The Neurological System

General Overview of the Human Nervous System

Introduction

Neurological disorders are a leading cause of disability and affect millions of people around the world. Before we go in to them, we must first understand the nervous system.

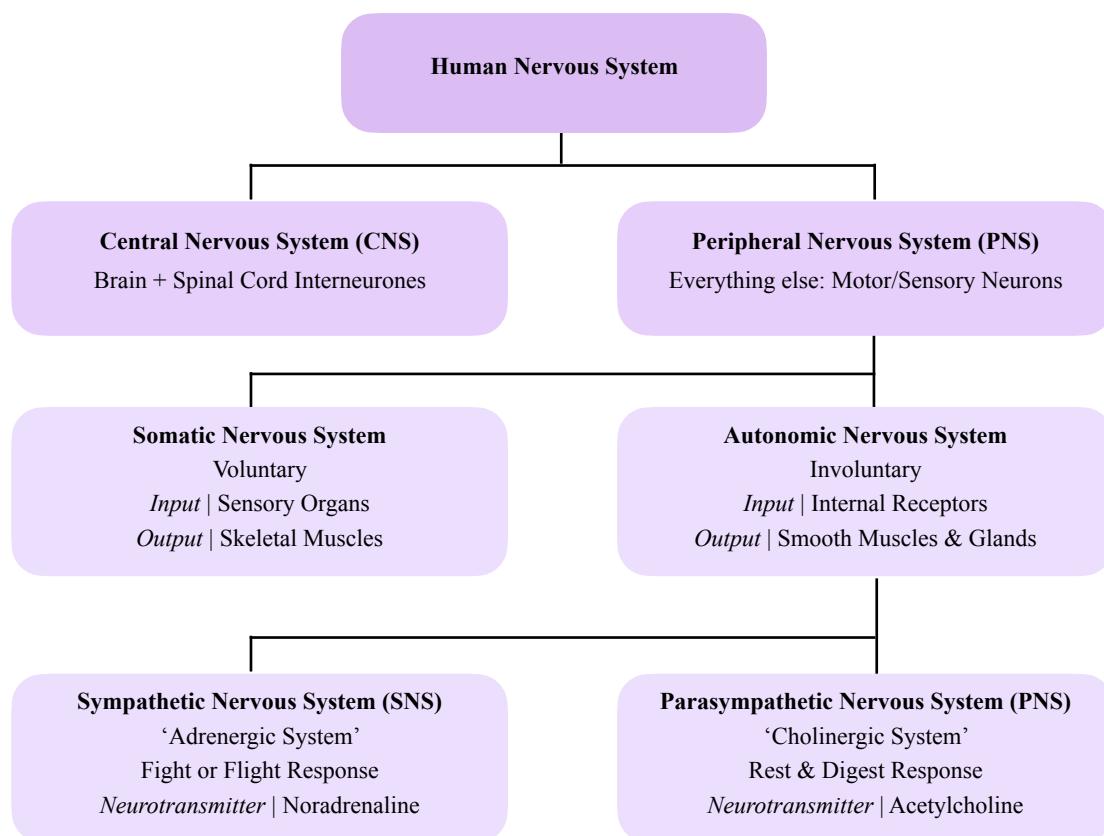


Living With Neurological Conditions

The consequences of having a neurological disorder often develop over time and can become increasingly severe. There are four main problems that exist: physical, cognitive, emotional/behavioural - take these into consideration during your counselling!

The Human Nervous System

The nervous system has two main parts: the central nervous system which is made up of the brain and spinal cord and the peripheral nervous system, which is made up of nerves that branch off from the spinal cord and extend to all parts of the body



	Central nervous system	Peripheral nerves and proximal ganglia	Target organ
Somatic nervous system			<p>Skeletal muscle</p> <p>N_1 (nicotinic acetylcholine) receptor</p> <p>Acetylcholine</p>
Autonomic nervous system	Parasympathetic	Preganglionic fiber	<p>Smooth muscle, cardiac muscle, gland</p> <p>Ganglion</p> <p>N_2 receptor</p> <p>Acetylcholine</p> <p>M (muscarinic acetylcholine) receptor</p> <p>Acetylcholine</p>
	Sympathetic	<p>Ganglion</p> <p>N_2 receptor</p> <p>Acetylcholine</p>	<p>Smooth muscle, cardiac muscle, gland</p> <p>α- and β-adrenergic receptors</p> <p>Postganglionic fiber</p> <p>Norepinephrine</p>
		<p>N_2 receptor</p> <p>Chromaffin cell</p> <p>Adrenal medulla</p> <p>Acetylcholine</p>	<p>Epinephrine</p>

Introduction to Neurons

Our brain consists of around 86 billion nerve cells — also known as neurons. These consist of a nucleus, cell body, dendrites, axon, myelin sheath and synapses.



Reflex Arc Neural Pathway

Neurons can be most simply organised in what we call a Reflex Arc Neural Pathway — which can be tested with a patellar reflex.

Three types of neurons exist:

Types of Neurons

Motor Neurons

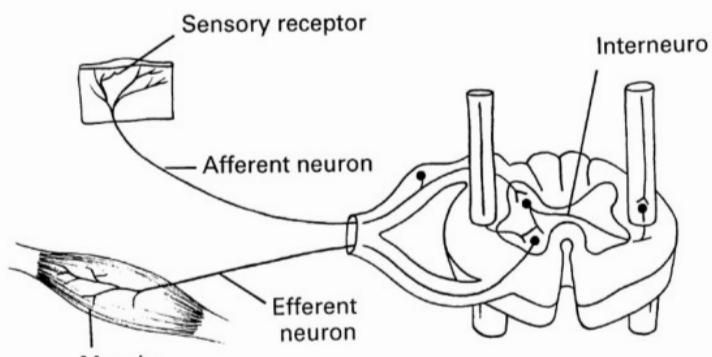
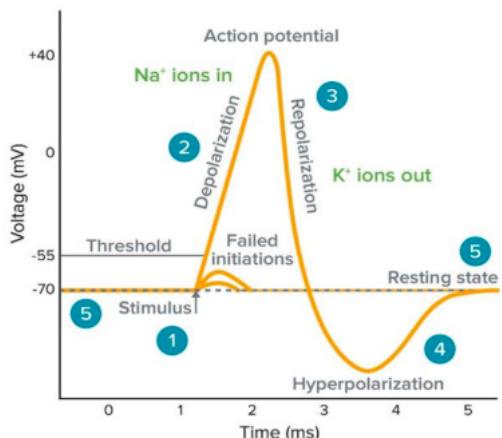
Provide an *efferent* pathway from the brain/spinal cord to the periphery (muscles, organs). Have short dendrites and long axons

Sensory Neurons

Provide *afferent* pathways from the periphery to the brain/spinal cord for processing. Have long dendrites and short axons

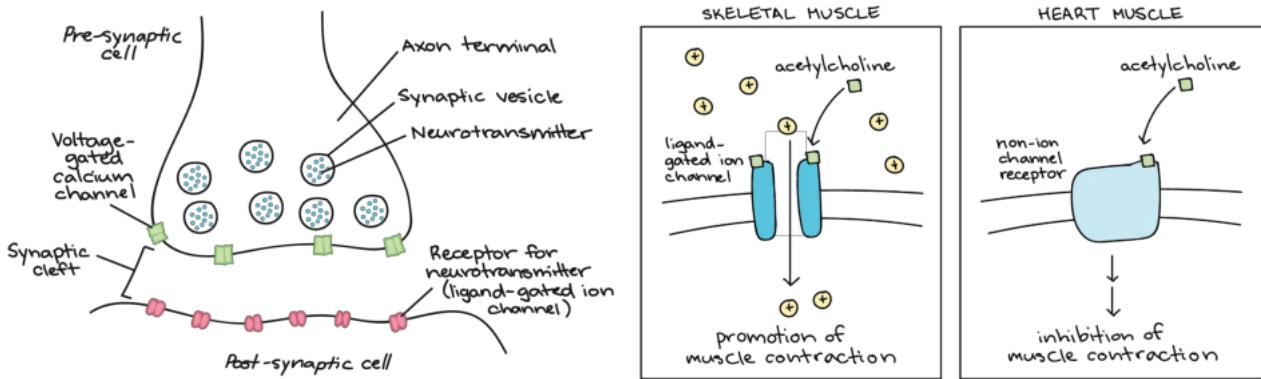
Interneurons

Provide a communicative pathway between sensory and motor neurons.



Cellular Communication

1. Cells communicate via excitability with an ‘all or nothing’ electrical response to the depolarisation of the cell membrane.
2. Information flows from one neuron to another across a synapse. Myelination allows the propagation of the message over a long distance at a high speed. As action potentials cannot cross this synapse, the electrical signal is converted into a chemical signal (neurotransmitters).
3. Effective synapse function depends on a way to ‘turn off’ the signal (neurotransmitter) once it has been sent, either by diffusion, reuptake, or degradation



PROCESS OF NEUROTRANSMISSION	
1. Synthesis and storage of Neurotransmitters	<ul style="list-style-type: none"> Neurotransmitters are the chemicals that transmit information between neurons They are produced in the axon terminals and cell body, and stored in synaptic vesicles
2. Release of neurotransmitter to the synaptic space	<ul style="list-style-type: none"> Neurotransmission begins with the arrival of an AP to the axon terminal of the presynaptic neuron A change in membrane potential leads to opening of voltage-gated Ca^{2+} channels, causing an influx of Ca^{2+} A signalling cascade is initiated to release NT into the synaptic cleft
3. Binding of neurotransmitter to receptors	<ul style="list-style-type: none"> NT binds to specific receptor in the postsynaptic membrane and opens ligand-gated Na^+ channel, causing a release of Na^+ ions into the neuron. This converts the signal back to an electrical AP to travel down the axon <p><i>Integration & Summation</i></p> <ul style="list-style-type: none"> Integration: postsynaptic neurons receives the sum of all of the excitatory and inhibitory input and ‘decides’ whether to fire the action potential (threshold must be met). Summation: is the basis for the processing power in the CNS <ul style="list-style-type: none"> Spatial summation: integration at different locations, at same time Temporal summation: integration at the same place, at slightly different times
4. Inactivation	<ul style="list-style-type: none"> The neurotransmitter is degraded in the synaptic cleft to prevent further activation of the receptor, resulting in termination of the signal (e.g. degradation of acetylcholine by acetyl cholinesterase)

NEUROTRANSMITTERS IN THE CNS		
Type		Description
Conventional	<p><i>Share Same Basic Features</i></p> <ul style="list-style-type: none"> Stored in synaptic vesicles Released when Ca^{2+} enters axon in response to an AP Bind to receptors on post synaptic terminal Some form of termination mechanisms 	<ul style="list-style-type: none"> Acetylcholine Amino acids: Glutamate, glycine, GABA Monoamines: Dopamine, NA, adrenaline, serotonin, histamine Purines: ATP, adenosine Neuropeptides: Enkephalins, endorphins, substance P, Neuropeptide Y
Non-Conventional	Different	<ul style="list-style-type: none"> Endocannabinoids Gasotransmitters: Carbon monoxide, nitric oxide
Excitatory	<p><i>Target neuron <u>more</u> likely to fire an AP</i></p> <p>Effect depends on receptor</p>	<ul style="list-style-type: none"> Glutamate is the main excitatory NT in CNS
Inhibitory	<p><i>Target neuron <u>less</u> likely to fire an AP</i></p> <p>Effect depends on receptor</p>	<ul style="list-style-type: none"> GABA is the main inhibitory NT (brain) Glycine is the main inhibitory NT (spinal cord)

Drugs & Neurotransmission

Aspects of neurotransmission (synthesis, storage, release, reuptake) is affected by many drugs:

Storage

- Drugs that facilitates storage: agonist
- Drugs that inhibit storage: antagonist

Release

- Increases release: agonist e.g. Amphetamine increases release of dopamine
- Prevents release: antagonist

Reuptake/breakdown

- Facilitates reuptake/breakdown: antagonist
- Inhibits reuptake/breakdown: agonist
 - e.g. selegiline prolongs action of dopamine by blocking degradation (MAO-B inhibitor)
 - e.g. cocaine blocks DA reuptake

A Note on γ -Aminobutyric Acid (GABA)

GABA is the major inhibitory neurotransmitter in the brain — with GABA_A receptor being the most abundant. GABA holds an intrinsic Cl⁻ channel which once activated, aims to decrease neuronal excitability and thus CNS function via an influx of Cl⁻ ions.

Drugs Potentiating GABA Transmission

Can cause:

1. Hypnotic Effects (Insomnia-Relief)
2. Sedation (Excitation Moderation/Calming Effect)
3. Anxiolytic (Anxiety-Relieving)
4. Seizure Control (Epilepsy-Relief)

SLEEP DISORDERS

Introduction

We will look into insomnia and narcolepsy. But before we will into those disorders - let's first look into how sleeping works:

The Physiology of Sleeping: The SCN & The RAS System

Sleeping is a natural and temporary state of unconsciousness - there are two major stages of sleep:

1. Rapid Eye Movement (REM) Sleep
2. Non-Rapid Eye Movement (Non-REM) Sleep

Reticular Activating System (RAS)

The overall structure that mediates various level of arousal and sleep-wake transitions is the reticular activating system (RAS). It does so by altering the brain's electrical activity such as the firing speed of neurons, and depending on how the RAS configures these signals, you may be more alert or less alert, more awake or less awake and so forth.

The RAS controls 3 things:

1. Motor Function
2. CV/Respiratory Control
- 3. Sleep/Wakefulness**

Damage to the RAS (e.g. stroke) = sleep problems

This has a role in narcolepsy and Parkinson's disease

However, the amount and timing of sleep is regulated by 2 major factors:

1. *Homeostatic Drive*: this describes the pressure drive or need to sleep: the longer you are awake, the greater your body senses the need to sleep. This is because of a chemical called adenosine - which seems to work by slowly building up in your blood when you are awake, making you drowsy over time and slowly dissipates while you sleep. However, if this process alone was in control of your sleep/wake cycles, in theory you would have the most energy when you wake up in the morning. And you would be tired and ready for sleep at the end of the day. There is thus another factor is involved:



Caffeine & Wakefulness

Caffeine seems to promotes wakefulness by blocking the receptors to adenosine.

2. *Circadian Rhythm*: this process is the body's biological clock for the sleep-wake cycle - it thus essentially determines the timing of sleep. The area of the brain that controls this is called the suprachiasmatic nucleus (SCN) also known as the master clock. It is found in the hypothalamus and is sensitive to signals of dark and light which allows it to regulate the day-night cycle. When the optic

nerve in the eyes senses light, the SCN triggers the release of cortisol and other hormones to help you wake up. At night, the SCN sends messages to the pineal gland to trigger the release of melatonin which makes you feel sleepy.



The Circadian Rhythm

The Circadian Rhythm causes highs and lows of sleepiness and wakefulness throughout the day. Typically, most adults feel the sleepiest between 2 a.m. and 4 a.m. and between 1 p.m. and 3 p.m. Getting plenty of regular sleep each night can help to balance out these sleepy lows.

Light Phase (Day)

ACh, Histamines, Dopamine, Serotonin, NA

Light activates the retinohypothalamic pathway which excites the SCN.

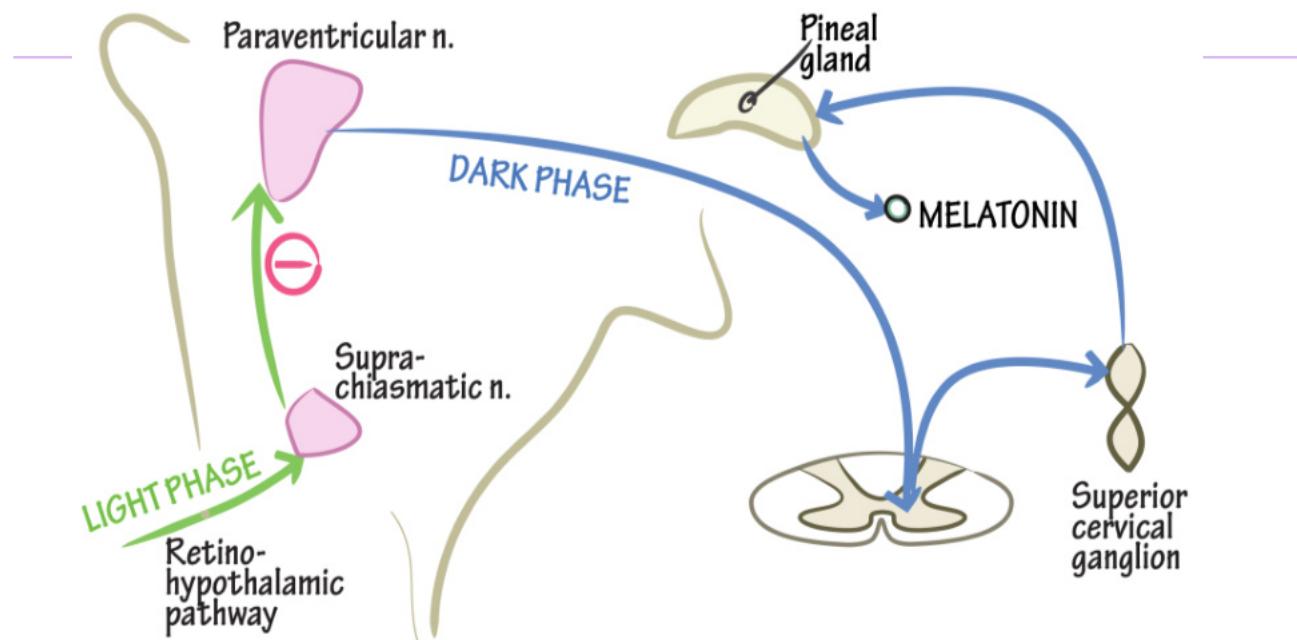
The SCN inhibits the paraventricular nucleus (which is in charge of the dark pathway). This inhibits the release of melatonin, promoting wakefulness.

Dark Phase (Night)

Melatonin, GABA

The paraventricular nucleus sits above the SCN. Projections from it excite the cervical spinal cord and superior cervical ganglion.

The latter in turn stimulates pineal gland to produce melatonin which helps promote sleep.



Insomnia

[National Sleep Foundation](#) [BPAC Insomnia Treatment Guidelines](#) [Pharmacist Melatonin Supply](#)

Description

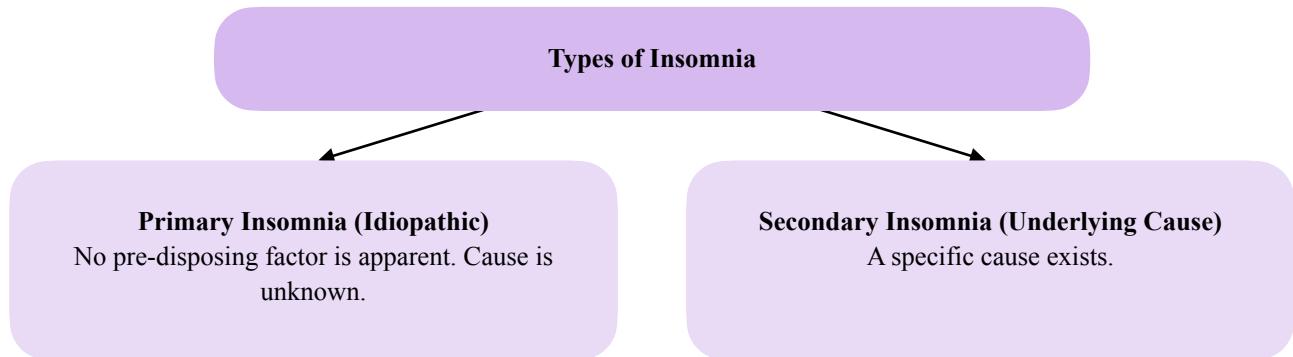
Insomnia, also known as sleeplessness, is a sleep disorder in which people have difficulty falling sleep (onset), maintaining sleep (maintenance), and/or not sleeping long enough. It is a variation in normal sleep pattern despite the opportunity and time.

The duration of insomnia can be classified as:

1. *Transient (2-3 days)*: acute situational/environmental stress e.g. shift work, jet lag
2. *Short Term (<3 weeks)*: lasting for days or weeks e.g. ongoing personal stress
3. *Long Term (> 3 weeks)*: lasting more than a month e.g. psychiatric illness, obstructive sleep apnoea

Pathophysiology

Insomnia is often considered a disorder of excessive activation of the arousal systems of the brain (ie, hyperarousal). Hyperarousal in the physiologic, emotional, or cognitive networks is believed to prevent sleep regulatory processes from naturally occurring. The cause of insomnia can be classified as:



Secondary causes include:

1. *Emotional*: depression, anxiety, PTSD
2. *Neurological*: Alzheimer's, Parkinsons
3. *Medical*: arthritis, dyspepsia, stroke, restless leg syndrome, menopause, sleep apnoea, hyperthyroidism
4. *Medicines*: pseudoephedrine, β -blockers, benzodiazepines overuse, TACs, SSRIs (esp fluoxetine), diuretics
5. *Common substances*: caffeine, nicotine, alcohol
6. *Other*: recent travel (timezone), daytime napping, night-shifts

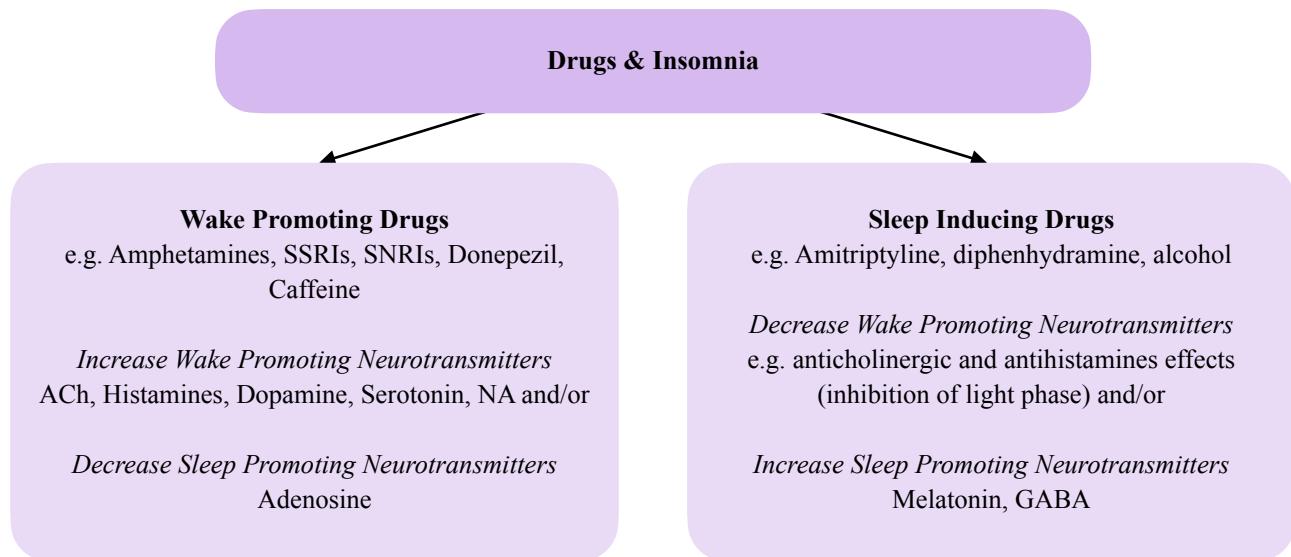


Address the Underlying Cause: Diuretic Example

Addressing the underlying cause of insomnia often may be enough instead of treating the insomnia directly. Diuretics for example can cause insomnia because of the potential for nighttime urination - a way to work around this is to not take any doses in the late afternoon!

A Focus on Medications

Medications are common culprits behind why someone may present with insomnia. While it is difficult to remember all the drugs that cause insomnia - remembering their respective mechanisms of action can help you determine whether it is causing a problem or not. Don't forget that alcohol and caffeine are also considered drugs!



Risk Factors

Patient

- Women
- Older individuals
- Those with co-morbid psychiatric and medical conditions

Signs & Symptoms

Insomnia is typically associated with the following:

- Irritability, depressed mood
- Daytime sleepiness, low energy/motivation, physical discomfort
- Impaired cognitive function (problems focusing and learning)
- Increased risk of motor vehicle collisions



Insomnia in Children

Insomnia in children may present differently - fear of the dark, nightmares can cause insomnia which leads to **bedwetting**

1/3 of adults experience one of the following:

- Sleep onset insomnia (younger people)
- Frequent nocturnal awakening (older people)
- Early morning wakening
- Obstructive sleep apnoea

Diagnosis

1. Sleep history: keep a sleep diary
2. Medical history
3. Physical examination: specific sleep symptoms, daytime symptoms, medicine/substance use, lifestyle, mental health and psychological stress

Non-Pharmacological Treatment

Cognitive Behavioural Therapy for Insomnia (CBTi)

- CBTi consists of behavioural changes to improve sleeping patterns and addressing any unhelpful thoughts or beliefs a patient may have about sleeping

Sleep Hygiene / ASLEEP

- Avoid alcohol, caffeine, nicotine (particularly within 6 hours of bedtime)
- Sleep (and sex) should be the only use of the bed
- Leave laptops, TVs and paperwork out of the bedroom
- Exercise regularly and be outdoors during the day
- Early rising — avoid sleeping in/daytime naps and rise earlier by 15-30 min.
- Plan for bedtime

Pharmacological Treatment

[Benzodiazepine Switching Guidelines](#) [Benzodiazepine Deprescribing Guidelines](#)

Insomnia pharmacotherapy can be classified based on whether the medication has a formal sleep indication and whether a prescription is required.

INSOMNIA PHARMACOTHERAPY			
Type	Mechanism of Action	Patient Counselling	Side Effects
[PRESCRIPTION] <i>Melatonin (Circadin, Vigisom)</i>	<p>Melatonin is produced in the pineal gland and facilitates sleep onset. It is under the control of the circadian rhythm (SCN); a late evening rise causes arousal to decline.</p> <p>Accreditation Required Prescription except when supplied:</p> <ul style="list-style-type: none">• For primary insomnia in adults ≥ 55 years• For up to 13 weeks• By a NZ accredited pharmacist• In a original pack• 3mg or 2mg if modified release (Circadin) <p>Special authority (only time its funded)</p> <ul style="list-style-type: none">• Children < 18• Persistent/distressing insomnia• Secondary to neurodevelopment disorders	<ul style="list-style-type: none">• Take 1 tablet once daily 1-2 hours before bedtime, after food (to reduce stomach upset)• Swallow whole, do not crush or chew.• May take a few days or longer for benefit.• Needs to be taken every night to be effective; aids in getting back to a good sleep habit• Do not drink alcohol• ASLEEP sleep hygiene• Do not drive or operate heavy machinery for 8 hours after taking• It is not funded - \$40-\$65 for a pack of 30 tablets	<p>Caution in renal/hepatic impairment Caution in elderly</p> <p><i>Interactions</i></p> <ul style="list-style-type: none">• Quinolones, carbamazepine, rifampicin• Alcohol and other hypnotics will be amplified.

<p>[PRESCRIPTION] <i>Benzodiazepine Receptor Agonists</i></p> <p>Triazolam, Temazepam, Diazepam, Flurazepam, Lorazepam</p>	<p>Benzodiazepines work to calm or sedate the person by acting as allosteric modulators of the GABA_A receptor.</p> <p>They bind at an allosteric BZD site on the GABA_A receptor (distinct from the GABA ligand attachment site) and triggers the opening of the Cl⁻ channel. This causes hyperpolarisation, therefore less excitability to fire AP</p> <p>This facilitates the onset/duration of sleep as well as alter the NREM:REM balance.</p>	<p><i>Long term use (> 4 weeks) is not recommended</i></p> <ul style="list-style-type: none"> Withdrawal symptoms can occur after 4-6 weeks of continuous use (switch short acting to long acting drugs to decrease severity) <p><i>Differing rates of onset/duration</i></p> <ul style="list-style-type: none"> Short duration of actions (temazepam, triazolam) are more associated with rebound insomnia in younger people. Longer half lives (diazepam, nitrazepam) can cause daytime sedation in older patients. 	<p><i>Generally</i></p> <ul style="list-style-type: none"> Rebound insomnia upon cessation Drowsiness, ataxia, muscle weakness (falls risk) Respiratory and CV depression (especially in respiratory disease e.g. COPD) Abuse potential as addictive → Use for ≤4 weeks with INTERMITTENT use <p><i>Withdrawal Symptoms</i></p> <ul style="list-style-type: none"> Physical: flu like symptoms, GI disturbances Psychological: insomnia, anxiety, depression <p><i>Caution</i></p> <p>Impaired hepatic function (e.g. low albumin increases potency)</p> <p><i>Interactions</i></p> <ul style="list-style-type: none"> OCs CYP Inhibitors (ketoconazole, macrolides) CYP Inducers (rifampicin, omeprazole, nifedipine)
<p>[PRESCRIPTION] <i>Non-Benzodiazepine Hypnotics ('z-drugs')</i></p> <p>Zopiclone, Zaleplon, Zolpidem</p>	<p>These act on GABA_A receptor on a distinct site from benzos to also cause an influx of Cl⁻, resulting in hyperpolarisation.</p> <p>These are usually given to people who go on long haul flights.</p>	<ul style="list-style-type: none"> Should only be used short term/ occasionally Long term use can cause dependence/tolerance Do not drink alcohol 	<ul style="list-style-type: none"> Incoordination Drowsiness Dizziness Confusion Amnesia
<p>[PRESCRIPTION] <i>Alternative Non-Insomnia Medications ('Off-label' use)</i></p>	<p><i>Wakeful Neurotransmitters Antagonist</i></p> <ul style="list-style-type: none"> Antidepressants (amitriptyline, mirtazapine, doxepin) Anti-psychotics (quetiapine) <p><i>Agonist of sleep neurotransmitters</i></p> <ul style="list-style-type: none"> Anxiolytics/anti-epileptics (alprazolam, clonazepam) 	<ul style="list-style-type: none"> Counsel on dose to decrease stigma 	<ul style="list-style-type: none"> Excessive sedation (long half-life)
<p>[PRESCRIPTION] <i>Anti-Histamines (H1)</i></p> <p>Promethazine (Phenergan)</p> <p>Diphenhydramine (Benadryl, Unisom)</p> <p>Doxylamine (Dozile)</p>	<p>Histamine is a potent wake promoting neurotransmitter</p>	<ul style="list-style-type: none"> Sedative effect may diminish over time If need to take off - reduce dose by taking it every second night for 3-5 days 	<ul style="list-style-type: none"> Daytime drowsiness (long half-life) Headache Psychomotor Impairment Anti-muscarinic effects Paradoxical excitation (children, elderly)

Formal Sleep Indication?			
Prescription Required?	No	Yes	
No	Dietary Supplements	<i>OTC / Sleep Aids</i> (e.g. Histamine Receptor Antagonists)	
Yes	Off-Label Sedating Medications	<i>Insomnia Medications</i> (e.g. Melatonin, Benzos & Non-Benzo Hypnotics)	

Osce Points

- Check for recent travel

Name: _____ Phone number: _____
Address: _____

1. Do you have trouble falling asleep, staying asleep or waking up early such that it interferes with your activities the following day (e.g. unrefreshed in the morning, fatigued, poor concentration or irritable)? If yes, how many nights per week? _____ How long have you had this? _____

2. When do you sleep well is this with the help of sleep medication? _____

3. Can you think of any reason for your problem sleeping? _____

4. Are you a shift worker?

5. During the past 2 weeks have you often been bothered by feeling nervous, anxious or on edge?

6. During the past 2 weeks have you often been bothered by not being able to stop or control worrying?

7. Do you snore very loudly at night? Don't know:

8. Do you find yourself falling asleep in the day, e.g. in waiting rooms or as a car passenger?

9. When you can choose do you go to bed late at night e.g. after midnight?

10. When you can choose (e.g. weekends) do you sleep late into the morning, after 10am?

11. Is there anything you do when sleeping e.g. sleep walking/talking, teeth grinding, restless legs (an irresistible urge to move the legs in bed), or anything unusual that is contributing to your sleep problems? _____

12. Do you have any significant health problems that affect your ability to sleep well, such as pain, breathing difficulty, acid reflux or cough?

13. During the past 2 weeks have you often been bothered by having little interest or pleasure in doing things?

14. During the past 2 weeks have you often been bothered by feeling down, depressed or hopeless?

15. In the last year, have you felt the need to cut down on the amount of alcohol you drink?

16. In the last year, have you ever drunk more alcohol than you meant to?

17. In the last year, have you ever used prescription, non-prescription or recreational drugs more than you meant to?

18. Which medicines do you take? _____

19. Time you go to bed: _____ Time you get up: _____ Hours sleeping: _____ Total hours in bed: _____
Ask about sleep hygiene/lifestyle, e.g. screen time 2 hours before bed and if waking, caffeine, room comfort

Stop Sleeping Pills Guide

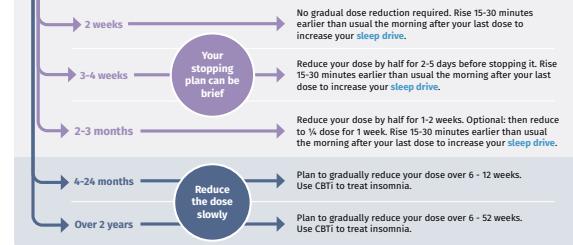


Advice

- 1 Estimate how long it will take to reduce your dose based on how long you have been using sleeping pills.
- 2 Using the **Stop Sleeping Pills Planner**, develop your dose reduction plan with your doctor and pharmacist.
- 3 Aim to reduce your dose on the same day of the week, every 1 or 2 weeks.
- 4 Your plan should be flexible. Make adjustments based on how you are feeling.
- 5 Reduce your dose the same amount each time or slow things down by making smaller dose reductions, lengthening the time between dose reductions, or both.
- 6 Monitor your sleep with a sleep diary. Use CBTi to help you sleep as you lower your dose.

Estimate the duration of your dose reduction schedule

How long have you been taking sleeping pills?



Sleeping pill

Name	Duration of use	Daily Dose	Estimated dose reduction duration

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How do sleeping pills compare?

Medicine	NZ Class	Onset of action	Average half-life Duration	Average Time to Develop Tolerance	Common ADR	Notes
Chlorpheniramine	POM for insomnia in those > 2 yr of age	Slow	Long 2 - 3 hr	3 days - 2 weeks 14 - 25 hr	Dry mouth, grogginess the next day	Max 10 doses
Cyclizine (e.g., Nausicain)	POM for insomnia	Rapid to Immediate	Short 30 min - 2 hr	3 days - 2 weeks	Dry mouth, grogginess the next day	Max 10 doses
Diphenhydramine (e.g., Unisom)	POM for insomnia in those > 2 yr of age	Immediate to slow	Short 1 - 4 hr	3 days - 2 weeks 4 - 8 hr	Dry mouth, grogginess the next day	doses > 50 mg do not produce better sleep Max 10 doses
Doxylamine (e.g., Dozile)	POM for insomnia in those > 2 yr of age	Immediate to slow	10 - 13 hr 1 - 2 hr	3 days - 2 weeks	Dry mouth, grogginess the next day	doses > 25 mg do not produce better sleep Max 10 doses
Melatonin (e.g., Circadin)	Rx with exemption for primary insomnia in those 55 yrs or older for up to 13 weeks	Immediate to slow	Very short 0.5 - 2 hr	None 1 hr	Uncommon - weakness, headache, respiratory infection, pain ache Long-acting formulation (product in NZ) is better for people having trouble staying asleep Take with food	mogadon
Promethazine (e.g., Allersoothe)	POM for insomnia in those > 2 yr of age	Rapid	Short 15 min - 1 hr	3 days - 2 weeks 2 - 3 hr	Dry mouth, grogginess the next day	25 - 75 mg nocte Max 10 doses
Temazepam	Prescription - controlled class C	Immediate to slow	Immediate 11 hr	2 - 4 weeks	Grogginess the next day	1 - 3 hr
Trimeprazine	POM for insomnia in those > 2 yr of age	Rapid	Short 15 min - 1 hr	3 - 6 hr	Dry mouth, grogginess the next day	Max 10 doses
Zopiclone	Prescription	Rapid	Short 30 min	4 weeks 4 - 6 hr	Dry mouth, bitter taste - to reduce take with orange juice	

Drug	Half-life; short = 6–12 hours; medium = 12–24 hours; long > 24 hours
Alprazolam	short
Clobazam	long
Clonazepam	long
Diazepam	long
Lorazepam	medium
Nitrazepam	long
Oxazepam	short
Temazepam	short
Triazolam	very short (< 6 hours)

Rebound insomnia (younger)

Narcolepsy

Description

Narcolepsy is a chronic sleep disorder characterized by overwhelming daytime drowsiness and sudden attacks of sleep.

Pathophysiology

The ability to regulate sleep-wake cycles is impaired, so the normal boundaries between sleeping and being awake are weak, leading to frequent lapses into sleep and the occurrence of elements of sleep while a person is awake. It is hypothesised that an autoimmune response occurs, killing orexin-producing nerve cells, which have a role in mediating wakefulness and alertness

Signs & Symptoms

People with narcolepsy often find it difficult to stay awake for long periods of time, regardless of the circumstances. Narcolepsy can cause serious disruptions in your daily routine. There are 5 key symptoms:

1. Daily sleepiness with episodes of dozing off (with little to no warning)
2. Episodes of muscle weakness (cataplexy) - triggered by strong emotions e.g. laughing, winning, anger
3. Inability to move at the start or end of sleep
4. Vivid hallucinations at the start or end of sleep e.g. visual, tactile, auditory
5. Fragmented sleep

NEURODEGENERATIVE MOTOR DISORDERS

Introduction

We will look into epilepsy & seizures, PD, MND and MS.

Epilepsy & Seizures

Description

Epilepsy is a neurological disorder leading to recurring, unprovoked seizures due to a temporary disturbance in the electrical activity of the brain. It characterised by a spectrum of conditions and it is not a mental illness.



Epilepsy ≠ Seizures

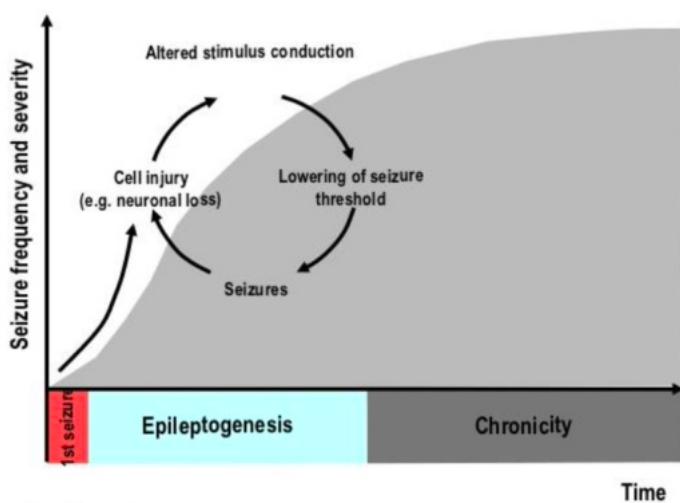
Seizures: an event that is the result of a disruption in the electrochemical activity of the brain, causing sudden abnormal and excessive firing of neurons — there is an excess of excitatory and/or failure of inhibitory neurotransmission.

Epilepsy: a neurological disease characterised by the tendency to have recurrent seizures.

Pathophysiology of Epileptogenesis

Anything that can alter the balance between excitatory/inhibitory neurotransmission will decrease seizure threshold. The temporary disturbance can be the result of the following, in which repeated seizures can cause neuronal cell death and promote more seizures:

1. An excess of excitatory neurotransmission **facilitated** (Glutamate → NMDA → Ca^{2+}) and/or
2. A **failure** of inhibitory neurotransmission (GABA → GABA receptor → Cl^-)



Glutamate and GABA play a critical role, however it is hypothesised that acetylcholine may also mediate signal transmission through nicotinic receptors.

Types of Epilepsy

The presentation of epilepsy is categorised based on the site of discharge and the extent of spread - and while this determines the signs & symptoms, people's experiences differ greatly. For some it may be a 'one-off' event and for others, a lifelong one (chronic).

TYPES OF EPILEPSIES		
Epilepsy	Description	Symptoms
Focal	<p>Focal epilepsies are when a seizure begins and remains limited/local to a particular area of the brain — this however does not mean that it cannot spread.</p> <p>Further classification based on awareness</p> <ol style="list-style-type: none"> 1. Simple: consciousness not affected 2. Complex: consciousness affected 	<ol style="list-style-type: none"> 1. <i>Simple Focal Epilepsies</i> <ul style="list-style-type: none"> • The person remains conscious and experiences strange sensations e.g. hearing things, tasting something, jerking movements • The person will remember the seizure afterwards and often confuse it as a 'daydream' or as being intoxicated. 2. <i>Complex Focal Epilepsies</i> <ul style="list-style-type: none"> • The person has an impaired awareness/respondiveness so may not remember what happened during the seizure.
Generalised	<p>Generalised epilepsies are those that affect the entire brain (both hemispheres, including the reticular formation) These kind of epilepsies may start as focal.</p> <p>Further classification based on movement</p> <ul style="list-style-type: none"> • Absence (petit mal): non-motor seizures • Myoclonic • Clonic • Tonic-Clonic (grand mal): motor seizures 	<ol style="list-style-type: none"> 1. <i>Absence (petit mal)</i> <ul style="list-style-type: none"> • Patients may stop what they are doing and stare into space — may feel like the person isn't really there or is mistaken for simple daydreaming • Patients may do the same movements over and over again (e.g. smacking lips) 2. <i>Myoclonic</i> <ul style="list-style-type: none"> • Person has short muscle twitches/jolts or increases in muscle tone 3. <i>Clonic</i> <ul style="list-style-type: none"> • Person has violent muscle contractions/convulsions (muscle spasm and jerks) 4. <i>Tonic-Clonic (grand mal)</i> <ul style="list-style-type: none"> • This is the most common kind of seizure. The body stiffens (tonic phase) and then the limbs begin to jerk rhythmically (clonic phase) • May lose consciousness
Unknown	Unknown onset seizures are the ones we cannot classify as either focal or generalised. Sometimes this classification is temporary until further information/testing results are obtained.	

Risk Factors

Causes of Epilepsy

1. Genetic (1/3)
2. Brain Injury (2/3)
 - TBI, tumours, stroke
 - Infections (meningitis, encephalitis)
 - Brain disorders (autism, dementia, cerebral palsy)

Remember: seizures are a feature of epilepsy

But can occur due to other reasons

Causes of Seizures

1. Epilepsy
2. Fever: febrile convulsions
3. Electrolyte disturbances: low Na
4. Substance use: illegal/recreational drugs, alcohol abuse
5. Hypoglycaemia
6. Certain medications
 - Tramadol, Quinolones, Lithium, Antidepressants, Antipsychotics
 - Alcohol/Benzodiazepine withdrawal (these lower seizure threshold because stopping causes hyper-excitability state)

Signs & Symptoms

While many types of epilepsy exist, seizures remain a common factor to them. Depending on the location and extent of the seizure, this can cause changes in:

Acronym [MABS]

1. *Motor*: movement
2. *Autonomic*: awareness and consciousness
3. *Behavioural*: behaviour
4. *Sensory*: sensation and feeling

Complications

1. Repeated epileptic discharge can result in cell death
2. Often seizures are not the main challenge for people — epilepsy is often associated with:
 - a. *Mood/Psychiatric disorders*: anxiety, **depression**
 - b. *Neurological disorders*: ADHD, cognitive disorders, migraines, sleep disorders
 - c. *Other*: CV, respiratory, inflammatory, **falls**, reproductive issues, **osteoporosis**, stigma
 - d. *Female patients*: hormonal changes can impact severity/frequency of epilepsy (puberty, menses, pregnancy, menopause)
 - e. *SUDEP*: sudden unexplained death in epilepsy patients

Diagnosis

Epilepsy can start at any age but is more likely to be diagnosed in childhood and senior years.

- **Electro-Encephalo-Graphy (EEG)**: visualises portion of brain causing the seizure — primary diagnosis
- History (seizure diary)
- Physical exam
- MRI: brain structure

Non-Pharmacological Treatment

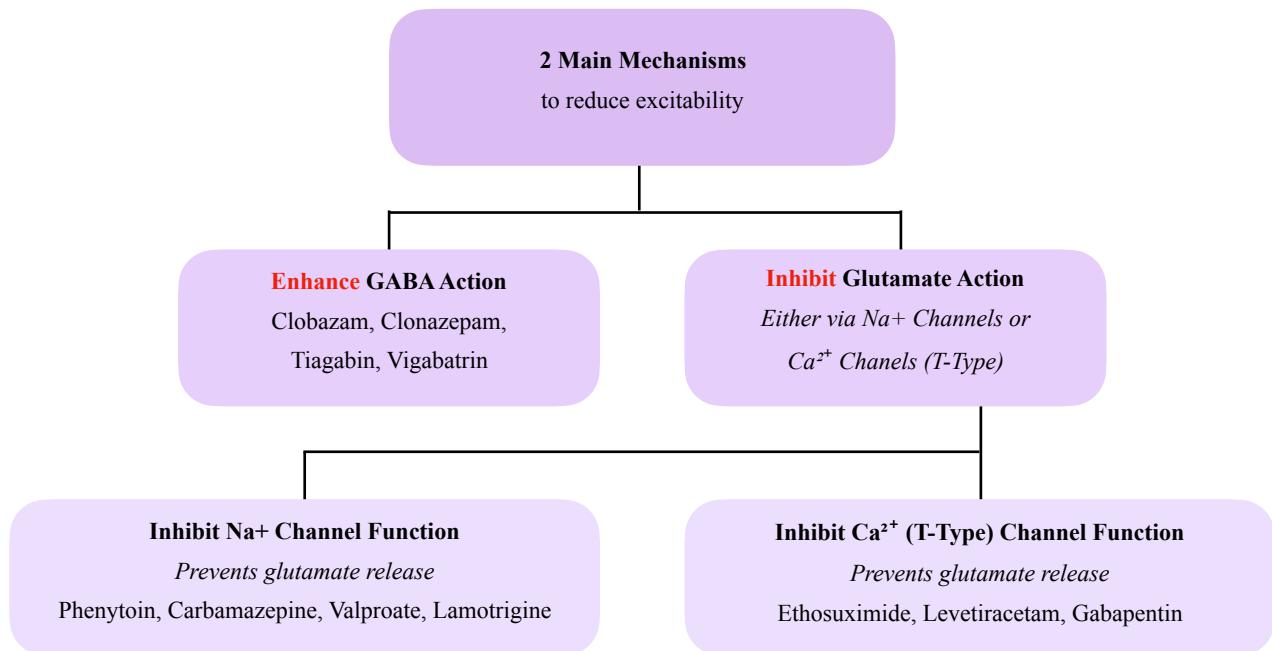
1. *Surgical removal of the focal area of the seizure — i.e. if drug resistant*
 - This can successfully eliminate drug-resistant seizures, provided the region affected is not too close to critical areas (e.g. those responsible for speech/muscle control)
2. *Vagal nerve stimulation to reduce seizure frequency*
 - This involves implantation of a unit that generates intermittent electrical currents to stimulate the vagus nerve. This is often reserved for patients who do not respond to drugs and/or are not surgical candidates.
3. *Ketogenic diet*
 - This diet consists of only dietary fats and protein with no added sugar. This consequently produces a keto-acidotic state which is effective in those with difficult-to-control seizures. However there are two concerns with this method: **palatability** is a concern and ketotic states are **difficult** to maintain.

Pharmacological Treatment

[Generalised Seizures NZF Treatment Guidelines](#),
[BPAC Prescribing Issues with Anti-Convulsants](#),
[Switching Antiepileptics](#),

[Focal Seizures NZF Treatment Guidelines](#)
[BPAC Anti-Convulsant Prescribing in Female Patients](#)
[Epilepsy Control NZF](#)

Epilepsy is treated primarily with anti-epileptics. Pharmacological interventions are initiated after a history of at least 2 seizures. The primary purposes of anti-epileptics is to raise the seizure threshold by making cells less excitable, thereby preventing signal propagation. It is thus possible to render patient seizure free with medications. **Monotherapy is best.** So how do anti-epileptics work?



EPILEPSY PHARMACOTHERAPY				
Class	Drug	Indication	Mechanism of Action	Side Effects
GABA Enhancement	Clobazam	Adjuncts	GABA_A R Activation Enhancement Benzodiazepines that act on the GABA receptor to suppress the discharge and spread of electrical activity.	'Think side effects of alcohol' Ataxia, memory impairment, sedation, slowed thinking
	Clonazepam	Adjuncts	GABA Uptake Inhibitor Tiagabine is a GABA uptake inhibitor, causing GABA to remain in the synaptic cleft	Confusion, difficulty speaking, mild sedation, paraesthesia <i>Overdose:</i> lethargy, respiratory depression, tachycardia
	Tiagabine	Adjunct for Focal	GABA Transaminase Inhibitor Prevents breakdown of GABA, resulting in its increased concentrations.	Visual disturbances, behaviour advisor effects <i>Overdose:</i> lethargy, respiratory depression, tachycardia
	Vigabatrin <i>Special authority</i>	Adjunct for Focal		
Glutamate Inhibition via Na ⁺	Phenytoin	Tonic-clonic, Focal	Tonic-clonic and focal seizures Not first choice due to poor side-effect profile and narrow therapeutic index (non-linear pharmacokinetics, <i>CYP inducer</i>) and therefore requires close monitoring. <i>Monitoring:</i> plasma concentrations in pregnancy and elderly (due to lowered protein binding), many drug interactions	<i>Toxicity</i> Nystagmus, diplopia, slurred speech, ataxia, confusion, hyperglycaemia <i>Side Effects</i> GI, drowsiness, tremor, dizziness, headache, gingival hypertrophy, hirsutism, acne
	Carbamazepine	Generalised tonic-clonic, Focal	Tonic-clonic and focal seizures — First line in pregnancy Pharmacologically similar to phenytoin <i>Interactions (substrate and autoinducer of CYP3A4)</i> Warfarin, clopidogrel, simvastatin, estrogen/progesterone, erythromycin	Dose related and dose limiting (minimised with modified release preparations) • Headache, N&V, ataxia, drowsiness, blurred vision • Hyponatraemia, blood, hepatic and skin disorders
	Sodium Valproate	All types	All forms — First line for generalised, TERATOGENIC Also has effects on increasing GABA concentrations. <i>Interactions</i> Anti-epileptics, antidepressants, antimalarials, antipsychotics, carbamazepine	<i>Side effects (fewer than others)</i> • Thrombocytopenia, transient hair loss, liver toxicity, pancreatitis • Weight gain, tremors, hair loss, GI disturbances • Do not use in pregnancy - risk of congenital malformations
	Lamotrigine <i>Not routinely indicated</i>	Focal, Generalised tonic-clonic, Absence	Most types — First line in child-bearing age females/pregnancy Lowest teratogenic risk <i>Interactions — Co-administration requires close monitoring</i> Valproate, Carbamazepine, phenytoin, phenobarbitone, primidone	<i>Side effects (manage with gradual dose titration)</i> Ataxia, dizziness, headache, insomnia, sedation, nausea, skin reactions (SJS & TEN hypersensitivity syndrome)
Glutamate Inhibition via Ca ²⁺	Ethosuximide <i>Not widely used</i>	Absence	Absence Seizures Specific block of T type calcium channels Either in monotherapy or in combination with other anticonvulsants	Nausea, anorexia, lethargy, dizziness, hypersensitivity
	Levetiracetam <i>Specialist Recommendation</i>	Focal	Partial +/- secondary generalisation — low teratogenic risk Newer kind of anticonvulsant: exact mechanism unknown, thought to bind to synaptic vesicle glycoprotein which decreases vesicle docking and NT release. Also inhibits presynaptic calcium channels (N-type)	Ataxia, dizziness, headache, tremor, behavioural disturbances, GI, suicidal ideation, psychiatric disturbances
	Gabapentin <i>Not routinely indicated</i>	Generalised tonic-clonic	Partial + secondary generalised tonic-clonic — more commonly used for neuropathic pain	Sedation, ataxia, weight gain, peripheral oedema
	Pregabalin <i>Not subsidised</i>	Partial seizures, Adjunct	Adjunct Blocks voltage gated calcium channels to decrease glutamate	
GABA and Glutamate activity	Topiramate <i>Not routinely indicated</i>	Generalised	Adjunct Blocks Na channels, inhibits glutamate activity, enhances GABA activity	Ataxia, confusion, dizziness, tiredness, weight loss
Benzodiazepine	Lorazepam (IV), Diazepam (rectal), Midazolam (IM)	Status Epilepticus	Life-threatening medical emergency	

A Note on other Anti-Epileptics

- Locasomide: Adjunct for focal seizures with/without secondary generalisation
- Phenobarbitone and primidone: no longer widely used due to CNS and respiratory ADRs
- Oxcarbazepine: not subsidised in NZ, therefore not widely used

Treatment Guidelines For Epilepsy

Based on NZF

Focal Seizures

If Newly Diagnosed

1. Lamotrigine or carbamazepine
2. Sodium valproate, levetiracetam
3. Adjunctive: Clobazam, oxcarbazepine, gabapentin, phenytoin, topiramate

Generalised Seizures

Absence Seizures (Petit Mal)

1. Ethosuximide or Sodium Valproate (unless childbearing aged female)
2. Lamotrigine (unapproved indication)
3. If adjunctive treatment fails: Clobazam, clonazepam, levetiracetam, topiramate, or zonisamide

Myoclonic Seizures

1. Sodium Valproate (unless childbearing aged female)
2. Levetiracetam or Topiramate
3. If adjunctive treatment fails: Clobazam, clonazepam, zonisamide

Tonic/Atonic Seizures

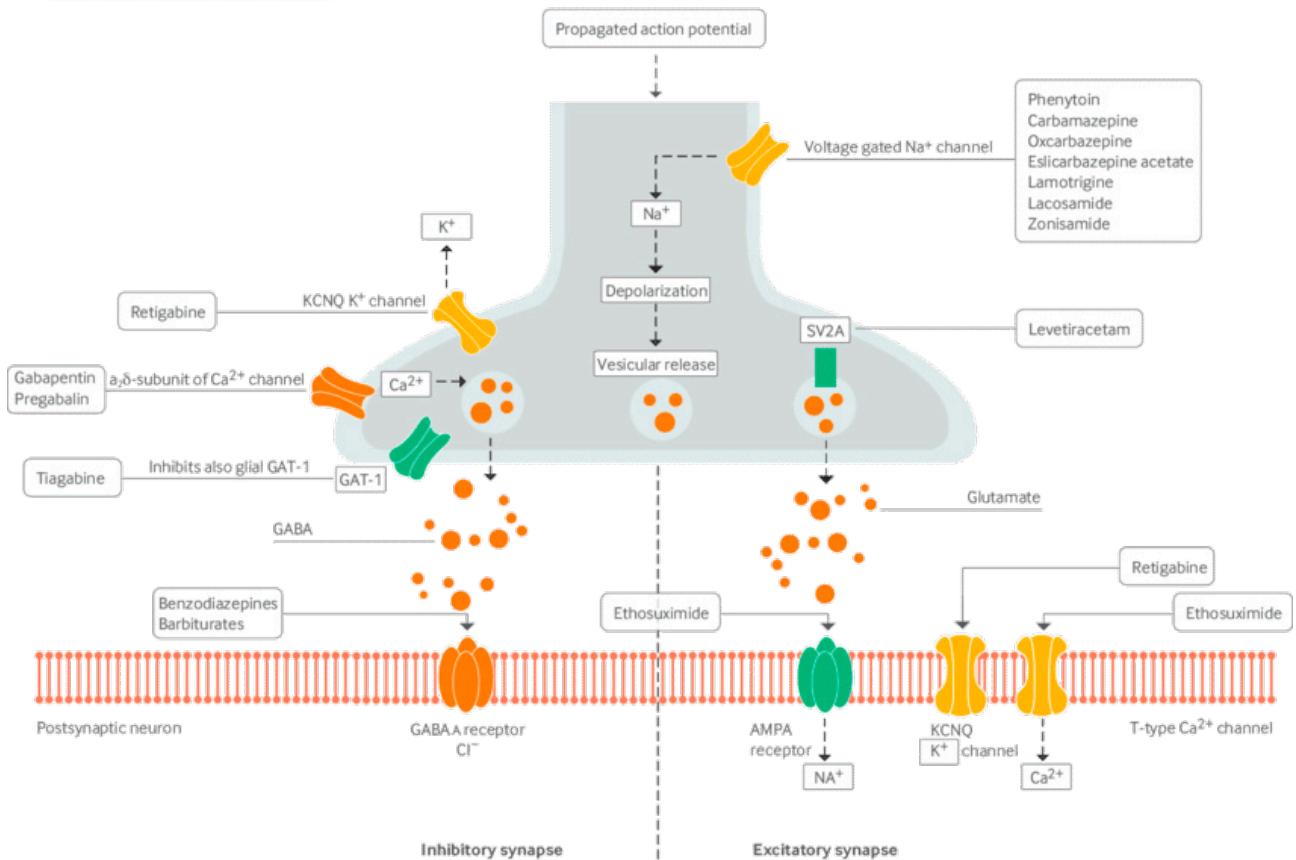
1. Sodium Valproate (unless childbearing aged female)
2. Lamotrigine (unapproved indication)
3. If adjunctive treatment fails: Rufinamide or topiramate

Tonic-Clonic Seizures (Grand Mal)

1. Sodium Valproate (unless childbearing aged female)
2. Lamotrigine (unapproved indication)
3. Other: Carbamazepine, oxcarbazepine, phenytoin
4. Adjunctive: Clobazam, levetiracetam, topiramate

CONSIDERATIONS WITH ANTI-EPILEPTICS	
Drug	Description
Driving	<p>Anti-convulsants are thus all dispensed STAT.</p> <p>Following a seizure in NZ, a 12 month stand down period is required from driving — this also applies to patients who experience a single seizure with no history of epilepsy. Patients may still hold a license for a private motor vehicle, however in most cases there will be a permanent loss for the license of a commercial vehicle.</p>
Alcohol	<p>A limited amount is acceptable (1-2 drinks to no more than 3-6 drinks per week).</p> <p>Alcohol withdrawal can lower seizure threshold and thus induce a seizure. However a limited amount is usually acceptable for the majority. Excessive amounts can induce seizures even in those with no history of epilepsy. The reason patients must be advised on alcohol allowed is because it is less riskier than missing a dose in order to drink.</p>
Monotherapy /Combination	<p>Monotherapy is always preferred if possible.</p> <p>When treatment with a first line agent has failed, a second drug may be trialled either by itself or as an adjunct. In the case of the latter, there should be evidence however that the first drug lacked efficacy — this is because treatment with a single drug is usually associated with better compliance, fewer ADRs, reduced likelihood of drug reactions, a lower teratogenic potential and is more cost effective.</p>
Switching Drug	<p>Regimens must be conducted in a step-wise manner to prevent breakthrough seizures</p> <p>Careful tapering and starting doses low and then increasing over a few weeks + close monitoring</p> <ul style="list-style-type: none"> • Be careful as many anti-epileptics interact with one another e.g. lamotrigine + valproate
Drug Withdrawal	<p>Must be gradual due to risk of rebound seizures</p> <p>Even in patients that have been seizure free for many years, seizure recurrence can occur upon withdrawal.</p> <ul style="list-style-type: none"> • Cessation of therapy should be gradual (may take months) and under specialist supervision (particularly with benzodiazepines and barbiturates due to risk of rebound seizures). • In situations where rapid withdrawal is necessary (e.g. experiencing adverse effects), add an additional anti-convulsant first to quickly obtain therapeutic levels.
Side Effects	<p>Anti-epileptics come with three types of side effects</p> <ol style="list-style-type: none"> 1. <i>Normal Side Effects - think 'alcohol side effects'</i> <ul style="list-style-type: none"> • Sedation, tiredness, dizziness, ataxia, tremors, slurred speech, confusion, dry mouth, nausea, diarrhoea, GI disturbances 2. <i>Idiosyncratic Reactions</i> <ul style="list-style-type: none"> • Idiosyncratic reactions are often the cause of emergency treatment cessation as they aren't dose or concentration related • Rash (can be life-threatening e.g. SJS, TEN), hepatotoxicity, haematological toxicities 3. <i>Chronic Adverse Effects i.e. after 6 months duration</i> <ul style="list-style-type: none"> • Peripheral neuropathy and cerebellar atrophy • Weight gain • Reduction in bone mineral density — fracture risk <p><i>Minimising the three types of side effects:</i></p> <p>There are a few strategies that can help minimise their occurrence:</p> <ol style="list-style-type: none"> 1. Slow release formulation to avoid rapid rises in serum concentrations 2. Start with a low dose and slowly increase over 1-2 week intervals 3. Use monotherapy if possible
Female Patients	<p>There are a few considerations for the use of anti-epileptics in female patients.</p> <ol style="list-style-type: none"> 1. <i>Hormone-related changes:</i> Puberty, menstrual cycle, pregnancy, and menopause can influence the severity and frequency of epilepsy 2. <i>Catamenial epilepsy:</i> increased seizures 3 days prior to menstruation due to progesterone/estrogen balance, pre-menstrual tension and fluid retention. Dose adjustments/timings will need to be considered. 3. <i>Contraception:</i> anti-epileptics are notorious hepatic enzyme inducers of the hormonal contraceptives, particularly carbamazepine and lamotrigine. Hormonal contraceptives are not recommended within 28 days of taking enzyme-inducing anti-epileptics 4. <i>Pregnancy:</i> some anti-epileptics are very teratogenic, particularly if more than 2 are used in the first trimester. Additionally, use of anti-epileptics need to be dose-adjusted in sight of increased drug clearance and close fetal growth/plasma concentrations monitoring is required. <ul style="list-style-type: none"> • First line in pregnancy is lamotrigine or carbamazepine • All women of childbearing age must not be given valproate • Considerations: folic acid, vitamin K supplementation

RESPONSE TO ANTI-EPILEPTIC DRUGS



Seizure First Aid

SEIZURE FIRST AID	
What	Description
1. Stay	<ul style="list-style-type: none"> Stay with the person until they are awake after the seizure — Most seizures end in a few minutes (< 5 minutes) Start timing the seizure, remain calm and check for medical ID
2. Safety	<ul style="list-style-type: none"> Move or guide person away from harmful objects and keep them safe
3. Side position	<ul style="list-style-type: none"> If the person is not awake and aware, turn them on their side. Don't block their airway Put something small and soft under their head Loosen tight clothes around neck.
4. Do not	<ul style="list-style-type: none"> Do not put anything in their mouth until they are awake (water, pills, food) Do not restrain!
Call 111 if the following occurs	
1	<p>Seizure lasts longer than 5 minutes (<i>status epilepticus</i>)</p> <ul style="list-style-type: none"> Status Epilepticus is a single epileptic seizure lasting more than 5 minutes or 2+ seizures within a 5 minute period without the person returning to normal between them. These are life threatening medical emergencies, particularly if treatment is delayed.
2	Repeated seizures or this is their first seizure
3	Difficulty breathing
4	Seizure occurs in water
5	Person is pregnant, injured or sick
6	Person doesn't return to usual state

Parkinson's Disease (PD)

Description

Parkinson's Disease (PD) is an age-related, chronic and progressive neurodegenerative disorder that affects parts of the brain that are associated with normal movement and balance, causing unintended or uncontrollable movements, such as shaking, stiffness and tremors. It is an extremely disabling condition that affect one's ability to perform daily tasks and activities.



Parkinson's Disease (PD)

Following dementia, Parkinson's Disease is the 2nd most common neurological disorder. Life expectancy of those affected by PD vary — depending on age of onset and concurrent comorbidity with dementia.

Pathophysiology

Parkinson's disease is the result of a dopamine deficiency in the brain. The two major pathological findings that we know of in Parkinson's cause this:

Loss of Dopamine-Containing Neurons *in the substantia nigra of the brain:*

Dopamine loss > 50% is where we begin to see symptoms as they cause degeneration of terminals in the striatum.

This was discovered in the post-mortem brains of patients with PD - which showed a loss of in the substantia nigra, thus indicating the loss of DA containing neurons.

Presence of Lewy Bodies *in the cytoplasm of the brain:*

Free radicals are by-product of DA metabolism that DA containing neurons fail to 'mop up' efficiently - resulting in the formation of Lewy Bodies.

These, in turn, are thought to cause functional changes in the way that dopamine-containing neurons.

Dopamine & Motor Function

So how does dopamine work? Dopamine (alongside Acetylcholine) is a neurotransmitter that overall modulates motor function. Motor function, simply put, can be described as communication that occurs from the basal ganglia (a structure that co-ordinates movement) to the motor cortex (a structure that enacts movement). This communication can occur in two possible pathways:

The Direct Pathway *Excitatory via Glutamate*

Allows voluntary movements via disinhibition of the thalamus

The Indirect Pathway *Inhibitory via GABA*

Prevents unwanted movements via inhibition of the thalamus

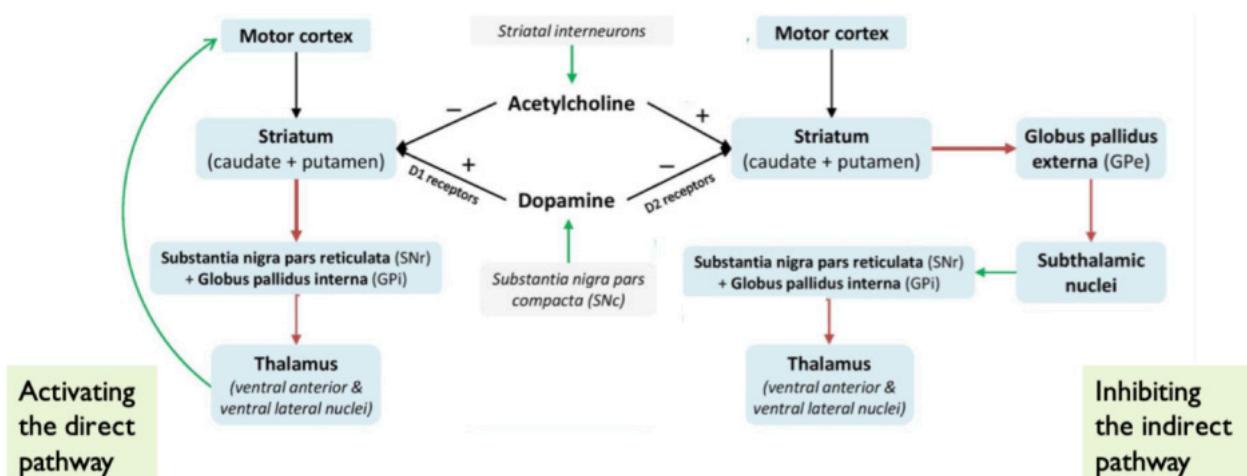
It is the balance between the excitatory (direct) and inhibitory (indirect) pathways that allows the production of smooth movement - this enabled by the actions of Dopamine and Acetylcholine.

1. DA will overall increase motor activity by activating the direct pathway and inhibiting the indirect.
2. ACh will produce the opposite by activating the indirect and inhibiting the direct.

Parkinson's and Dopamine

In Parkinson's Disease, the reason we thus observe destabilised motor control is because there is a degeneration of nigrostriatal dopaminergic pathways - no dopamine means:

1. Reduced activation of the direct pathway = **less voluntary movement**
2. Reduced inhibition of the indirect pathway = **less voluntary movement**



Risk Factors

1. *Idiopathic* (90%): cerebral ischaemia, head injury, viral infection
2. *Genetic*: mutations in 2 key gene families (a-synuclein, parkin)
3. *Toxin Exposure*: herbicides, pesticides ([paraquat](#), rotenone)
4. *Age* > 60 years
5. *Gender*: males > females
6. *Medicines*: dopamine reducing drugs - see next page



Smoking & Parkinson's Disease

Smoking, much like in Ulcerative Colitis (UC), is also a protective factor for Parkinson's Disease.

Medications & Parkinson's Disease

Medications that reduce dopamine level (such as risperidone or chlorpromazine) can either:

1. Worsens **pre-existing idiopathic PD** or
2. Induces PD-like symptoms in non-PD patients (high rate of recovery following medication cessation)

DRUG INDUCED PARKINSONISM	
Risk Level	Description
High Risk Drugs	<p>D₂ Receptor Antagonists</p> <ol style="list-style-type: none"> 1. <i>Antipsychotics</i>: typicals > atypical 2. <i>Antiepileptics</i>: sodium valproate 3. <i>Antiemetics</i>: metoclopramide, prochlorperazine → use domperidone or cyclizine or ondansetron <p>Dopamine Depleters</p> <ol style="list-style-type: none"> 1. <i>Tetrabenazine (Huntington's Disease)</i>: VMAT inhibitor that can cause PD symptoms in those with HD 2. <i>Methyldopa</i> (centrally acting anti-hypertensive)
Intermediate Risk Drugs	<p>Intermediate Risk Drugs</p> <ol style="list-style-type: none"> 1. <i>(Non-)CCBs</i>: verapamil, diltiazem — Ca²⁺ is required for NT (dopamine) release 2. <i>Mood Stabilisers</i>: lithium
Low Risk Drugs	<p>Low Risk Drugs</p> <ol style="list-style-type: none"> 1. <i>SSRIs</i>: fluoxetine

Signs & Symptoms

As we've established, symptoms of PD are the result of reduced DA levels. Most common at diagnosis:

1. Tremors or Shaking (72%)
2. Changes in/difficulty walking (42%)
3. Changes in handwriting; micrographia (40%)
4. Fatigue (37%)

FEATURES OF PARKINSON'S DISEASE			
Symptom		Description	
Precursor to PD	Micrographia	Writing that is little and slopes upwards	
Primary Motor Symptoms At diagnosis and/or later <i>Presence of these is often enough to make a diagnosis</i>	Resting Tremors (pill-rolling tremor)	<ul style="list-style-type: none"> • Slow, rhythmic tremor which occurs at rest • Affects hand, foot, or leg — can also occur in the jaw, chin, mouth, or tongue • Lessens during sleep or when the body part is actively in use. 	
	Bradykinesia	Slow movements	
	Ataxia Rigidity/Stiffness	<ul style="list-style-type: none"> Muscles remain contracted and can't relax. The rigidity makes it hard to move parts of the body. This can lead to changes in posture, walking (gait) or balance problems. • Impaired balance and coordination, sometimes leads to falls. • May also cause pain 	
	Reduced facial expression	Movement in the face is reduced, feeling like you are wearing a mask.	
Early Non-Motor Symptoms May precede diagnosis	Hyposmia	Reduced sense of smell	
	Fatigue	Most disabling symptoms and is affected by slow movement, muscle stiffness, depression, changes in movement or sleeping, and even medications.	
	Depression	PD affects production of dopamine, norepinephrine, and serotonin in the brain	
	Rapid Eye Movement Sleep Behaviour Disorder (RBD)	RBD is characterised by complex motor enactment of dreams and is a potential prodromal marker of PD. Of note, patients with PD observed during RBD episodes exhibit improved motor function, relative to baseline states during wake periods.	
	Constipation	PD can affect and slow down the digestive tract.	
	Pain	Types of pain in PD: musculoskeletal, neuropathic, dystonic, akathisia, central pain	
Late Symptoms 5-10 years after symptom onset	Treatment Resistant Axial Symptoms	Freezing	A feeling that the feet are 'glued' to the ground. May suddenly not be able to move forward for several seconds or minutes.
		Postural Instability	PD causes issues with balance, which causes unsteadiness when standing.
		Falls	PD increases the risk of falls
		Dysphagia	Swallowing impairment reduces QoL, complicates medication intake and leads to malnutrition and aspiration pneumonia — a major cause of death in PD.
	Psychiatric Disturbances	Anxiety	Common fears and worries that go along with PD may trigger anxiety. One is a fear of being unable to function independently.
		Psychosis	Parkinson's disease Psychosis (PDP) has strong links to disease progression, and may need antipsychotics (quetiapine, clozapine - do not cause worsening of motor function)
	Autonomic Disturbances	Postural hypotension	PD can affect blood pressure resulting in orthostatic hypotension.
		Sialorrhoea (drooling)	Excessive pooling or spillage of saliva out of the mouth.
		Urinary Urgency	Frequent and urgent need to urinate, even when the bladder is not full.
		Nocturia	There exists a relation between nocturia and poor sleep quality, falls, and institutionalisation.
		Sexual Dysfunction	Medication side effects, progressing disease and non-motor symptoms, such as anxiety or apathy, can decrease sex drive, erections and orgasm.
	Cognitive Impairment	Mild Cognitive Impairment	Feelings of distraction or disorganisation can accompany cognitive impairment, along with finding it difficult to plan and accomplish tasks. It may be harder to focus in situations that divide your attention, like a group conversation.
		Dementia	Parkinson's disease dementia (PDD) can occur as Parkinson's advances, after several years of motor symptoms.

Non-Pharmacological Treatment

Therapy

- Occupational Therapy e.g driving assessment
- Speech Therapy

Exercise should be encouraged

1. Strategy training e.g. instruction with reinforcement to use longer stride length
2. Management of musculoskeletal issues e.g. weakness and loss of range of movement
3. General promotion of physical activity with specific interventions for falls prevention

Pharmacological Treatment

[JAMA - Pharmacological Treatment of Parkinson Disease](#), [NZF Dopaminergic Drugs used in PD](#)

It is important to note that there is **no cure** for Parkinson's Disease. Pharmacological therapy simply centres around slowing down the progression of the disease and improving the patient's quality of life. There are 5 classes of medications that we can use:

Increase Dopamine Levels

1. Levodopa (L-DOPA) +/-
2. Peripheral Decarboxylase Inhibitors (PDIs): Carbidopa or Benserazide
3. D₂R Agonists: Pramipexole, Ropinirole, Apomorphine, Amantadine)
4. Selective MOA-B inhibitors: Selegiline

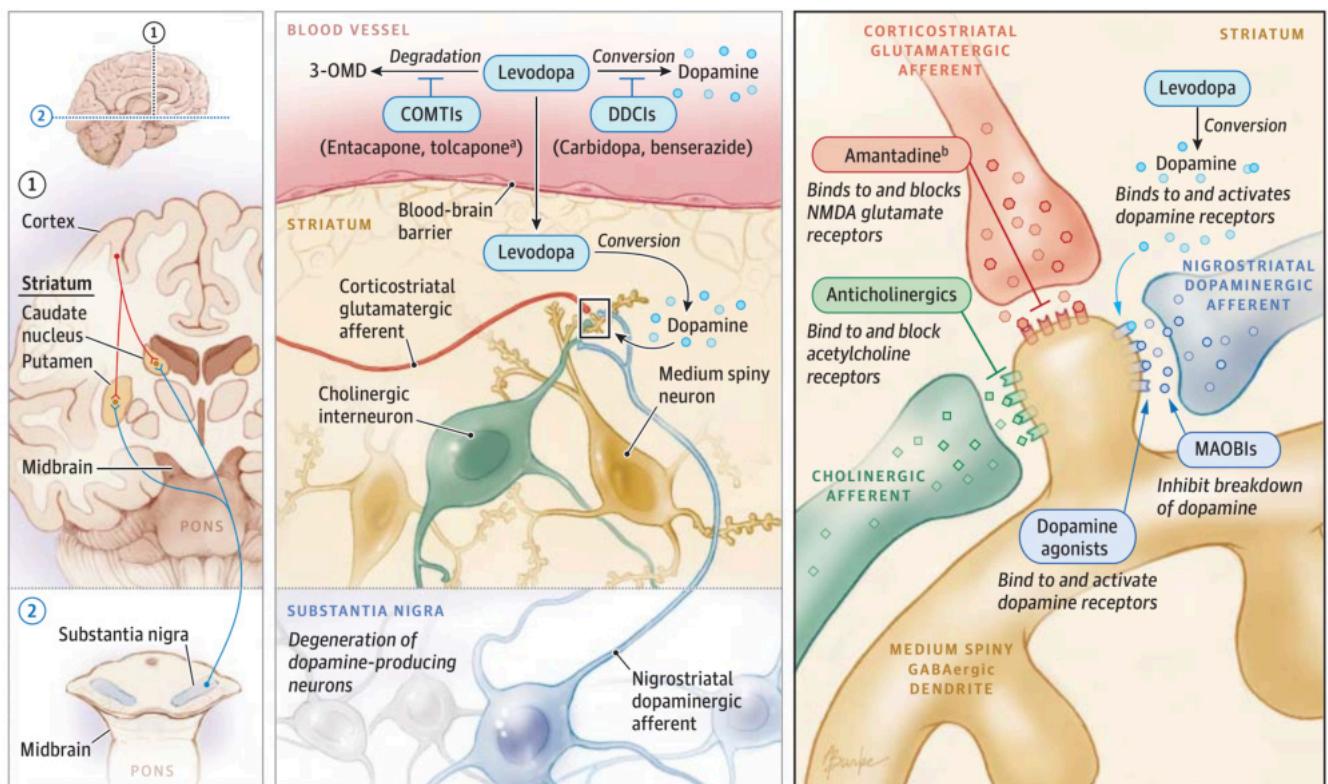
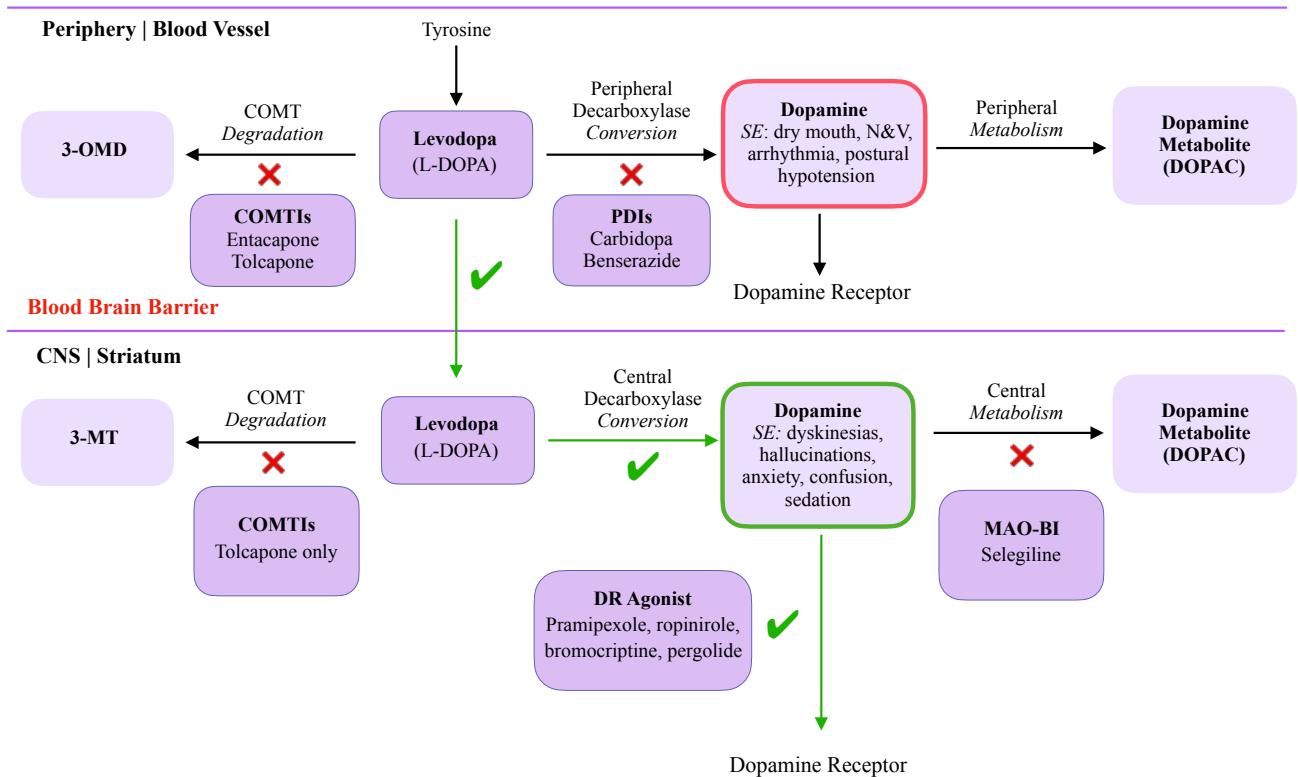
Decrease Acetyl Choline Levels

5. Antimuscarinics: Benztropine, Procyclidine

Other: Antiemetics

Nausea is a common peripheral side effect of giving dopamine as a treatment to Parkinson's. The indicated anti-emetics are ondansetron, cyclizine and domperidone - although domperidone is a dopamine agonist, it does not easily cross the BBB thus blocking the peripheral effects of dopamine effectively.

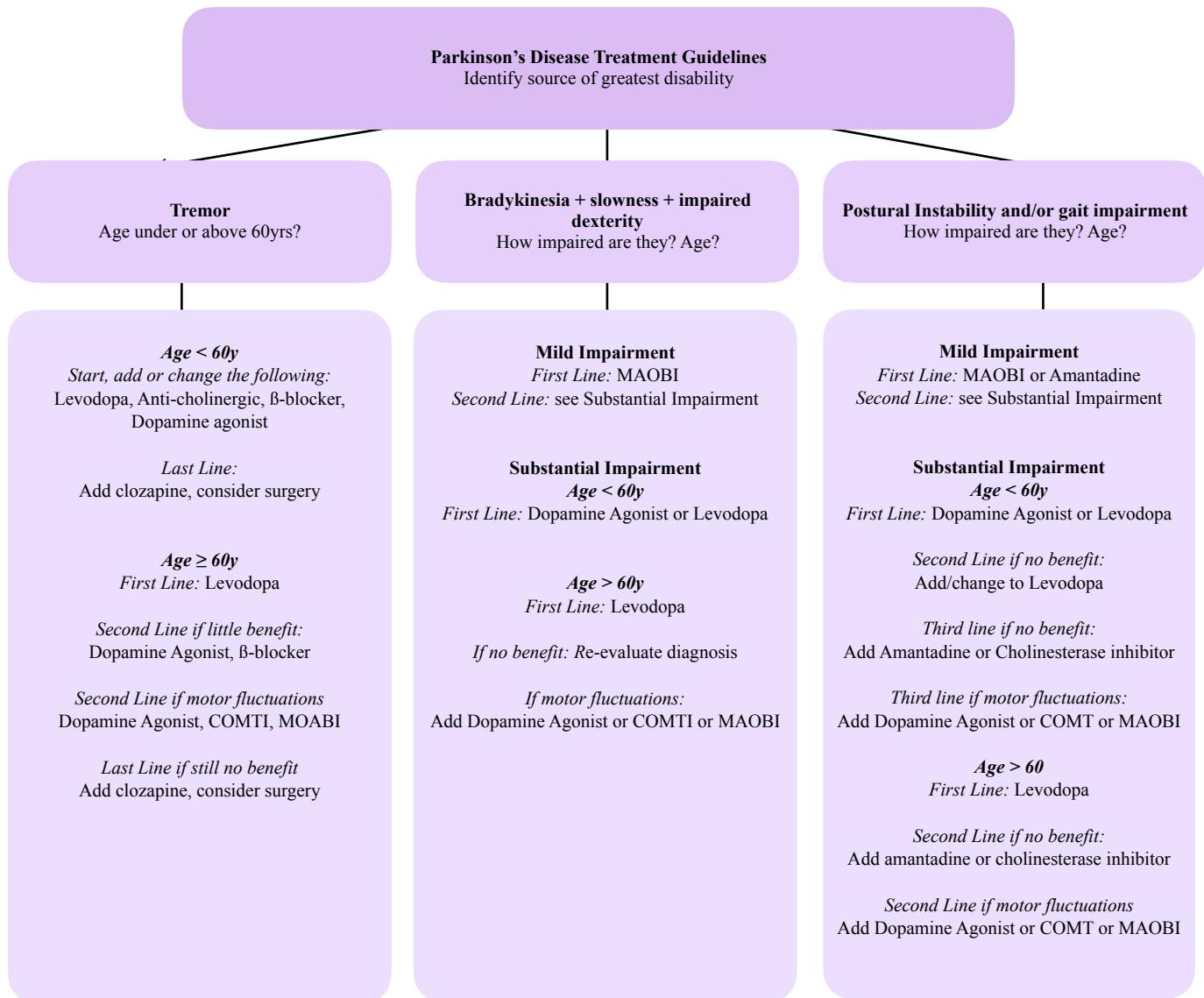
Mechanism of Action of Drugs Used in Parkinson's Disease



PHARMACOLOGICAL TREATMENT OF PARKINSON'S DISEASE				
	Class	Drug	Mechanism of Action	Side Effects
Dopamine	L-DOPA + PDI	[PRESCRIPTION] <i>Co-Careldopa</i> Levodopa + Carbidopa (Sinemet)	Dopamine Supply: Levodopa Dopamine cannot cross the BBB. As L-DOPA is the immediate precursor that can cross the BBB, it aims to replenish the dopamine deficiency that occurs in Parkinson's Disease. Its formulation allows it to be decarboxylated to dopamine by dopamine decarboxylase to allow it to reach concentrations in the BBB. However as dopamine decarboxylase also exists in the periphery: 1. Dopamine released in the periphery causes many peripheral side effects 2. Peripheral decarboxylation means only 1% of the oral dose reaches the brain	Peripheral formation of DA (if L-DOPA is given alone) <ul style="list-style-type: none">• Dry mouth• N&V (Anorexia)• Arrhythmias• Postural hypotension (dopamine is a vasodilator)
		[PRESCRIPTION] <i>Co-beneldopa</i> Levodopa + Benserazide (Madopar)	Peripheral Decarboxylase Inhibitors (PDIs): Carbidopa, Benserazide L-DOPA is thus administered with peripheral decarboxylase inhibitors such as (carbidopa, benserazide) which: 1. Decreases dose required and increase concentration in the brain 2. Decreases peripheral side effects	Excessive DA in the CNS if L-DOPA + PDI/COMTI <ul style="list-style-type: none">• Dyskinesias• Hallucinations• Anxiety, confusion, psychosis• Sedation, sudden onset of sleep
	L-DOPA + COMTI	[PRESCRIPTION] Levodopa <i>and</i> ; Entacapone (Comtan) or Tolcapone (Tasmar)	Catechol-O-methyltransferase (COMT) inhibitors prevent dopamine breakdown, and therefore double the half life of L-DOPA. <ul style="list-style-type: none">• Entacapone prevents peripheral breakdown• Tolcapone prevents peripheral & central breakdown	
	Dopamine Receptor Agonists	[PRESCRIPTION] <i>Pramipexole (D2R)</i> (Rampipex)	L-DOPA sparing therapy These imitate the actions of dopamine when levels are low and improve PD symptoms by fooling the brain into thinking dopamine is available. They can delay the need for L-DOPA and therefore prevent motor fluctuations. <ul style="list-style-type: none">• They may have fewer motor complications but are less effective and have more side effects• May be added to L-DOPA to decrease 'off' time	Peripheral and CNS <ul style="list-style-type: none">• N&V, hypotension, constipation, peripheral oedema• Dyskinesias• Sudden onset of sleep (caution in driving)• Psychosis (treat with quetiapine/clozapine)• Impulse control disorders (concern in young people)• Punding
		[PRESCRIPTION] <i>Ropirinole (D2R)</i> (Ropin)	To note: <ul style="list-style-type: none">• Amantadine: useful to treat L-DOPA induced dyskinesia in late disease• Apomorphine: helpful for unpredictable 'off' periods with L-DOPA in late disease.	<i>Apomorphine:</i> Causes severe N&V, pre-medicate for 2 days with domperidone
		[PRESCRIPTION] <i>Amantadine (DR)</i> (Symmetrel)		
		[PRESCRIPTION] <i>Apomorphine (D_{1/2}R)</i> (Mayne, Movapo)		
	Selective MAO-B Inhibitors	[PRESCRIPTION] <i>Selegiline</i> (Eldepril)	L-DOPA sparing therapy By inhibiting the monoamine oxidase type B enzyme involved in the metabolic pathway of dopamine, it causes a decrease in the breakdown of DA in the striatum. <ul style="list-style-type: none">• Decreased breakdown of DA in striatum (like COMTI)• Decreased dose requirement (1/3)• Prolonged duration of action• Potential first line for young onset patients w/ minor symptoms (e.g. small tremor)• Management of 'wearing off'	Nausea, dry mouth, dyspepsia, constipation, transient dizziness
Acetylcholine	Anti-muscarinics	[PRESCRIPTION] <i>Benztropine</i> <i>Procyclidine</i>	Anti-muscarinics restore balance by decreasing the relative central cholinergic excess created by the dopamine deficiency. While they have little effect on movement (bradykinesia), they are helpful in the management of tremors, rigidity, and sialorrhea.	Anticholinergic effects <i>Peripheral:</i> constipation, dry mouth, blurred vision, urinary retention <i>Central:</i> confusion, memory impairment, restlessness (elderly)

Treatment Guidelines

First line treatment depends on: main debilitating symptoms, severity, and patient's age.



Strong evidence supports:

- Levodopa and dopamine agonists for motor symptoms at all stages of Parkinson disease
- Dopamine agonists and drugs that block dopamine metabolism are effective for motor fluctuations
- Quetiapine, Clozapine is effective for hallucinations (careful of EPSE)
- Cholinesterase inhibitors may improve symptoms of dementia and antidepressants
- Pramipexole may improve depression

Note: If you drop blood pressure by too much, this may cause not enough dopamine to perfuse to the brain

A Note on L-DOPA Motor Fluctuations

Many people with Parkinson's disease (PD) experience motor fluctuations as a complication to L-DOPA use after 5-10 years due to the progression of their disease. These are a broad term which describe variations in the movement ability and/or symptoms of the patient throughout the day due to fluctuating dopamine levels.

They occur due to the gradual loss of dopamine producing cells over time, brain [DA] levels slowly become more dependent on [L-DOPA] levels in the blood, therefore the latest dose of medication. This is why these are seen after many years rather than in patients in an earlier stage of the disease.

Motor fluctuations are a combination of the following two things:

1. On Time: L-DOPA working, symptoms controlled
2. Off Time: L-DOPA not working, symptoms return

As the disease progresses (e.g. due to the excessive loss of dopamine neurons), motor fluctuations then become less related to the dose timing and the patient experiences more 'off time' than they did at the beginning. Thus later on, motor fluctuations begin to encompass the following five things:

- | | |
|--|----------------|
| 1. Delayed On | 4. Dyskinesias |
| 2. Wearing Off (end of dose deterioration) | 5. Dystonia |
| 3. Freezing | |

TYPES OF MOTOR FLUCTUATIONS			
Motor Fluctuation		Description	Recommendation
Late Disease	On Phenomenon	Patient experiences a good response to medication and thus periods of good symptom control.	
	Off Phenomenon	Also known as 'end of dose deterioration', these are periods where benefit from Parkinson disease medications wear off and symptoms reemerge.	Initially symptoms can be controlled with 2-3 daily doses of L-DOPA, but over time this becomes less efficient. We can: <ol style="list-style-type: none"> 1. Use sustained release preparations 2. Add a D2R (e.g. apomorphine) to decrease 'off time' 3. Add a COMT Inhibitor (e.g. entacapone, tolcapone) 4. Patients with YOPD are the most sensitive to L-DOPA motor fluctuations. Antimuscarinics are preferred in those situations. <p>Note: SR preps become useful then after time harmful with disease progression</p>
Even Later Disease	Delayed On	This is a delay in the medication taking an effect. More noticeable with controlled release formulations and high protein meals due to a delay in the absorption of the drug.	
	Wearing Off	The effect of L-DOPA fades quicker, patient might be tempted to take their next dose sooner.	
	Freezing	This is an uncontrolled temporary inability to move within seconds to several minute. It is common when 'off' but it is not the same as an off period and becomes more frequent as the disease progresses	
	Dystonias	Involuntary muscle spasms which can last for a short time or many hours. Occur either when the medicine is wearing off or when dopamine levels peak.	Apomorphine is useful for unpredictable 'off time' in late disease
	Dyskinesias	Sometimes, people experience involuntary movements e.g. twitches, jerking, twisting when medication levels are at their highest point.	Amantadine is useful for treating L-DOPA induced dyskinesias in the late disease.

Motor Neuron Disease (MND)

Description

Also known as Lou Gehrig's Disease, Charcot's Disease, Amyotrophic Lateral Sclerosis, Motor Neuron Disease (MND) is a progressive degenerative neurological condition that affects both lower and upper **motor efferent neurons**. Nerve cell death causes the body to no longer activate the effector muscles, causing them to weaken and waste away.

Classifications of Motor Neuron Disease				
Type	Notes	Presentation	Upper Affected	Lower Affected
MND (ALS)	Most common	<ul style="list-style-type: none">• Muscle weakness• Stiffness• Overactive reflexes• Rapidly changes emotions	Yes	Yes
Progressive bulbar palsy (PBP)		<ul style="list-style-type: none">• Speech and swallowing muscles affected• Limb muscles affected over time	Yes	Yes
Progressive Muscular Atrophy (PMA)	Slower progression, hardest to diagnose	<ul style="list-style-type: none">• Muscle wasting and weakness• Absent reflexes• Loss of weight and muscle twitching	No	Yes
Primary Lateral Sclerosis	Rare		Yes	No

Pathophysiology

Motor neurons form the efferent pathway.

- *Upper*: originate in brain, responsible for motor movement
- *Lower*: originate in spinal cord, prevent excessive muscle movement

There are three theories as to how MND develops:

1. *Excessive glutamate receptor activation* (causing excitotoxic cell death)
2. *TDP-43 dysfunction* (RNA splicing protein)
3. *Oxidative stress caused by free radicals*

Risk Factors

1. Most cases of MND are sporadic; with no clear identifiable cause
2. Some cases are hereditary
3. Other:
 - *Age* > 40 years old
 - *Sex*: Males > Females
 - *Viral infection*
 - *Other*: immune mediated damage, premature motor neuron ageing, loss of growth factors

Signs & Symptoms

Degeneration of upper and lower neurons typically cause issues with swallowing, chewing, tongue movement, facial expression, breathing, coughing, limb movement. Note that cognition is largely unaffected, however 15% of patients with MND develop frontotemporal dementia.

1. Lower Motor Neurons

- Atrophy: muscle wasting
- Flaccidity: muscle weakness
- Fasciculation: muscle twitching

2. Upper Motor Neurons

- Spasticity: muscles are constantly contracted (increased stiffness/tone) causing difficulty initiating or controlling muscle movement

Complications: Death due to respiratory failure (by respiratory muscles)

Diagnosis

- History
- Nerve conduction studies (identify motor neurons affected)
- Electromyography (muscle atrophy)

Pharmacological Treatment

There is currently no cure or treatment that significantly alters disease course. Treatment aims to control symptoms, retain function, and improve quality of life.

1. *Riluzole*: inhibits glutamate release and prevents its action on NMDA receptors
2. *Endavarone* (not available in NZ): free radical scavenger i.e. antioxidant

Multiple Sclerosis (MS)

Multiple Sclerosis BPAC Management

Description

An autoimmune disorder in which the immune system eats away at the protective covering of nerves (myelin sheath). The resulting nerve damage and affected conduction disrupts communication between the brain and the body.



Note

An important distinction to Motor Neuron Disease is that MS affects **sensory neurons** (MND affects motor neurons)

Pathophysiology

It is theorised that the autoimmune response is triggered by an agent with a similar antigenic structure to myelin basic protein (MBP), triggering self-tissue recognition therefore causing multiple areas of scarring in the myelin (in the brain, spinal cord, and optic nerve).

- These areas of scarring cause healing patches of inflammation, however this triggers further autoimmune attacks, further exacerbating the state of the sheath.
- With the progression of demyelination, the axon is eventually revealed. The immune system thus eventually begins to cause axonal damage. This is much less reversible than myelin damage.

Risk Factors

- **Caucasian**
- Female
- People in cooler climates (potential role of sunlight exposure)
- Near relatives of MS (Note: MS is **not** an inherited disease)
- Viral infection? Vitamin D levels? Sunlight exposure?

Signs & Symptoms

Depends on the locations of the affected axons e.g. brain, spinal cord, optic nerve

- Optic neuritis, weakness, spasticity, ataxia, bladder & bowel dysfunction

Non-Pharmacological Treatment

- Review diet if continual weight loss occurs or evidence of malnutrition
- Review Vitamin D intake

Pharmacological Treatment

Much like MND, no cure exists for MS. Treatment aims to reduce symptoms but is ineffective in primary/secondary progressive MS. While early treatment is associated with reduced disability, it is important to note that relapsing-remitting MS occurs in majority of people (85%) i.e. relapse after a period of improvement.

First Line

1. Ocrelizumab: targets CD20+ B cells involved in myelin damage
2. Fingolimod: reduces migration of lymphocytes to lesions
3. Teriflunomide: reduce proliferation of activated T and B cells
4. Dimethyl Fumarate: Anti-oxidative which upregulates glutathione expression (free radical scavenger)
5. Natalizumab: prevents lymphocyte from interacting with receptor

Second Line

1. Interferons: reduce immune response directed at myelin
2. Glatiramer acetate: structurally similar to aspects of MBP, acting as a decoy

Other (Available but unfunded)

1. Cladribine
2. Nabiximols
3. Fampridine
4. Steroids

Chronic Pain Management

1. TCAs e.g. amitriptyline
2. Anti-convulsants e.g. carbamazepine, gabapentin

Severe Spasticity Management

- Baclofen

NEURODEVELOPMENTAL DISORDERS

Introduction

We will look into ADHD and ASD.

Attention Deficit Hyperactivity Disorder (ADHD)

Description

Attention Deficit Hyperactivity Disorder (ADHD) is a chronic mental health condition that can cause attention difficulty, hyperactivity and impulsiveness. ADHD often begins in childhood and can persist into adulthood. It may contribute to low self-esteem, troubled relationships and difficulty at school or work.

Pathophysiology

The exact pathophysiology of ADHD is not clear and is hypothesised to be due to abnormalities in dopaminergic and noradrenergic pathways, resulting in low levels of these neurotransmitters.

Risk Factors

Family history, prematurity, low birth weight, intrauterine growth restriction, brain injury, genetic syndromes

Signs & Symptoms

- Trouble focusing on activities and becoming easily distracted
- Low attention span while playing or doing schoolwork
- Fidgeting, squirming, or otherwise having trouble sitting still
- Constantly needing movement or frequently running around
- Engaging in activities loudly or disruptively
- Excess talking and interrupting other people
- Substance use disorders
- Antisocial personality disorder

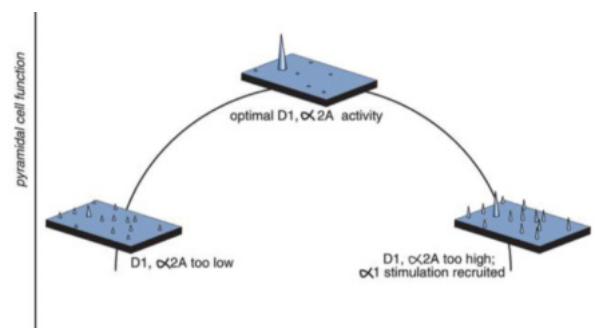
Diagnosis

- Adults: ICD-10, DSM-V

Non-Pharmacological Treatment

Behavioural Therapy

- Psychological, psychosocial, and behavioural interventions
- Talk therapy: Counselling



Pharmacological Treatment

Goldilocks Theory: Need the right dose (MODERATE) amount of methylphenidate for the individual

1. *1st Line*: Methylphenidate
2. *2nd line*: Dexamfetamine, lis-dexamfetamine (less abusable), atomoxetine

3. 3rd Line: Guanfacine (Not in NZ), Clonidine
4. Some evidence: Modafinil, TCAs, bupropion

	Medicine	Mechanism of Action	Side Effects
First Line	[CONTROLLED DRUG B2] <i>First Line</i> Methylphenidate <i>Ritalin - Normal (Tab), LA (Cap)</i> <i>Rubifen - Normal (Tab), SR (Cap)</i> <i>Concerta (Tab)</i> <i>Teva (ER)</i>	Increases dopamine and norepinephrine in prefrontal cortex <i>Immediate Release</i> Onset: 20-60 minutes Duration: 2-4 hours <i>Sustained Release</i> Onset: 30 min to 2 hours Duration: 12 hours	Nervousness, irritability, difficulty falling asleep or staying asleep, dizziness, N/V, loss of appetite, weight loss
Second Line	[CONTROLLED DRUG B1] Dexamfetamine Lis-Dexamfetamine (Prodrug)	Prevents re-uptake, increases release, and stimulates reverse-transport of dopamine in synaptic clefts in the striatum. <i>Dexamfetamine (IR)</i> Onset: 20-60 min Duration 3-6 hours <i>Lisdexamfetamine</i> Onset: 20-60min Duration 13+ hours	Nausea, diarrhoea, dry mouth, abdominal cramps, anorexia, weight loss, taste disturbance, cardiovascular issues
3rd Line	[PRESCRIPTION] Atomoxetine	Selective inhibition of presynaptic norepinephrine re-uptake in the prefrontal cortex. Onset: 4-6 weeks	Anorexia, dry mouth, nausea, vomiting, abdominal pain, constipation, dyspepsia, flatulence, cardiovascular issues
3rd Line	[PRESCRIPTION] Clonidine	Thought to stimulate postsynaptic α -2 adrenergic receptors and increases noradrenaline signalling to normal levels.	Constipation, dry mouth, N/V, postural hypotension

Monitoring

Methylphenidate, dexamfetamine, lis-dexamfetamine

- Discontinue treatment if no benefits seen in 1 month
- Height, weight, BP, HR
- Insomnia, appetite changes (decreased hunger leading to weight loss)
- Development of tics

Autism Spectrum Disorder (ASD) / Asperger's Syndrome

Description

Autism Spectrum Disorder (ASD) is a lifelong neurodevelopment condition characterised by a greater or lesser degree of impairment in language and communication skills, as well as repetitive or restrictive patterns of thought and behaviour. It is a spectrum and developmental condition, meaning that some people are affected more than others and it looks different at different ages. Autism is not an illness or disease and **cannot be ‘cured’.**

Some autistic people also have intellectual disabilities, Attention Deficit Hyperactivity Disorder (ADHD), and/or learning difficulties. Others have mental health issues, mostly commonly anxiety and depression.

Signs & Symptoms

People with ASD have a delay or difficulty in three areas of development, and can often be identified from birth to 3 years old:

1. *Language skills*: they have trouble understanding and using spoken language and non-verbal communication such as facial expressions and body language.
2. *Social behaviour*: they have trouble understanding social interactions, which affects their ability to play or interact with others.
3. *Cognitive and thinking skills*: they have trouble thinking and behaving flexibly, and may engage in restricted, obsessive or repetitive behaviours.

Risk Factors

- Genetics: gene mutations, genetic disorders, family history
- Sex: males > females
- Premature babies
- Parent’s age

Non-Pharmacological Treatment

Early intervention is beneficial to identify appropriate support and therapies

- Behavioural and communication therapies
- Educational therapies
- Family therapies

Pharmacological Treatment

No cure!

- Medications to control presenting symptoms e.g. hyperactivity, anxiety, depression

COGNITIVE IMPAIRMENTS

Ageing

Cognitive changes are an inevitable part of advancing age, with peak processing efficiency/abstraction ability being achieved in the 20's. Following this, there is a slow loss in mental processing speed and an associated reduction in our information processing ability.

Fluid Intelligence

Solving New Problems - age affects this form.

Staying mentally active can maintain this intelligence.

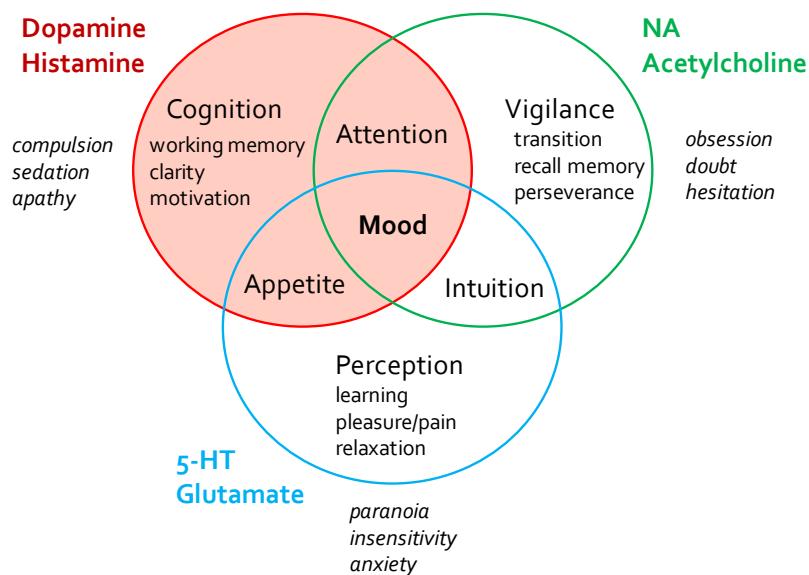
Crystalline Intelligence

Using Learned Knowledges and Experiences

Relies mostly on memory.

Pathophysiology

Cognition is a term that refers to the mental processes involved in gaining knowledge and understanding through thought, experience, and the senses — which declines with age. It is made of 5 broad categories; these are high-level functions of the brain which encompass perception, reasoning and problem solving, learning, memory, and language. A balanced brain chemistry (dopamine, histamine, NA, ACh, 5-HT, glutamate) is required for an adequate cognitive function.



Normal advancing age can result in a number of neurophysiological changes:

- Minor deposition of β -amyloid peptide and neurofibrillary tangles
- Loss of synapses and neuronal networks
- Mild cerebral atrophy

- Slight ventricular enlargement
- Mild hippocampal atrophy

A Note on Cognitive Enhancers (Nootropics)

Nootropic also known as ‘cognitive enhancers’ are drugs that some people use in an attempt to improve memory, increase mental alertness and concentration as well as boost energy levels and wakefulness.

There are many different nootropics. Some are pharmaceutical drugs that are designed to treat conditions such as sleepiness or narcolepsy, and to improve attention and focus in people with attention disorders. However, some healthy people use these drugs in an attempt to improve their cognitive performance.

Psychiatric disorders may develop with inappropriate use.

- Caffeine, nicotine, amphetamines
- Enzogenol, neuroberry (MAO inhibitor)
- Methylphenidate (rx: narcolepsy, ADHD, ADD)
- Modafinil (rx: narcolepsy)
- Piracetam (rx: myoclonus)

Subjective Cognitive Decline (SCD)

Description

Subjective Cognitive Decline (SCD) is the self-reported experience of worsening or more frequent confusion or memory loss, but there is no significant impairment shown on cognitive testing and no significant decline in daily functioning.



Do Not Dismiss!

At the end of the day, even if of no concern, SCD is a form of cognitive impairment and may be one of the earliest noticeable symptoms of Alzheimer's disease and related dementias.

Signs & Symptoms

A concern that something is different and a bit wrong, however;

- No significant impairment shown on cognitive testing
- No significant decline in daily functioning

Complications

Risk factor for preclinical Alzheimer's Disease

SCD may be associated with an increased risk of future cognitive decline and biomarker abnormalities

- Decline in memory rather than other domains of cognition
- Onset of SCD within the last five years
- Age of onset >60 years
- Have concerns (worries) associated with SCD
- Feeling of worse performance than others of the same age group

Mild Cognitive Impairment (MCI)

Description

Mild cognitive impairment (MCI) is a clinical stage on the **continuum** between the expected cognitive decline of normal ageing and the more serious decline of dementia. It is defined as the impairment in 1 or more cognitive domains above what is seen in normal ageing (such as memory, language or visual/spatial perception). These individuals are still able to maintain the ability to independently perform most activities of daily living.

COGNITIVE IMPAIRMENT COMPARISON		
SCD	MCI	Dementia
In SCD, there is no significant impairment shown on cognitive testing and no significant decline in daily functioning.	<ul style="list-style-type: none"> In MCI, there is a preservation of the person's independence in functional abilities and lack of significant impairment in occupational or social functioning Not all cases of MCI are precursors to dementia and not all are progressive (high reversal rates) 	<ul style="list-style-type: none"> A person with a dementia or major neurocognitive disorder (DSM-IV) will display more significant deficits on their cognitive tests (>2 SD from the mean) and their functioning will have significantly declined

Risk Factors

Risk Class	Risk Factor	
Patient	<ul style="list-style-type: none"> Age >65 Male 	
Environmental	<ul style="list-style-type: none"> Cognitively or physically sedentary Lower educational level 	
Genetics	<ul style="list-style-type: none"> Presence of apolipoprotein E allele Family history of cognitive impairment 	
Medical Conditions	<ul style="list-style-type: none"> Presence of vascular risk factors (hypertension, hyperlipidaemia, coronary artery disease, and stroke) Chronic health conditions e.g. HTN, HPLD, CAD, OA, COPD, depression, diabetes 	
Reversible Causes of MCI	<ul style="list-style-type: none"> Polypharmacy (regular use of ≥ 5 medicines) Hypotension/Orthostatic Hypertension Depression Hypothyroidism Vitamin B12 Deficiency Hypo / hyperglycaemia 	<ul style="list-style-type: none"> Dehydration Sensory loss (visual/hearing impairment) Obstructive sleep apnoea Normal pressure Hydrocephalus Atrial Fibrillation Infection

Signs & Symptoms

Patient presentation can depend on the:

- Subtype of MCI
- Other co-morbid factors
- Daily activities

Function	Description
Memory	Losing household items, forgetting conversations or upcoming plans, repeating questions, more reliant on notes and reminders, forgetful of parked car, disorientated while driving, leaving household appliances on, forgetting details of recent events
Language	Word finding difficulties
Visuospatial	Difficulty parking or judging distance of the car in front, difficulty staying in their lane
Attention	Easily distracted, difficulty multi-tasking, go off-track during a conversation
Executive function	More difficulty preparing meals, difficulty organising a dinner party or travel plans, making errors when paying bills, more confusion around the use of technology, fix-it jobs take longer

Complications

- While MCI is a risk factor for dementia, not all cases are precursors and not all are progressive
- Quite high reversal rates actually exist, with 30% to 50% of patients originally diagnosed with MCI reverting back to “normal cognition” or remaining stable at follow-up assessments.

Screening

The MACE: Mini Addenbrookes

All patients with suspected MCI should undergo a comprehensive history and physical examination, looking at cognitive functioning, functional status, medications, neurological and psychiatric symptoms and also undergo necessary blood tests and neuroimaging.

- If positive of MCI on screening: blood tests & neuro-imaging are required to rule out reversible causes
- Referral to a clinical psychologist/neuropsychologist for a full neuropsychological assessment

Diagnosis

DSM-V: Mild Neurocognitive Disorder

1. Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains (e.g. complex attention, executive function, learning and memory, language, perceptual motor, or social cognition)
2. The cognitive deficits **do not interfere** with capacity for independence in everyday activities (but greater effort, compensatory strategies, or accommodation may be required)
3. The cognitive deficits do not occur exclusively in the context of a delirium episode
4. The cognitive deficits are not better explained by another mental disorder

Factors Affecting the Validity of Cognitive Screening Tests

- Bad administering and scoring tests (the MACE has clear instructions and a “good practice checklist”)
 - The effect of third party observers
 - Time of day
 - Hearing/noise
 - Culture/Different Language versions
 - Education

Benefits of an Early Diagnosis

- There may be reversible causes that can be treated and prevent further progression
- Has important therapeutic implications should disease modifying therapies become available
- Helps patients and families understand the cause of their cognitive concerns
- Allows the patient and family to plan ahead and to be involved in shared decision making
- Encourages patients to make the most of their time
- Patient can be encouraged to appoint an Enduring Power of Attorney
- Helps to reduce risk e.g. driving, gun safety, work safety etc.
- They can be involved in research

Non-Pharmacological Treatment

1. Lifestyle modifications, address reversible causes of MCI

- Vascular risk factor control, medicines review, manage depression/anxiety, assess/treat sleep disorders
- Physical exercise, socialising, reduce alcohol consumption
- Cognitive training/workouts (Elevate, Brain HQ, Luminosity), engage in meaningful mental stimulation and intellectual activity, education around external memory aids e.g. diary, reminder notes
- Minimise risk: driving assessments, occupational therapy assessment around safety in the kitchen, managing finances, counselling patients regarding work roles that may involve risk

2. Coping: Forgetfulness Group-SDHB

3. Education & Support: Referral to Alzheimer's Society



Vitamins?
There is no evidence to suggest that vitamins and various supplements help (unless there is a clear vitamin deficiency)

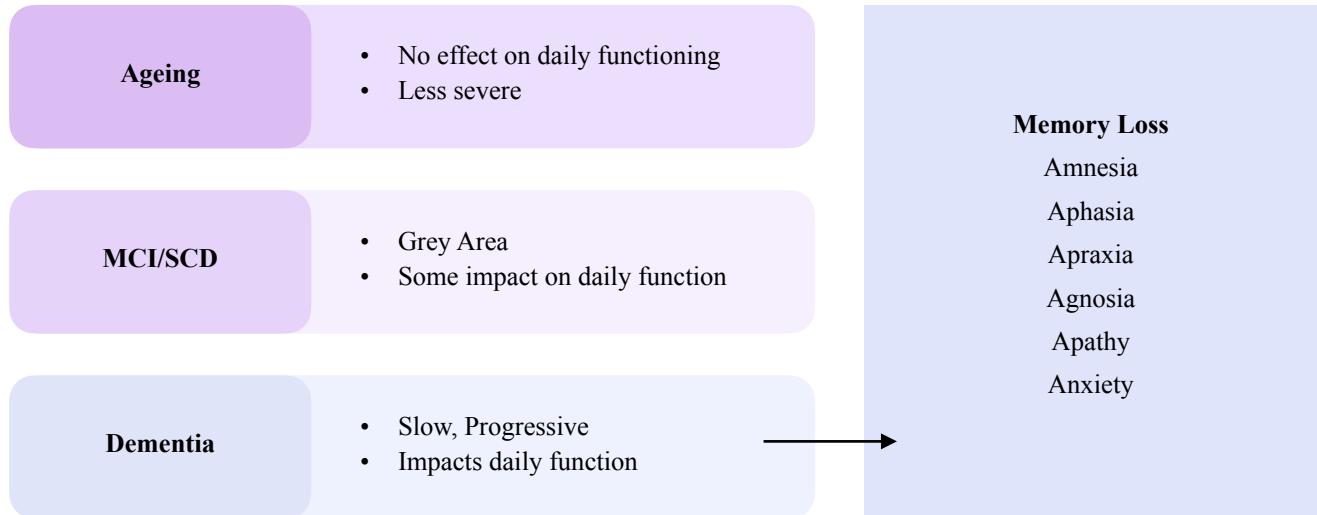
Pharmacological Treatment

Currently no pharmacological options approved.

Dementias

Description

Dementia is an umbrella term used to describe a range of symptoms associated with cognitive impairment — to such an extent that it interferes with a person's quality of life. Dementia is not a normal part of ageing but is common amongst older people (~85 years old).



Dementia encompasses the following medical conditions:

Dementia Type	Description	Associated Symptoms
Alzheimer's Disease (50-75%)	The most common dementia diagnosis among older adults. It is caused by changes in the brain, including abnormal buildups of proteins, known as amyloid plaques and tau tangles.	Short term memory loss, difficulty finding words, behavioural changes, impaired functioning, reduced insight
Vascular Dementia (20-40%)	Associated with cerebrovascular disease A form of dementia caused by conditions that damage blood vessels in the brain or interrupt the flow of blood and oxygen to the brain.	Memory loss typically less than AD. Defects in language, decision-making, information processing. Mood changes and apathy
Lewy Body Dementia (10-25%)	Associated with parkinsonian features A form of dementia caused by abnormal deposits of the protein alpha-synuclein, called Lewy bodies.	Visual hallucinations, postural hypotension, incontinence, sexual dysfunction, falls, sleep disturbances
Frontotemporal Dementia (10-15%)	Associated with MND A rare form of dementia that tends to occur in people younger than 60. It is associated with abnormal amounts or forms of the proteins tau and TDP-43.	Changes in personality and behaviour (disinhibition and impulsiveness)
Mixed Dementia	A combination of two or more types of dementia.	

Please note: medical conditions such as stress, anxiety, depression, and delirium can cause serious memory problems that resemble dementia, as can side effects of certain medicines.

Signs & Symptoms

Dementia memory loss comes with:

- *Aphasia* (impaired speech)
- *Apraxia* (impaired voluntary action)
- *Agnosia* (impaired sensation e.g. people, objects, location)
- *Behavioural changes* (apathy, anxiety)
- *Physical signs* (gait disturbances)

Differential Diagnosis

Dementia, Delirium and Depression all share common symptoms and often co-exist in older people.

Therefore before a definitive diagnosis of dementia can be made, other causes of cognitive impairment need to be ruled out (delirium, depression).

DIFFERENTIAL DIAGNOSIS OF THE 3 D'S			
Feature	Dementia	Depression	Delirium
Onset Timing	Chronic and generally insidious	Variable, may coincide with life events	Usually a sudden change from normal
Duration	Months to years	Weeks to months	Hours to days (less than 1 month)
Progression	Slow, progressive	Variable, uneven	Rapidly fluctuates, can be normal at times
Attention/ Concentration	Generally normal, or mildly affected	May be impaired	Severely affected, fluctuates, distractible
Psychomotor Activity	Normal	Normal or reduced	Agitated, lethargic or swings between both
Sleep	Sometimes disturbed	Unrefreshing, early morning wakening	May be drowsy or alert - often with day/night reversal
Speech	Normal in early stages	May be slowed	Often incoherent, muddled, slow or rapid
Orientation	Usually impaired (unless very mild)	Normal	Disorientated
Thought Content	Scarcity of thought, words hard to find	Often themes of hopelessness	Disorientated, incoherent

Alzheimer's Disease (AD)

Description

Alzheimer's disease (AD) is a neurodegenerative disease that affects brain cell connections and the cells themselves, resulting in the destruction of memory and many other important mental functions. AD usually starts slowly and progressively worsens.



Most Common Form of Dementia

It is the cause of 50-75% of cases of dementia and the most common cause of dementia in people above 65 years old.

Pathophysiology

The main hallmark changes are neurofibrillary tangles (tau protein) and amyloid deposition and formation of plaques (amyloid β protein). These cause the loss of tissue in the cortex (cognition) and a decrease in hippocampal volume (memory), which are areas of the brain heavily involved with memory processing.

1. Amyloid Proteins

Amyloid proteins in a normal brain are involved in neural/growth and repair. However in AD, an imbalance is thought to occur between their production and clearance, resulting in the formation of plaque deposits. This disrupts cell signal (brain function) and causes inflammation, which is hypothesised to facilitate the formation of neurofibrillary tangles.

2. Neurofibrillary Tangles

Tau proteins in a normal brain are involved in microtubule assembly and vesicle transport. However in AD, they aggregate to form neurofibrillary tangles. These cause decreased signalling and neuronal apoptosis.

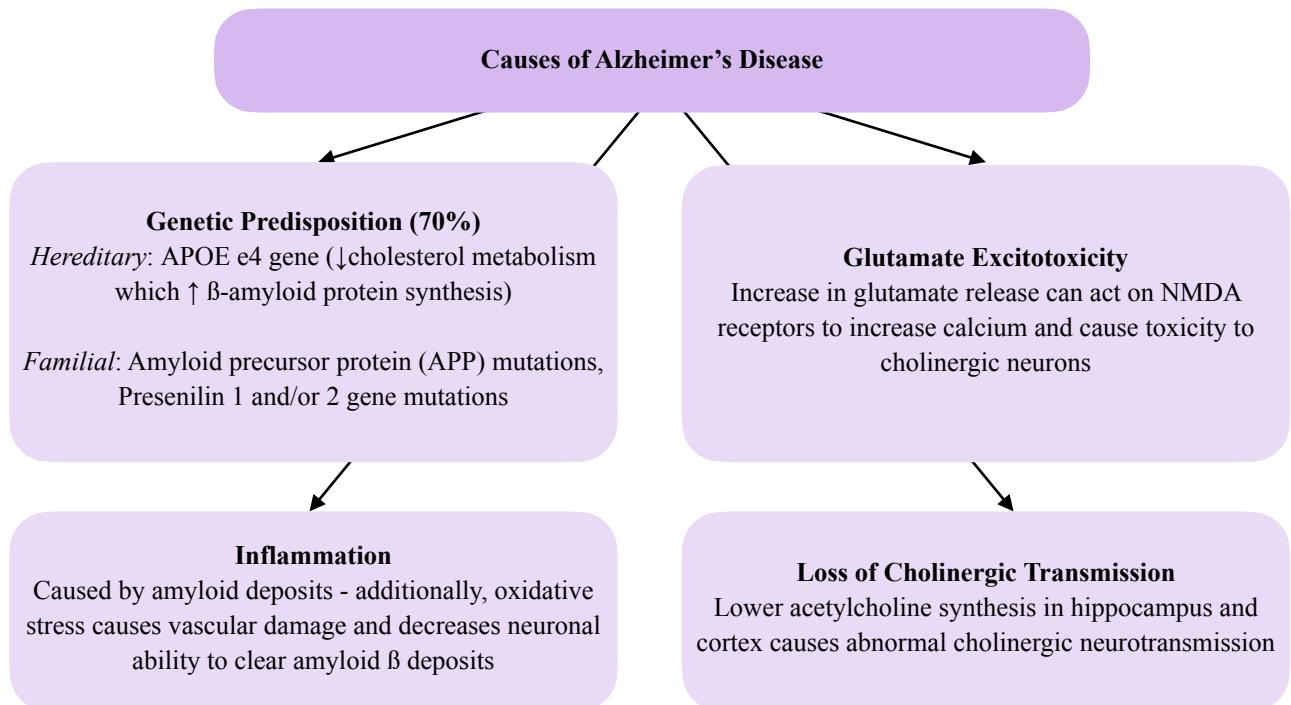
Signs & Symptoms

The most common early symptom is difficulty in remembering recent events. As the disease advances, symptoms can include problems with:

- Language
- Disorientation (including easily getting lost)
- Mood swings
- Loss of motivation
- Self-neglect, and
- Behavioural issues.

Risk Factors

The following promote neuronal damage:



Diagnosis

1. Cognitive assessment *Mini-ACE (MACE)*: ≤ 25 likely dementia, ≤ 21 almost certain of dementia
2. Neuroimaging: CT or MRI
3. Blood test
4. Review of other health conditions

Non-Pharmacological Treatment

1. Exercise and diet
2. Maintaining independence as well as social engagement and connection
3. Massage and relaxation

Pharmacological Treatment

BPAC Alzheimers Disease Treatment Guidelines

There is currently no treatment available that can prevent the onset of Alzheimer's disease or its progression. The aim of treatment is to regulate levels of neurotransmitters in brain regions which control learning and memory, and symptomatic/behavioural treatment where appropriate.

1. Cholinesterase Inhibitors
2. Glutamate Antagonists
3. Anti-Amyloid B Monoclonal Antibody
4. Antipsychotics

5. Benzodiazepines

Drug	Mechanism of Action	Side Effects
[PRESCRIPTION] <i>Cholinesterase Inhibitors</i> Donepezil (Donepezil Rex) Galantamine (Reminyl) Rivastigmine (Exelon, Rivastigmine)	Restores cholinergic transmission — mild/moderate symptoms Prevents the breakdown of ACh, therefore prolonging its effect at the synapse in order to improve/preserve cognition, behaviour and function by ~ 6 months • <i>Donepezil (first line)</i> : severe AD symptoms • <i>Rivastigmine</i> : good for hallucinations	<ul style="list-style-type: none"> Cholinergic syndrome Risk of heart block/sinus bradycardia with BBs, digoxin, amiodarone, CCBs (CHECK PULSE at each visit monthly, then 6 monthly. ECG prior to tx)
[PRESCRIPTION] <i>Glutamate Antagonists</i> Memantine (Ebixa)	Inhibits excitotoxicity — moderate/severe symptoms Non-competitive NMDA receptor antagonist	<i>Influenza like symptoms</i> Constipation, hypertension, dyspnoea, headache, dizziness, drowsiness
[PRESCRIPTION] <i>Anti-amyloid B monoclonal antibody</i> Adalimumab (Humira)	New potential therapy Proposed to reduce amyloid plaques; disease modifying	
[PRESCRIPTION] <i>Antipsychotics</i> Risperidone (Risperidone) Olanzapine (Zypine) Quetiapine (Quetapril)	Non-Cognitive symptoms of AD Good for delusions, hallucinations, anxiety, challenging behaviour (aggression, agitation) — only treat if severely distressed or immediate risk of harm. Avoid haloperidol	Antipsychotics can cause an increased risk of stroke and death in the elderly & have anticholinergic effects (can worsen cognition, cause delirium, increase risk of falls)
[PRESCRIPTION] <i>Benzodiazepines</i> Lorazepam (Ativan)	Avoid long acting benzo's (diazepam) as they can worsen cognitive symptoms	

Monitoring

Cognitive tests are used to monitor both the progression of Alzheimer's disease and the treatment effect of pharmacological agents.

1. Mini Mental State Examination (MMSE)
2. Addenbrooke's Cognitive Examination-Revised (ACE-R)

Vascular Dementia

[Vascular Dementia Mayo Clinic](#)

Description

Vascular dementia is a general term describing problems with reasoning, planning, judgment, memory and other thought processes caused by brain damage from impaired blood flow to your brain. You may develop vascular dementia after a stroke which blocks an artery in your brain, but not always.

Lewy Bodies Dementia (DLB)

[LB Dementia ALZ](#)

Description

Dementia with Lewy bodies (DLB) is a type of progressive dementia that leads to a decline in thinking, reasoning and independent function. Protein deposits, called Lewy bodies, develop in nerve cells in the brain regions involved in thinking, memory and movement (motor control). Its features may include spontaneous changes in attention and alertness, recurrent visual hallucinations, REM sleep behaviour disorder, and slow movement, tremors or rigidity.

Frontotemporal Dementia

[NHS FT Dementia](#)

Description

Frontotemporal dementia is an uncommon type of dementia that causes problems with behaviour and language. This type of dementia tends to start at a younger age than other dementias (45-65 yrs). Like other types of dementia, frontotemporal dementia tends to develop slowly and gradually worsens over several years.

BRAIN INJURIES

Introduction

Brain injuries, in NZ, are a leading cause of death and disability in young adults in children.

These type of injuries are often acquired:

- Contact sports e.g. rugby, netball
- Strokes, aneurysms, infections (meningitis)
- Hypoxia, brain tumours, neurotoxic disorders (drugs, alcohol, pesticides, gases, solvents)

Traumatic Brain Injury (TBI)

Description

Traumatic brain injury (TBI), is a form of acquired brain injury that occurs when a sudden trauma causes damage to the brain e.g. violently hit by an object or the object pierces the skull and enters brain tissue. It is a form of a primary brain injury. Note that a concussion is a type of TBI.

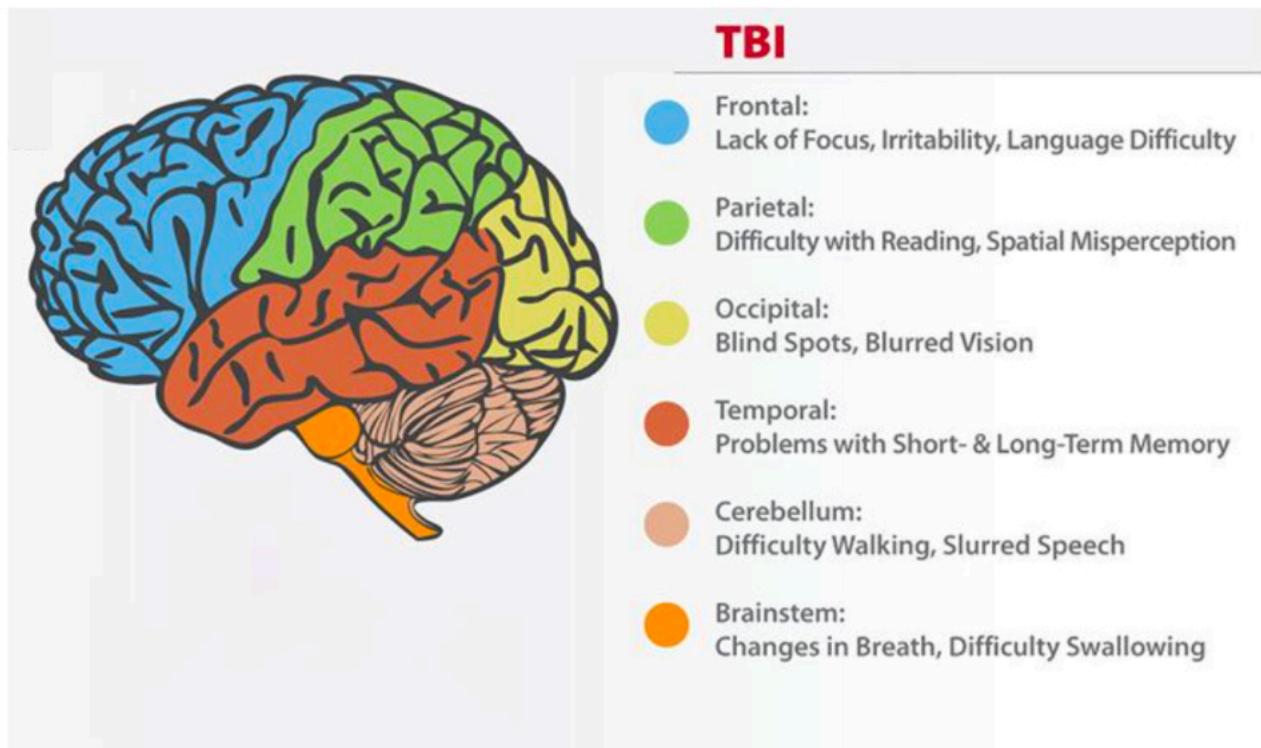
Pathophysiology

Damages of neuronal tissues associated with TBI fall into two categories:

	Description
Primary Injury (Biomechanics)	<p>Pathophysiology: Primary brain injuries describe the displacement of physical structures in the brain due to an initial insult which is characterised by an external transfer of kinetic energy. Examples: skull fracture, concussion, haemorrhage Location: Focal (limited) or diffuse</p>
Secondary Injury (Biology)	<p>Pathophysiology: Secondary brain injuries may occur following a primary injury. It describes the subsequent biological processes that occur following the initial insult. Kinetic energy is transferred through structures within the brain (nerves, neurons, axons, astrocytes) and can cause direct damage. A cascade of events (known as the secondary injury) is triggered.</p> <ol style="list-style-type: none">1. <i>Examples:</i> The events depend on the primary injury and often includes a reduced cerebral blood flow (CBF)<ol style="list-style-type: none">a) Cerebral ischaemia → swelling and hypoxiab) Excitotoxicity mediated cell death → neuroinflammation → synaptic re-organisation<ol style="list-style-type: none">i. Neuroinflammation: raised intra-cranial pressure (ICP), reduced cerebral perfusion pressure (CPP)ii. Synaptic re-organisation: leads to seizures

Signs & Symptoms

Depend on the extent of damage and location



Complications



TBI & Delirium

Almost a half of patients with mild to moderate head injuries may develop delirium in the first 4 days after a TBI.

Diagnosis

Glasgow Coma Scale: Assesses impairment of conscious level in response to defined stimuli — a lower score is worse

Goal of Treatment

Aim to decrease morbidity/mortality risk and thus optimise long term functional outcomes

1. Establish airway, maintain ventilation/circulation during resuscitation
2. Maintain balance between oxygen delivery and consumption
3. Prevent/minimise secondary neuronal injury
4. Prevent/treat associated medical complications

These are predictive of the outcome

- CPP = MAP - ICP (high CPP to avoid ischaemia)

- Maintain BP > 90mmHg (prevent hypotension)
- Avoid hypoxia as it can cause reduced CBF

Pharmacological Treatment

In order to protect the CPP, there are three ways we can reduce the raised ICP:

1. Osmotic Agents Infusion
2. Decompressive Craniotomy
3. Medically Induced Coma

We can also provide treatment/prophylaxis for complications:

1. Seizures: levetiracetam, phenytoin
2. Nosocomial (hospital) infections (LRTs, VAP, surgical site infections)
3. Deep Vein Thrombosis (DVT): heparins
4. Stress Ulcers: PPIs such as omeprazole (careful of risk of pneumonia)

Drug	Mechanism of Action	Side Effects
[PRESCRIPTION] Osmotic Agents Mannitol	Hyperosmolar therapy Plasma expanding effects which decreases blood viscosity, increases CBF • Osmotic concentration gradient across BBB: fluid moves out of brain and into intravascular compartment where it can be removed out of the body	• Hypotension (diuresis) • Renal dysfunction
[PRESCRIPTION] High Dose Barbiturates Pentobarbital	Medically Induced Coma Lack of oxygen supply to the brain can be resolved by decreasing the brain's metabolic demand for it i.e inducing a coma with barbiturates: • Decreased regional CMRO ₂ (cerebral metabolic rate of oxygen consumption) • Decreased lipid peroxidation • Alter blood vessel tone	• Hypotension due to peripheral vasodilation
[SURGICAL] Decompressive Craniectomy	Surgical Removal of Portion of Skull Removal of a portion of the skull to allow expansion of the swelling while avoiding secondary neuronal injury.	• Risk of vegetative state.

Delirium

Description

Delirium is an acute state of medical confusional in medically unwell patients. It is considered a psychiatric emergency in which there is a serious disturbance in mental abilities that causes confused thinking and reduced environmental awareness. The onset of delirium is usually rapid — within hours or a few days.

Pathophysiology

Not fully understood but triggers all cause a disrupted neurotransmission. Cholinergic deficiency is often known to induce delirium.

Signs & Symptoms

Inability to pay attention, disorientation, an inability to think clearly, and fluctuations in the level of alertness (consciousness).

Complications

Delirium is not always transient and reversible, and it can result in:

- Functional impairment e.g. long term cognitive impairment
- Increased costs
- Institutionalisation e.g. prolonged hospitalisation
- Death
- Psychological stress

Risk Factors

PINCH ME

- Pain e.g. severe/chronic/terminal illness, surgery, inflammation, acute stress response
- Infection e.g. fever, pneumonia, sepsis, UTI
- Nutrition e.g. malnutrition, changes in metabolic balance (low Na)
- Constipation
- Hydration
- Medications e.g. **anticholinergics**, alcohol, overdose, drug intoxication/withdrawal, chronic disease
- Environment e.g. unfamiliar place, poor senses (eyesight/hearing), memory issues

Other: older persons, **dementia**, brain injury, neuronal injury (hypoglycaemia, hypoxaemia), lack of sleep

Differential Diagnosis

As symptoms of delirium and dementia can be similar, input from a family member or caregiver may be important for a doctor to make an accurate diagnosis.

1. [4AT - Rapid Clinical Test for Delirium Detection](#)
2. [DSM-5 Criteria for Delirium](#)

Non-Pharmacological Treatment

Orienting patient with time and date can help with delirium!

Pharmacological Treatment

1. Address Underlying Cause

- TBI?

2. Decrease Anticholinergic Burden:

- Increasing ACh levels (i.e. cholinesterase inhibitor) can **reverse** anticholinergic caused delirium

3. Sedatives

- Benzodiazepines (e.g. lorazepam)
- Antipsychotics (e.g. haloperidol, risperidone, olanzapine, quetiapine)



Caution: Benzodiazepines & Antipsychotics

Benzodiazepines can worsen delirium but can allow investigations, treatment, prevent the patient from endangering themselves or others, relieve agitation/anxiety. Likewise, *antipsychotics* increase the risk of stroke in the elderly but can help manage behavioural changes/mental status.

HEADACHES

[Healthline Types of Headaches](#), [BPAC Headache Guidelines](#), [Health Navigator A Quick Headache Guide](#)

Overview & Summary of Headaches

Introduction to Headaches

A headache is a painful sensation in any part of the head, ranging from sharp to dull, that may occur with other symptoms. They are often associated with pain, disability, damaged quality of life and financial cost.

Primary Headache

Not a result of underlying disease

Cause is idiopathic/unknown

Secondary Headache

A result of underlying condition

e.g. injury, dehydration, caffeine or alcohol withdrawal, infection, medication, hunger

Headaches can be episodic or chronic:

1. *Episodic headaches* may occur every so often but no more than 15 days in one month. They can last anywhere from half an hour to several hours.
2. *Chronic headaches* are more consistent. They occur more than 15 days in a month. In these cases, a pain management plan is necessary.

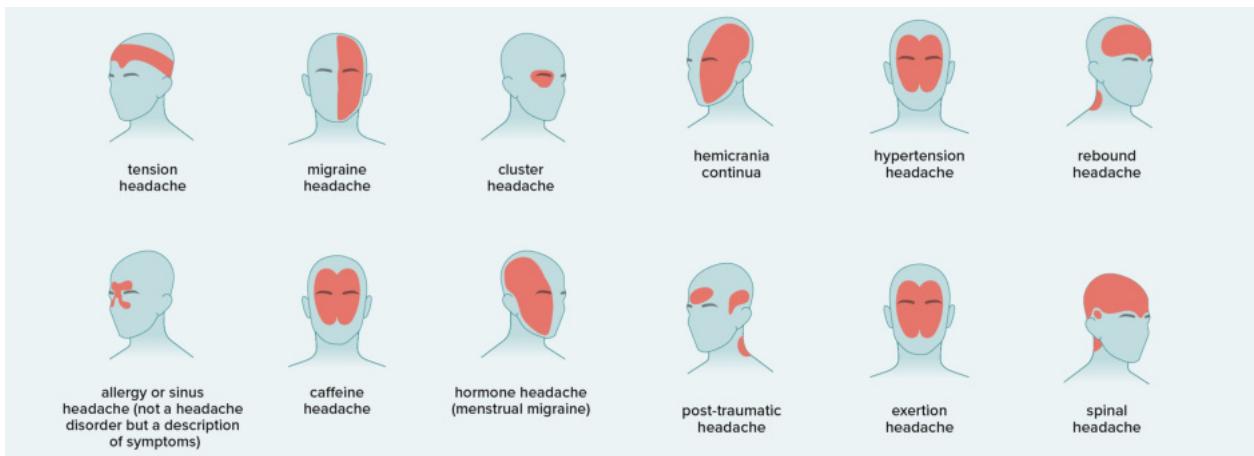
Pathophysiology

The brain tissue does not have nociceptors, therefore headache is typically the result of pain originating in surrounding structures e.g. blood vessels, meninges, muscle fibres, facial structures, cranial or spinal nerves.

Risk Factors

1. *Emotional*: stress/anxiety, tension, shock/excitement
2. *Physical*: tiredness, poor posture, low blood sugar, strenuous exercise
3. *Environmental*: bright lights, smoking, loud noises, changes in climates (humidity, cold)
4. *Medicines*: HRT, COC, nitrates

Types of Headaches



Comprehensive Comparison of All Headaches

Headache Type	Description	Signs & Symptoms	Causative Factors	Non-Pharmacological Treatment	Pharmacological Treatment
Tension Headaches	Tight band around head <ul style="list-style-type: none"> Most common type of headache Mild-moderate pain 	<ul style="list-style-type: none"> Dull, steady aching pain Sensation of tightness or pressure across the forehead or on the sides and back of the head Tenderness in the scalp, neck and shoulder muscles 	<ul style="list-style-type: none"> Stress Poor posture Excessive sleep Working too hard 	<ul style="list-style-type: none"> Avoid causative factors 	<ul style="list-style-type: none"> Paracetamol, NSAIDs <i>Prophylaxis:</i> naproxen
Sinus Headaches	Dull pain which worsens when leaning forward <ul style="list-style-type: none"> Often associated with other sinusitis symptoms (e.g. fever, stuffy nose, pressure, congestion) 	<ul style="list-style-type: none"> Dull, severe pain behind eyes, cheekbones, forehead, nose-bridge Pain worsens when leaning forward 	<ul style="list-style-type: none"> Allergies that cause sinus congestions Infection (sinusitis) 	<ul style="list-style-type: none"> Warm compress Saline spray/drops, vaporisers/steam Avoid triggers 	<ul style="list-style-type: none"> OTC decongestants Antihistamines Analgesics, NSAIDs
Medication Overuse (Rebound) Headache	Use of too much pain relief medication to treat headaches <ul style="list-style-type: none"> Improves with pain relief medication but then return as your medication wears off 	<ul style="list-style-type: none"> May feel like tension or migraine headache 	<ul style="list-style-type: none"> Paracetamol/NSAIDs should not be used > 15 days / month Triptans for migraines should not be used for more > 10 days / month 		<ul style="list-style-type: none"> Withdrawal: Improves within 2-4 weeks of withdrawal of the overused medicine but can worsen before improving
Cluster Headaches	Pain typically over one eye <ul style="list-style-type: none"> Rare and intense type of headache which can be extremely disabling Can occur several times a day for a period of time / at a particular time of the year / disappear for months/ years 	<ul style="list-style-type: none"> Sudden and intense pain around or behind one eye or on one side of the head Can last 15 min - 3 hours Warning Signs: nasal congestion on one side, droopy eyelids, watery eyes 	<ul style="list-style-type: none"> Alcohol Seasons: cold wind Head blown in face (hairdryers) Increased risk in males 	<ul style="list-style-type: none"> Oxygen Avoid alcohol Nerve stimulation, surgery 	<ul style="list-style-type: none"> Triptans <i>Prophylaxis:</i> verapamil

High Altitude Headaches	Elevated Altitudes <ul style="list-style-type: none">The exact cause is unknown and unsure if it is linked to lower oxygen levels (hypoxia) at higher altitudes	<ul style="list-style-type: none">May be associated with other symptoms of altitude sickness: N/V, dizziness, loss of appetite			
Menstrual Migraines / Hormonal Headaches	Associated with falling levels of estrogen <ul style="list-style-type: none">Usually start in the 2 days leading up to a period or the first 3 days of a period.		<ul style="list-style-type: none">MenstruationMenopausePregnancyOral contraceptives	<ul style="list-style-type: none">Small, frequent snacks to keep blood sugar level upRegular sleepAvoid stress	<ul style="list-style-type: none">Continuous regimen of COCsHRTEstrogen therapy
Chronic Migraines	Headaches occurring ≥15 days/month				
Migraines (with/without aura)	<p>Unilateral severe headache</p> <ul style="list-style-type: none">The exact cause of migraines is unknown, but they are thought to be the result of abnormal brain activity temporarily affecting nerve signals, chemicals and blood vessels in the brain.	<ul style="list-style-type: none">Throbbing headache typically affecting one side of the headOften accompanied by nausea, disturbed vision, high sensitivity to light and noise <p><i>Migraines with Aura (WARNING SIGN)</i></p> <ul style="list-style-type: none">Proceeding symptoms of sensory disturbances (flashing lights, zigzag lines, blind spots)Other: fatigue, sleep disturbances, restless, irritability, anxiety, dizziness, mood swings, food cravings, tingling or numbing feelings.	<p><i>Risk Factors:</i></p> <ul style="list-style-type: none">Family history, age (peak at 30s), females <p><i>Causative factors</i></p> <ul style="list-style-type: none">Sensory: Bright lights, strong smellsCertain foodsMedications: OC, HRT, GTNSleep disturbancesHormonal changesAlcohol, caffeineEmotional triggersPhysical triggers		<ul style="list-style-type: none">Paracetamol, NSAIDsTriptansOpioidsAntiemetics<i>Prophylaxis:</i> β-blocker, TCA, antiepileptic

Emergency Care (Red Flags)

Seek emergency care if:

- Abrupt, severe headache that comes on suddenly and gets worse within minutes (especially if > 50 yo)
- Headache with fever, stiff neck, mental confusion, seizures, double vision, weakness, numbness, changes in consciousness or speaking difficulties
- Headache after head injury

Differentially Diagnosing Headaches

Abbreviation	Example	Clinical significance
Initial Onset of Headache	Childhood or adulthood?	<p>If headaches begun in childhood</p> <ul style="list-style-type: none"> Primary headache is likely <p>If headaches begun after 50 years of age</p> <ul style="list-style-type: none"> Secondary cause is much more likely
Frequency & Timing	Establish onset, length of time, frequency and if there is there a pattern such as headache in the morning or evening or weekdays only	<ul style="list-style-type: none"> Headache associated with the menstrual cycle or at certain times (e.g. weekend, holiday) suggests <i>migraine</i>. Headaches that occur episodically at the same time of day or night suggest <i>cluster headache</i>. Headaches that occur on most days with the same pattern suggest <i>tension-type headache</i>.
Location of Pain	Unilateral, bilateral or occipital	<ul style="list-style-type: none"> Tension-type headaches are generally bilateral and migraine is generally unilateral. Occipital pain in TTHs suggests involvement of the neck. Cluster headache is nearly always unilateral in the frontal and ocular areas (can also be felt in the temporal areas). Migraine headache is unilateral in 70% of patients but can change from side to side and from attack to attack.
Severity of Pain	Assess severity, if the headache is getting worse and what effect on daily life is it having	<ul style="list-style-type: none"> Pain is a subjective personal experience and there are therefore no objective measures. Using a numeric pain intensity scale should allow you to assess the level of pain the person is experiencing: 0 represents no pain and 10 the worst pain possible. Dull and band-like suggests tension-type headache. Severe to intense ache or throbbing suggests haemorrhage or aneurysm. Piercing, boring, searing eye pain suggests cluster headache. Moderate to severe throbbing pain that often starts as dull ache suggests migraine.
Type of Onset	Acute or gradual	Tension-type headaches tend to develop over hours, often through the day. Sudden onset of acute pain, e.g. a “thunderclap” headache, is consistent with a subarachnoid haemorrhage.
Characterisation	Throbbing or pressing	Migraines are often throbbing or pulsating while tension-type headaches are pressing.
Triggers	Triggers such as drinking caffeine, stress, poor posture or taking prescribed medicines, and what provides relief, e.g. lying down, sleep, OTC medicines	<p>Identification of triggers allows for self-management. Relieving factors may guide treatment. It is important to note the frequency of administration and effectiveness of any OTC products to determine if medicine overuse headache is a possibility.</p> <ul style="list-style-type: none"> Pain that worsens on exertion, coughing and bending suggests a tumour. Food (in 10% of sufferers), menstruation and relaxation after stress are indicative of migraine. Lying down makes cluster headache worse.
Radiation	Pain may affect areas other than the head, such as the neck, eye or face	Tension-type headache may radiate from the neck. Trigeminal involvement may cause pain to radiate to the face.
Attack Duration	Hours? Days?	<ul style="list-style-type: none"> Typically, migraine attacks last between a few hours and 3 days. Tension-type headaches last between a few hours and several days, such as 1 week or longer. Cluster headache will only normally last 2–3 hours.
Associated symptoms	Visual disturbances, nausea, fear of light and/or noise, fever, cough, jaw claudication, neurological deficits	<ul style="list-style-type: none"> Migraine can be associated with visual disturbances. Fever and cough with a headache suggests an infection. Jaw claudication suggests giant cell arteritis. Neurological deficits may be consistent with an intracranial tumour.

Diagnosis

1. [MIDAS](#) scoring (Migraine disability assessment)
2. Headache diaries may be helpful (see [The Migraine Trust](#))

Overview of Pharmacological Options

Various pain relief options exist for the treatment of headaches as well as nausea caused from it:

1. *Paracetamol*
2. *NSAIDs*: ibuprofen, diclofenac, naproxen
3. *Opioids*: codeine, tramadol, DHC
4. *Triptans*: Rizatriptan, sumatriptan, zolmitriptan
5. *Antiemetics*: metoclopramide, prochlorperazine



Pharmacist-Medications

Accredited pharmacist can supply 2 tablets of sumagran for migraines and 10 buccal tablets of prochlorperazine for nausea associated with migraines.

Primary Headaches

Description

Primary Headaches have no known underlying cause - we will look into tension-types, clusters, migraines and ice pick headaches.

Tension-Type Headaches (TTH)

Description

A tension-type headache (TTH) is generally a mild to moderate pain that's often described as feeling like a tight band around the head.

Episodic Tension-Type Headaches

- Episodic tension-type headaches can last from 30 minutes to 7 days (a week.)
- Frequent episodic tension-type headaches occur less than 15 days a month for at least three months - these may become chronic.

Chronic Tension-Type Headaches

- These last hours and may be continuous.
- If your headaches occur 15 or more days a month for at least three months, they're considered chronic.

Causes

They are associated with **stress**, poor posture, excess sleep, working too hard, muscle tension.

Signs & Symptoms

The pain generally has a limited impact on the individual and presents as:

- Dull, steady aching
- Sensation of tightness or pressure across the forehead or on the sides and back of the head
- Tenderness in the scalp, neck and shoulder muscles

Differential Diagnosis

From Migraines

Differential diagnosis can be tricky as they can occur concurrently however TTH's are not associated with:

- Visual disturbances, N&V
- Aggravation from routine activities e.g. physical exercise
- Increased sensitivity to light or sound (uncommon photophobia or phono-phobia)
- Pain isn't 'throbbing'

Non-Pharmacological Treatment

Non-pharmacological interventions are first line in the management of TTHs and focus on managing musculoskeletal tension.

First Line: Physiotherapy (if MSK issue)

1. Massage, mobilisation, manipulation, postural awareness

Lifestyle management:

1. *Routine:* Sleep well, use appropriate pillows, adjust work station, use lumbar support, use heat packs
2. *Social:* Don't smoke, limit alcohol, caffeine, sugar
3. *Exercise* regularly, aim to increase movement
4. *Diet:* Eat regular, balanced meals

Other

1. Biofeedback Training
2. Cognitive Behavioural Therapy (CBT)
3. Other Relaxation Techniques e.g. deep breathing, yoga, meditation

Pharmacological Treatment

BPAC Headache Treatment Guidelines

OTC Analgesia (use should limited to **no more than 2 days** per week)

1. *NSAIDs:* Naproxen, Ibuprofen, Aspirin (**not in pregnancy**)
2. *Paracetamol* (less effective but considered if GIMIRI risk with NSAIDs)



Medication Rebound Headaches

We will look into these headaches a bit later on - note for now the limit on the use of analgesia to prevent it from happening. It is also the reason why medications such as Opioids & Triptans are not recommended for use in TTHs, simply because of the high risk for rebound headaches.

Prophylaxis of recurring tension-type headache

1. 3 week course of Naproxen 250-500mg bd is considered for the prophylaxis of recurrent TTH
2. Alternative: course of TCA e.g. amitriptyline or nortriptyline

Cluster Headaches

Description

Cluster headaches are characterised by severe burning and piercing pain that occurs around or behind one eye on one side of the face at a time. It is a rare type of headache that is extremely disabling - it is considered to be the most excruciating pains to exist.

These headaches occur in a series:

- A series of cluster headaches can be daily for months at a time and in the months between clusters, people are symptom-free.
- During a cluster, most people experience one to four headaches a day, usually around the same time each day. Thus after one headache resolves, another will soon follow.
- Each individual headache can last from 15 minutes to 3 hours.
- These headaches often occur around the same time each year - particularly in the spring and fall

Signs & Symptoms

Patient can experience:

- Swelling, redness, flushing, and sweating on the side that's affected by the headache
- Nasal congestion and eye tearing (or droopy eyelid) on the same side as the headache
- People may be found banging their head against the wall until pain stops.

Risk Factors

- Males (3x more likely)
- Season: spring/fall (cold wind)
- Alcohol
- Head blown in face e.g. hairdryers

Non Pharmacological Treatment

1. Oxygen 100% for 10-20 minutes
2. Complete avoidance of alcohol during cluster episodes
3. Invasive options: nerve stimulation, surgery

Pharmacological Treatment

BPAC Cluster Headache Treatment Guidelines

First Line Treatment:

1. Sumatriptan 6mg subcut



Note

Analgesics, ergotamine and triptans have no place in the treatment of cluster headaches.

Prophylactic/Chronic Headache Treatment

These should be commenced as soon as a new cluster starts.

1. Verapamil
2. Other: prednisone, lithium

Migraines +/- Aura

Description

A *migraine* is a headache that can cause severe throbbing pain or a pulsing sensation, usually on one side of the head. It's often accompanied by nausea, vomiting, and extreme sensitivity to light and sound.

For some people, a warning symptom, known as an *aura*, occurs before or with the headache. An aura can include visual disturbances, such as flashes of light or blind spots, or other disturbances, such as tingling on one side of the face or in an arm or leg and difficulty speaking.

Pathophysiology

Though migraine causes aren't fully understood, genetics and environmental factors appear to play a role. Changes in the brainstem and its interactions with the trigeminal nerve, a major pain pathway, might be involved. So might imbalances in brain chemicals — including serotonin, which helps regulate pain in your nervous system.

Signs & Symptoms

Migraines progress through four stages. Not everyone who has migraines goes through all stages.

1. *Prodrome* - constipation, mood changes, food cravings, neck stiffness, increased urination fluid retention, yawning
2. *Aura* - may occur before and during the migraine, person experiences various shapes, bright spots or light flashes, vision loss, pins/needles sensations, weakness/numbness in the face or one side of the body, difficulty speaking.
3. *Attack* - lasts from 4-72 hours, person experiences pain one or both sides of the head that throbs/pulses alongside symptoms listed in the description.
4. *Post-drome* - following the attack, person feels drained, confused and washed out for up to a day and sudden head movement may bring on the pain again.

Refer: < 18 and > 65, more than 6 attacks a month

Risk Factors

1. Family History
2. Age (peak at 30s)
3. Females (although improvement following menopause)

Triggers

There are a number of migraine triggers, including:

- *Hormonal changes in women*: see hormonal headaches
- *Drinks*: alcohol (wine), caffeine
- *Emotional*: **stress**/anxiety, tension, shock/excitement
- *Sensory stimuli*: bright or flashing lights, loud sounds. Strong smells, secondhand smoke

- *Sleep changes*
- *Physical factors:* intense exertion e.g. sexual activity, poor posture, tiredness, low blood sugar
- *Weather changes*
- *Medications:* OCs, HRT, GTN, Marivet, Donepezil
- *Foods:* additives (MSG), skipping meals, **aged cheeses, citrus fruit, chocolate** and salty and processed foods

Diagnosis

- See [MIDAS scoring](#) (migraine disability assessment)
- Headache Diaries (see [The Migraine Trust](#))

Non-Pharmacological Treatment

1. Eat small, frequent snacks to keep your blood sugar level up. Missing meals or going too long without food can trigger attacks. Have a small snack before going to bed, and always eat breakfast.
2. Have a regular sleep pattern, and avoid too much or too little sleep. Get a good night's sleep with 10 tips to beat insomnia
3. Avoid stress. If this proves difficult, find ways to deal with stress, such as taking regular exercise and using relaxation strategies.
4. CBT (if anxiety/stress)
5. Acupuncture
6. Oxygen
7. Transcranial Magnetic Stimulation (TMS)
8. Regular exercise

Pharmacological Treatment

Pain Relief

1. *First Line:* Simple Analgesics e.g. NSAIDs (ibuprofen, diclofenac or naproxen), Paracetamol
2. *Second Line or Combination:* Triptans e.g. Rizatriptan (first choice), Sumatriptan, Zolmitriptan
3. *Other:* Opioids e.g. codeine, tramadol, DHC

Migraine Prevention Prophylaxis:

These are for patients who suffer **at least 2 attacks** a month and suffer significant disability from it.

1. *First Line:* Beta-Blockers e.g. propanolol)
2. *Alternative First Line:* TCAs (amitriptyline)
3. *Second Line:* Anti-Epileptics (sodium valproate or topiramate)

Other

1. *For Nausea/Vomiting:* Antiemetics e.g. Metoclopramide, Domperidone or Prochlorperazine



Antiemetics in Headaches

Headaches can reduce *peristalsis* which can affect the absorption of medicines, the above anti-emetics are preferred as they promote gastric emptying.

Medications	Eligibility & Dosing	Counselling	Referral
[PHARMACIST ONLY] Sumatriptan Sumagram	Sumagram Questionnaire Migraine Disability Assessment Test • 2 tablets	<ul style="list-style-type: none">Take ONE 50mg tablet at the first sign of a migraine attackSwallow whole with a large glass of waterEffect seen within 30 minTake with or without foodIf symptoms improve but return, take a second tablet after 2 hours (i.e. wait at least 2 hours after the first tablet was taken)If not effective, do NOT take a second tabletDo not take more than 2 tablets for the same attackMay cause tingling, dizziness, drowsiness, flushing, fatigueTriptans are not recommended in breastfeeding	Refer if < 18 or > 65 If frequent migraines i.e. >6 per month (may need to consider preventative meds) Tightness in any part of the body
[PHARMACIST ONLY] Prochlorperazine	<ul style="list-style-type: none">POM for N/V associated with migraines• 10 buccal tablet pack	<ul style="list-style-type: none">Take 1-2 tablets twice dailyPlace tablet between upper lip and gum, and leave to dissolveBest not to eat or drink fluids while the tablet is dissolving as you may swallow portions or all of the tabletEffect seen in 60 min	

Migraine Prevention

1. β -blockers: propranolol
2. TCAs: amitriptyline, nortriptyline
3. Neuroleptics: Sodium valproate, gabapentin, topiramate
4. Verapamil
5. Oxygen
6. Other: Botulinum toxin type A, pizotifen, Erenumab
7. Non-Pharmacological: TMS, acupuncture

Ice Pick Headaches

Description

An ice pick headache is an uncommon headache disorder. It causes a sudden, sharp, stabbing head pain (or a quick series of pains).

Signs & Symptoms

This pain comes on unexpectedly and lasts a few seconds. People who have these headaches equate the pain to being stabbed in the head or eye with an ice pick.

Non Pharmacological Treatment

- External hand warming

Pharmacological Treatment

Healthline Headaches

Ice pick headaches can be difficult to treat because they last for such a short duration. Most ice pick headaches are over before you have a chance to do much about them - thus preventative measures are a common approach to reduce frequency/intensity of future headaches.

- Indomethacin
- Gabapentin
- Cyclooxygenase-2 (COX-2) inhibitors
- Melatonin

Secondary Headaches

Description

A secondary headache is the result of another condition (e.g. psychiatric, cardiovascular) causing traction on or inflammation of pain-sensitive structures.

Sinus (Allergy) Headaches

Description

A sinus headache is simply put, a migraine with nasal symptoms. While allergies themselves do not cause headaches, they can cause sinus congestion. The resulting pressure, pain and **infection** (sinusitis) from the blockage can lead to these type of headaches.

Risk Factors

- People with seasonal allergies (allergic rhinitis) are more likely to suffer from migraines
- Common cold

Signs & Symptoms

Pain depends on the sinus affected and is accompanied by congestion, thick mucus discharge, fever and a swollen/puffy face.

- A dull ache may be felt behind the eyes or cheekbones, forehead, nose-bridge.
- Patients may describe their face as ‘hurting’ particularly with sudden movement or leaning forward.

Diagnosis

Congestion is a tell-tale sign. Its absence likely indicates that it is not a sinus headache.

Non-Pharmacological Treatment

Relieve sinus pressure:

1. Warm compress to painful areas of the face
2. Saline nasal spray or drops
3. Vaporisers or inhale steam from a pan of boiled water
4. Reduce potential triggers e.g. alcohol, caffeine, specific foods such as chocolate, lack of sleep, stress

Pharmacological Treatment

1. OTC Decongestants
2. Anti-Histamines
3. Analgesics
4. Steroids (inflammation)

Hormonal (Menstrual) Headaches

[Hormonal Headaches NHS](#)

Description

Many women experience headaches associated with falling levels of estrogen and progesterone release.

Signs & Symptoms

Migraine is most likely to develop in either the **2 days** leading up to a period or the **first 3 days** during a period. The attacks are typically more severe than migraines at other times of the month and are more likely to come back the next day.

Risk Factors

Periods are not the only trigger of hormone headaches. Other causes include:

1. *Oral Contraceptives*

- Some women find their headaches improve while they're on the pill, but others report more frequent attacks, especially in the pill-free week.

2. *Menopause*

- Headaches usually worsen as you approach the menopause, partly because periods come more often and partly because the normal hormone cycle is disrupted

3. *Pregnancy*

- Headaches can get worse in the first few weeks of pregnancy, but they usually improve or stop completely during the last 6 months; they do not harm the baby

Non-Pharmacological Treatment

1. Eat small, frequent snacks to keep your blood sugar level up.
2. Have a regular sleep pattern
3. Avoid stress

Pharmacological Treatment

- Continuous regimen of OCs
- HRT
- Estrogen therapy (gel/patches)

Medication-Overuse (Rebound) Headaches

Description

Medication overuse headaches or rebound headaches are caused by regular, long-term use of medication to treat headaches, such as migraines.



What About Analgesia For Non-Headache Related Purposes?

If you have a headache disorder, any medication you take for pain relief can cause rebound headaches. Pain relievers taken regularly for another condition, such as arthritis, haven't been shown to cause medication overuse headaches in people who never had a headache disorder.

Pathophysiology

Pain receptors (nociceptors) instead of being switched off when analgesics are taken, are in fact switched on. The consequence is a cycle where patients take more and more painkillers that are stronger and stronger to control the pain.

Signs & Symptoms

Pain that is dull, nagging and:

- Occur every day or nearly every day, often waking you in the early morning
- Improves with pain relief medication but then return as your medication wears off
- *Other:* N&V, restlessness, difficulty concentrating, memory problems, irritability

Prevention

- Paracetamol/NSAIDs should not be used **> 15 days** per month for headaches
- Triptans for migraines should not be used for more **> 10 days** per month
- Caffeine containing medicines

Non-Pharmacological Treatment

Withdraw Overused Medicine

Improves within 2-4 weeks of withdrawal of the overused medicine but can worsen prior to improvement being seen. This is important to counsel on.

Post-Traumatic Headache

Description

Post-traumatic headaches are a secondary headache attributed to trauma or injury to the head that develops within seven days following trauma. They can develop after any type of head injury. They usually last up to 6 to 12 months after your injury occurs. They can become chronic.

Signs & Symptoms

Feel like migraines or tension headaches.

Hypertension Headaches

Revisit *Chapter 8 — Cardiovascular System* for more information on Hypertension.

Description

This kind of headache signals an emergency. It occurs when your blood pressure becomes dangerously high.

Signs & Symptoms

A hypertension headache will usually occur on both sides of your head and is typically worse with any activity. It often has a pulsating quality.

Pharmacological Treatment

1. Anti-hypertensives



CHAPTER 17

THE PSYCHIATRIC SYSTEM



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Chapter 17

The Psychiatric System

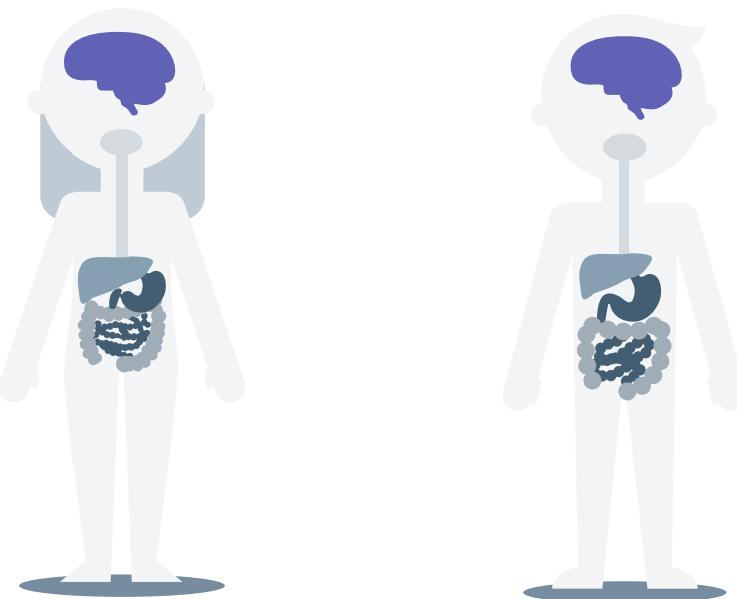
General Overview of Mental Health

Chapter Resources

Excellent resources for this chapter are [The Maudsley Prescribing Guidelines in Psychiatry](#) and the [DSM-V](#)

Introduction

Mental health is defined by the WHO as “a state of well-being in which every individual realises his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community”.



The Global Burden

However, the current situation is that mental illness holds a large global burden. Stigma is often the main barrier to receiving effective mental healthcare — pharmacists with a good knowledge of mental health can help resolve this and provide adequate care. So what better place to start than with Anxiety & Depression.

MOOD & AFFECTIVE DISORDERS

Understanding Mood Temperaments

Introduction

Mood disorders or affective disorders are common psychiatric disorders that have external display of mood or emotion felt internally - the two disorders that we will cover under this section are the Anxiety & Depressive Disorders. These kind of disorders are often co-morbid with pain, sleep or substance abuse disorders and are described by marked disruptions in emotions. These disruptions can be categorised in the following way:

Depression	Middle/Normal Temperament	Mania		
Depression	Dysthymia	Normal	Hypomania	Mania
Depression Most common mood disorder defined by the occurrence of at least one single major depressive episode.	Middle/Normal Temperament This is where most people exist	Mania Mood disorder marked by periods of great excitement or euphoria, delusions, and overactivity		
Depressive/Dysthymia Temperament Consistently below normal but not pathological. Includes stable characteristics such as being sad/apathetic. At risk for developing a mood disorder later on in life.		Hyperthermic/Hypomania Temperament Consistently above normal but not pathological, includes stable characteristics such as extroversion, optimism and impulsiveness. At risk for developing a mood disorder later on in life.		

Pathophysiology of Anxiety & Depression

No one knows just what causes affective disorders. They could be hereditary (depression/anxiety in first degree relatives) or due to environmental factors (e.g. life changes, poverty, unemployment, social isolation, substance abuse, chronic illness or other physical illnesses, stress, trauma, certain physical illnesses, certain medicines) - they could be biological, learnt, we just aren't sure.



The Role of Stress

Stress is linked to many mental health disorders that exist. However the degree of stress matters i.e. small amounts may be protective and build resilience while excessive amounts can induce sensitisation and therefore increase the risk for psychiatric illnesses.

Let's try to understand the structures and neurotransmitters involved:

The Amygdala

The amygdala, a pair of small, almond-shaped clusters of neurons near the base of the brain, is thought to be the starting point of anxiety reactions and also play a major role in depression. It originally functions to manage the storage of memories according to the strength of emotional reaction associated with them. When triggered, it sends distress signals to other parts of the brain — which eventually activates the fight or flight response.

The Monoamine Theory of Anxiety & Depression

In addition to the activation of the amygdala, it is theorised that anxiety/depression are the result of a functionally deficient monoaminergic transmission in the CNS; serotonin (5-HT), noradrenaline (NA), and dopamine (DA).

This is where things get confusing - the issue is that there is no convincing evidence that a monoamine deficiency is what causes anxiety/depression as no 'real' deficit exists. Instead it is possible that it is the **activity** of the monoamine transmitters that are deficient, causing **up-regulation** of the post-synaptic receptors and therefore leading to mood disorders.

This is supported by the fact that not only do we observe a variation in individual response, but we also a delayed therapeutic effect in depression - despite the medications for anxiety and depression being mostly the same, the anti-depressant effect of SSRIs is much, much shorter than their anxiolytic effect (~up to 12 weeks or more in anxiety vs up to 4-6 weeks in depression).

Differential Diagnosis - Anxiety vs Depression

Core symptoms of anxiety (excessive fear, worry) differ from depression (depressed mood/pleasure, loss of interest) but there is a considerable overlap. This can make diagnosis difficult. The symptom overlap that occurs between depressive disorders and anxiety disorders in addition to the fact they often occur concurrently means that diagnosis can often be very difficult. This is however out of our scope.

Summary of Anti-Depressants/Anxiolytics

Drug Profiles

Medications used to treat depression and anxiety are mostly the same - it is the treatment guidelines that differ. Regardless, they all mainly aim to address the monoamine deficiency theory. We will cover here the medications available, please find the guidelines under the respective disorders.

ANTIDEPRESSANT/ANXIOLYTICS PROFILES						
Drug	Receptor	Cardiac	Nausea	Sedation	Overdose	Sexual Dysfunction
Amitryptyline	5-HT, NA, DA	+++	++	+++	+++	++
Imipramine	5-HT, NA	++	++	+	+++	++
Clomipramine	5-HT, NA	++	++	++	+	+++
Fluoxetine	5-HT, DA	-	++	-/+	-	++
Paroxetine	5-HT, NA	-	++	-/+	-	+++
Citalopram	5-HT	-	+++	-	-	++
Venlafazine	5-HT, NA, DA	++	++	+	++	++
Mirtazapine	5-HT, NA, DA	-/+	-/+	++	-/+	-/+
Bupropion	NA, DA	-/+	+	-/+	++	-
Moclobemide	5-HT, NA, DA	-	+	-	-	+

Overview

PHARMACOLOGICAL TREATMENT OF ANXIETY & DEPRESSIVE DISORDERS			
Drug	Mechanism of Action	Side Effects	Counselling
Benzodiazepines Diazepam, Lorazepam	Helps with worsening of symptoms when SSRI initiated (however rarely needed) Provide rapid symptomatic relief from acute anxiety states. Only use to treat anxiety that is severe, disabling or subjecting the individual to extreme distress.	Potential for physical dependence/withdrawal symptoms	Short term use only (2-4 weeks)
SSRIs Citalopram, escitalopram, sertraline, fluoxetine, paroxetine fluvoxamine, duloxetine	Although different mechanisms of action, they aim to enhance serotonergic input to the amygdala in order to alleviate symptoms. SSRIs selectively inhibit the re-uptake of serotonin (5-hydroxytryptamine, 5-HT) in the pre-synapse, increasing the available serotonin in the brain. This leads to down regulation of receptors.	Insomnia/sedation, anxiety, depression , weight loss/gain, nausea, sexual dysfunction , hyponatraemia.	See next page
SNRIs Venlafaxine	5-HT and NA re-uptake inhibitor - which increases the effects of those neurotransmitters at the synapse.	Constipation, N/V, anorexia, weight changes, HTN, palpitation, vasodilation, dizziness, dry mouth, insomnia, nervousness, drowsiness, headache, anxiety, sensory disturbances, tremor, sexual dysfunction	
NaSSA Mirtazapine	Presynaptic alpha2-adrenoreceptor antagonist which increases central noradrenergic and serotonergic neurotransmission	Feeling sleepy, drowsy, dizzy, tired, increased appetite, weight gain, dry mouth, feeling faint, trouble sleeping, constipation	Take at night
TCAs Amitriptyline, Clomipramine, Imipramine (Tofranil)	Inhibit reuptake of NA and/or 5-HT which increases their concentration in the synaptic cleft and therefore changing neurotransmission in the brain Note: Imipramine is the less sedative TCA	Sedation, confusion, motor incoordination, blurred vision, dry mouth, urinary retention, constipation, ventricular dysrhythmias, QT prolongation, cardiotoxicity Contraindicated in CVD.	Potential toxicity in overdose.
MAOI Moclobemide	Reversibly inhibits monoamine oxidase A, thereby causing synaptic accumulation of monoamine neurotransmitters (noradrenaline, dopamine, and serotonin)	Sleep disturbances, dizziness, gastro-intestinal disorders, headache, restlessness, agitation	Take with food
α2-δ ligands Pregabalin, gabapentin	Binds to α 2- δ subunit of voltage sensitive Ca channels which reduces Ca influx and decreases release of excitatory neurotransmitters e.g. glutamate	Nausea, vomiting, gingivitis, diarrhoea, abdominal pain, dyspepsia, constipation, dry mouth and throat, flatulence, increased appetite, weight gain, anorexia, hypertension, vasodilation, oedema, dyspnoea	
NDRI Bupropion (Zyban) [Unapproved]	Dopamine and noradrenaline re-uptake inhibitor.	Also used in smoking cessation	Swallow whole, do not crush or chew
5-HT_{1A} agonist Buspirone	5-HT _{1A} agonist		Short term use only
Atypical Antipsychotics Quetiapine, Olanzapine, Risperidone	5-HT _{2A} /DA ₂ antagonists	Extrapyramidal symptoms, cardiovascular effects, metabolic effects, hyperprolactinaemia, priapism	

Things to Note about SSRIs/SNRIs

- Symptomatic improvement frequently **takes longer than treating depression**. This is because while the blockade or release of a particular neurotransmitter is immediate, the clinical effect takes weeks-months to develop due to secondary adaptive changes
- It gets worse before it gets better; SSRIs often worsen anxiety/depression in the first couple of weeks - monitor patients for suicidal ideation. A benzodiazepine for the first month can help with the initial exacerbation
- Despite the worsening, SSRIs are less toxic than TCAs, particularly in overdose
- People with anxiety disorders may be especially prone to adverse effects and thus high initial doses of SSRIs in particular may be poorly tolerated
- Time taken for post-synaptic receptor desensitisation correlates with tolerance to most ADRs



Navigating Insomnia and/or Sleepiness with Mood Disorder Medications

Medication used here have the potential to cause either **sedation** or **insomnia**. In the case of the first, advise patients to take their doses **at night**. And in the case of the second, advise to take in the **morning**.

Monitoring

It will usually take up to 12 weeks for full benefit, whether cognitive-behavioural therapy (CBT) or medication is used.

Anxiety Disorders

Description

RANZCP Anxiety Clinical Practice

Anxiety is a normal emotion that is experienced by everyone at some time. However, when symptoms become excessively distressing or disabling, or reduce quality of life, in the context of the absence of any clear external threat, they become part of what we call an anxiety disorder. These disorders, simply put, refer to a group of mental disorders characterised by feelings of **fear or worry**, the main types are:

ANXIETY DISORDERS		
	Classification	Description
Main Anxiety Disorders (DMS-V)	Main Anxiety Disorders <ol style="list-style-type: none"> 1. Generalised Anxiety Disorders (GAD) 2. Panic Attack Disorders (PAD) 3. Social Anxiety Disorders (SAD) 4. Phobias No longer considered anxiety disorders formally according to DSM-V: <ol style="list-style-type: none"> 1. Obsessive-Compulsive Disorder (OCD) 2. Post-Traumatic Stress Disorder (PTSD) 	Anxiety disorders can: <ul style="list-style-type: none"> • Occur on their own • Be co-morbid with other psychiatric disorders (particularly depression) • Be a consequence of physical illness such as thyrotoxicosis or • Be drug induced (e.g. by caffeine)

Signs & Symptoms

Symptoms can be psychological, physical or a mixture of both. However, as established earlier, there are 2 core symptoms involved in all anxiety disorders; **fear, worry**.

SUMMARY OF ANXIETY DISORDERS			
	GAD	SAD	Panic
Core Symptoms	<ol style="list-style-type: none"> 1. Anxiety & Fear: panic, phobias <ul style="list-style-type: none"> • Regulated by the amygdala-centered circuit (overactivation) • Associated with autonomic symptoms such as increased HR & BP • Long term activation increases risk of cardiovascular disease 2. Worry: anxious, misery, apprehensive, expectations, catastrophisation, obsessions <ul style="list-style-type: none"> • Regulated by the cortico-striatal-thalamic-cortical (CSTC) loop • Associated with the breathing circuit — person feels suffocated, RR increases • Long term activation can exacerbate asthma <p><i>Note: Core symptoms of GAD (anxiety, worry) differ from depression (depressed mood/pleasure), however overlapping symptoms make diagnosis difficult.</i></p>		
Disease-Specific Core Symptoms	<ul style="list-style-type: none"> • Generalised anxiety, worry, increased arousal, difficulty concentrating • Persistent symptoms most days for at least 6 months 	<ul style="list-style-type: none"> • Marked fear about one or more social situations and exposure to possible scrutiny by others. • Exposure usually provokes immediate situation-related panic attack and phobic avoidance of those situations 	<ul style="list-style-type: none"> • Begins as a series of unexpected (spontaneous) panic attacks; abrupt surge of intense fear or discomfort • Is followed by ≥ 1 month of persistent concern about further attacks or worry about consequences of another attack • This leads to significant maladaptive behavioural changes
Physical Symptoms	<ul style="list-style-type: none"> • Sleep problems, fatigue, irritability, muscle tension, restlessness 	<ul style="list-style-type: none"> • Blushing, diarrhoea, sweating, tachycardia, trembling, stumbling over words. 	<ul style="list-style-type: none"> • Abdominal distress, chest pain/discomfort, chills, dizziness, heat sensations, nausea, palpitations, SOB, sweating, trembling • Note: Many present to A&E thinking they have a heart attack but they are experiencing chest pain and a panic attack

Non-Pharmacological Treatment

The mainstay of treatment is CBT +/- medication.

1. CBT (first line)
2. Exercise
3. Applied Relaxation
4. *Preparations:* chamomile, gingko biloba, lavender oil, riluzole

Summary of Pharmacological Treatment

As established, pharmacological treatment aims to increase the monoamines in which a 'deficit' seems to exist. However please note, anxiety spectrum disorders tend to be chronic and treatment is often only partially successful. The usage of CBT and other forms of therapy is thus important.

First Line

1. *SSRIs:* citalopram, escitalopram, sertraline, fluoxetine (**if <18 yo**), paroxetine, fluvoxamine, duloxetine
2. *SNRIs:* venlafaxine

Second Line

3. *Benzodiazepines (short term):* diazepam, lorazepam, clonazepam, alprazolam
4. *NaSSAs:* mirtazapine, mianserin
5. *TCAs:* amitriptyline, nortriptyline, desipramine, clomipramine, imipramine
6. *MAOI:* moclobemide, phenelzine
7. *Anti-epileptics:* pregabalin, gabapentin
8. *NDRI (NA):* Bupropion — also used in smoking cessation



Did You Know?

Combination of mirtazapine and venlafaxine is known as "Californian Rocket Fuel"

Other

9. *5-HT_{2C} antagonist:* agomelatine
10. *Serotonin modulator:* vortioxetine (Brintellix)
11. *5-HT_{1A} agonist:* buspirone
12. *SDAs (5-HT_{2A}/DA₂ antagonists)* i.e. atypical antipsychotics: quetiapine, olanzapine, risperidone
13. *SARI (5-HT_{2A}):* atomoxetine
14. *β-blockers* for symptomatic relief: atenolol, propranolol

Key/prominent symptom(s)	Preferred antidepressant
Anxiety	SNRIs SSRIs
Cognitive difficulties (learning, memory, decision-making)	Duloxetine Vortioxetine
Sleep disturbances (e.g. Insomnia)	Agomelatine Mirtazapine
Fatigue	Bupropion
Pain	Duloxetine TCAs
Melancholia (psychomotor slowing, diurnal mood variation)	TCAs
Psychotic symptoms (mood congruent delusions)	Antipsychotic medication in addition to antidepressants
Atypical symptoms (Increased sleep, increased appetite)	MAOIs

How to Select an Anxiolytic

Selection criteria frequently based on side-effect profile, rather than efficacy.

SSRIs should initially be prescribed at **half the normal starting dose for the treatment of depression**.

The dose should then be titrated upwards into the normal antidepressant dosage range as tolerated.

Generalised Anxiety Disorders (GAD)

Description

Generalised Anxiety Disorder (GAD) is characterised by persistent and excessive worry about a number of different things. People with GAD may anticipate disaster and may be overly concerned about money, health, family, work, or other issues. Individuals with GAD find it difficult to control their worry.

Pharmacological Treatment

Crisis Management

- Benzodiazepines

First Line Treatment (in order of preference)

1. SSRIs: fluoxetine, sertraline
2. SNRIs
3. Pregabalin

Second Line Treatment (not in order of preference)

- Agomelatine
- β -Blockers (**tremors, tachycardia**)
- Buspirone
- Hydroxyzine
- Antipsychotics e.g. quetiapine
- TCAs: clomipramine, imipramine
- NaSSA: mirtazapine
- MAOI: phenelzine, vortioxetine

Monitoring

Will take 12 weeks to improve — assess efficacy of treatment at 12 weeks

Panic Attack Disorders (PAD)

Description

A panic attack is a sudden and intense surge of fear or anxiety in a short period of time. It usually peaks within ten minutes but symptoms can last much longer.

People having panic attacks sometimes believe they are having heart attacks, losing their minds, or even dying. They sometimes can't predict when or where an attack will occur, and between episodes many worry intensely and dread the next attack. When people have repeated panic attacks, or become very fearful of having further panic attacks, this is called Panic Disorder.

Signs & Symptoms

People who have full-blown, repeated panic attacks can become very disabled as they start to avoid places or situations where panic attacks have occurred. For example, if a panic attack happened while driving they may develop a fear of driving and avoid it completely.

Risk Factors

1. Substance Induced

- Intoxication (stimulants)
- Withdrawal (alcohol, benzos)
- Adverse effects of OTC meds e.g. decongestants, β -adrenergic inhalers, stimulants
- Caffeine-based products e.g. energy drinks, coffee

2. Medical Conditions

- Hypo/hyperthyroidism, hypo/hyperparathyroidism arrhythmias, ventricular dysfunction, seizure disorders, pulmonary emboli, electrolyte disturbances, menopause, Cushing's syndrome

Pharmacological Treatment

Crisis

- Benzodiazepines (**NICE does not recommend in Panic Disorders**)

First Line Treatment (in order of preference)

1. SSRIs (patients may experience an initial exacerbation of panic symptoms)
2. SNRIs: Venlafaxine

Second Line Treatment (not in order of preference)

- Mirtazapine
- MAOI: moclobemide, phenelzine
- TCAs: **clomipramine**, desipramine, imipramine, lofepramine

Social Anxiety Disorder (SAD)

Description

Social anxiety disorder is an intense, persistent fear social situations e.g. eating in public or public speaking. This fear can affect work, school, and other daily activities. It can even make it hard to make and keep friends.

Signs & Symptoms

Patients often experience a fear of humiliation or embarrassment and will exhibit avoidance behaviour e.g. never eating in restaurants and anxious participation e.g. feeling sick on entering a restaurant. Majority eventually develop a concurrent mood, anxiety or substance use disorder.

Physical Symptoms

- Diarrhoea
- Sweating
- Tachycardia
- Trembling
- Stumbling over words



Differential Diagnosis

Blushing is the principal physical indicator and distinguishes SAD from other anxiety disorders.

Pharmacological Treatment

First Line Treatment (in order of preference)

1. SSRIs: any
2. SNRIs: venlafaxine

Second Line Treatment (no order of preference)

- Atypical antipsychotics: olanzapine
- β -Blockers (**autonomic symptoms**): atenolol
- Benzodiazepines (**PRN**): clonazepam
- Anti epileptics: gabapentin, pregabalin, levetiracetam
- MAOI: phenelzine, moclobemide

Phobias

Description

A phobia is a type of anxiety disorder that causes an individual to experience extreme, irrational fear about a situation, living creature, place, or object. When a person has a phobia, they will often shape their lives to avoid what they consider to be dangerous.

TYPES OF PHOBIAS	
Medical Term	Description
Alektorophobia	fear of chickens
Astraphobia	fear of extremely loud natural noises, eg thunder and lightning
Auto/Monophobia	fear of being alone or lonely
Cynophobia	fear of dogs
Gametophobia	fear of being married
Iatrophobia	fear of doctors
Pharmacophobia	fear of medication
Scopophobia	fear of being stared at
Trypanophobia	fear of medical procedures involving injections or hypodermic needles.

Obsessive-Compulsive Disorders (OCD)

Description

Obsessive-compulsive disorder (OCD) is a mental illness that causes repeated unwanted thoughts or sensations (obsessions) or the urge to do something over and over again (compulsions). Some people can have both obsessions and compulsions.

Signs & Symptoms

1. *Obsessional thinking* e.g. constantly thinking the door has been left unlocked
2. *Compulsive behaviour* e.g. constantly going back to check

Pharmacological Treatment

First Line Treatment (in order of preference)

1. SSRIs: any
2. TCAs: clomipramine

*Second Line Treatment (**add to SSRI**)*

- Antipsychotics: aripiprazole, risperidone, haloperidol
- Anti-epileptics: lamotrigine, topiramate
- Other: acetyl-cysteine

Post-Traumatic Stress Disorders (PTSD)

Description

Post-traumatic stress disorder (PTSD) is a mental health condition that's triggered by a terrifying event — either experiencing it or witnessing it. The condition may last months or years, with triggers that can bring back memories of the trauma accompanied by intense emotional and physical reactions.

Signs & Symptoms

Symptoms may include nightmares or flashbacks, avoidance of situations that bring back the trauma, heightened reactivity to stimuli, anxiety or depressed mood.

Pharmacological Treatment

First Line Treatment (in order of preference)

1. SSRIs: paroxetine, sertraline, fluoxetine
2. SNRIs: venlafaxine

Second Line Treatment (not in order of preference)

- Antipsychotics: olanzapine, risperidone, quetiapine,
- MAOI: phenelzine
- NaSSA: mirtazapine
- Alpha blockers (**nightmares, sleep disturbances**): prazosin
- TCAs: Amitriptyline, imipramine

Depressive Disorders

Introduction

Depressive disorders are an affective mental health disorder characterised by persistently depressed mood or loss of interest in activities, causing significant impairment in daily life.



St John's Wort - Is Your Patient Using It?

St John's wort is a herb that is sold as a natural health product in NZ for the treatment of depression mainly. Its use, however, has long been of rising concern because of the many serious interactions it shares with other drugs - so much so many countries like France have chosen to ban it. Always screen your patients for potential OTCs/Herbals/Vitamins they may be on - particularly this one.

Signs & Symptoms

The core symptoms of depression are depressed mood/pleasure and loss of interest

1. *Emotional*: misery, apathy, pessimism, low self-esteem, guilt, loss of motivation, indecision, inadequacy
2. *Biological*: loss of libido, slowed thought, sleep disturbance, appetite changes

Goal of Therapy

Mainly prevention of suicide outcomes

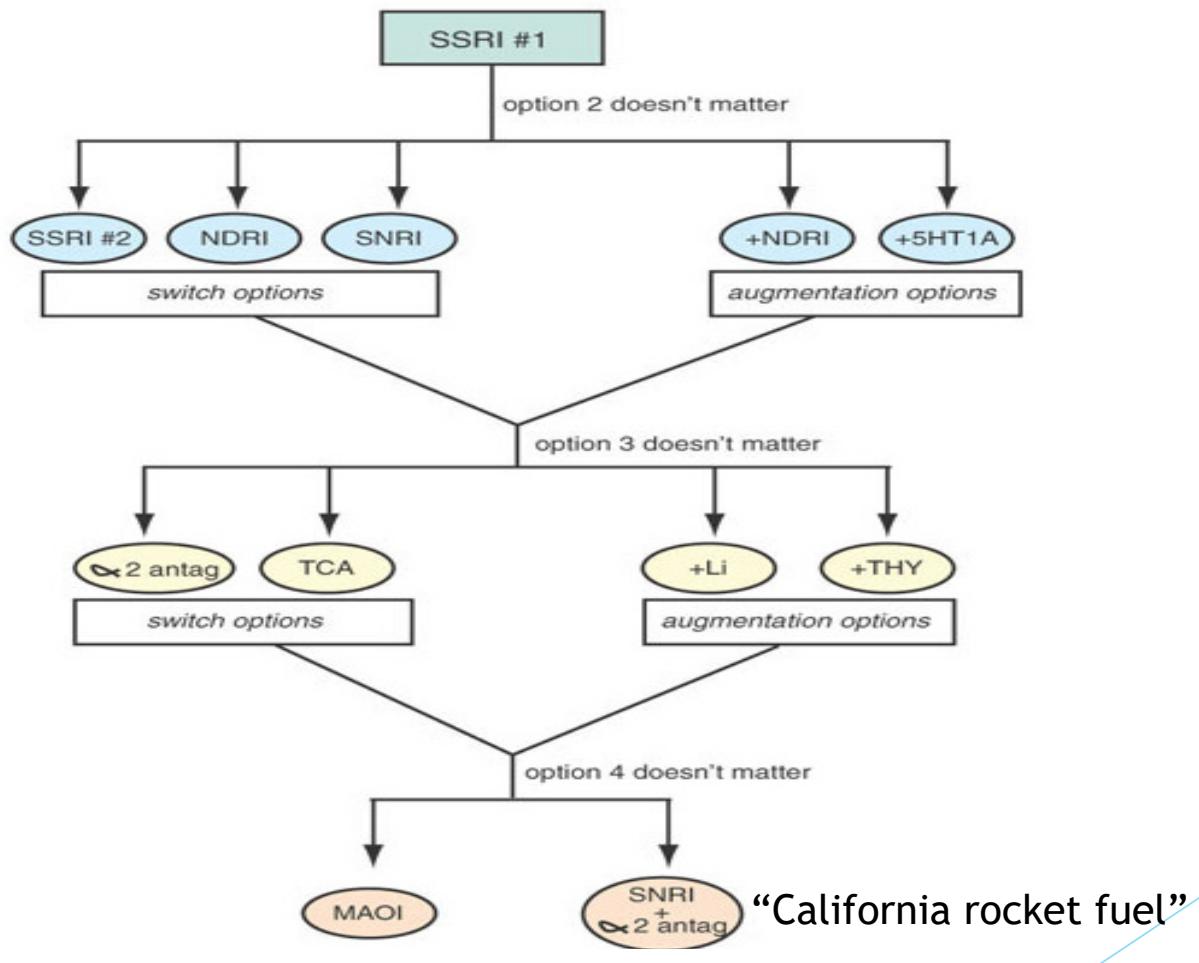
Non-Pharmacological Treatment

1. CBT (or IPPT or DBT)
2. Social support helps prevent/buffer suicide/depression the most
3. Exercise
4. Good diet
5. Hanging out with people and continuing on doing things you like
6. Managing stress
7. Minimising alcohol or other substances intake
8. Get enough sleep

Pharmacological Treatment

Treatment options are the same as for anxiety, however guidelines differ slightly. Alongside CBT, antidepressants here are used to reduce the risk of suicide — they are a prophylaxis for further depressive episodes and are recommended only in moderate-severe depression/dysthymia.

Antidepressant Prescribing Guidelines



Switching Antidepressants

BPAC Guidelines to Switching Antidepressants

Antidepressant Switching Table								
Changing to Changing from	short-acting SSRI [a]	fluoxetine	TCA [b]	venlafaxine	mirtazapine (or mianserin)	bupropion	moclobemide	Irreversible nonselective MAOIs [c]
short-acting SSRIs [a]	Stop 1 st SSRI [d] then start 2 nd SSRI the following day	Stop 1 st SSRI [d] then start fluoxetine	Cross taper cautiously with very low dose TCA [f] [g]	Stop SSRI [d] then start venlafaxine the next day at 37.5mg/day and increase very slowly	Withdraw before starting mirtazapine cautiously	Withdraw then start bupropion	Withdraw, wait 1 week, start moclobemide	Withdraw and wait 1 week
fluoxetine [h]	Stop fluoxetine, wait 4-7 days, start SSRI at low dose [e]	—	Stop fluoxetine, wait 4-7 days, start TCA at very low dose and increase very slowly [f][g]	Stop fluoxetine, wait 4-7 days, start venlafaxine at 37.5mg/day and increase very slowly	Stop fluoxetine, wait 4-7 days, start mirtazapine cautiously	Stop fluoxetine, wait 5 weeks, start bupropion	Stop fluoxetine, wait 5 weeks, start moclobemide	Stop fluoxetine and wait 5 weeks [h]
TCA [b]	Halve dose, add SSRI, then slowly withdraw TCA [g]	Halve dose, add fluoxetine, then slowly withdraw TCA [g]	Cross taper cautiously	Cross taper cautiously starting with venlafaxine 37.5mg/day [g]	Withdraw, start mirtazapine cautiously	Cross taper cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
venlafaxine	Cross taper cautiously starting with low dose SSRI [e]	Cross taper cautiously starting with fluoxetine 20mg on alternate days	Cross taper cautiously with very low dose TCA [g]	—	Withdraw, start mirtazapine cautiously	Withdraw, start bupropion cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
mirtazapine/ mianserin	Withdraw then start SSRI	Withdraw then start fluoxetine	Withdraw then start TCA	Withdraw then start venlafaxine	—	Withdraw, start bupropion cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
bupropion	Withdraw then start SSRI	Withdraw then start fluoxetine	Withdraw then start TCA at a low dose.	Withdraw, start venlafaxine at 37.5mg and increase slowly	Withdrawn, start mirtazapine cautiously	—	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
moclobemide	Withdraw, wait 24 hours, start SSRI	Withdraw, wait 24 hours, start fluoxetine	Withdraw, wait 24 hours, start TCA	Withdraw, wait 24 hours, start venlafaxine	Withdraw, wait 24 hours, start mirtazapine	Withdraw, wait 24 hours, start bupropion	—	Withdraw and wait 24 hours
Irreversible nonselective MAOIs	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks

[a] Short-acting SSRIs are citalopram, escitalopram, paroxetine, and sertraline.
[b] TCAs are amitriptyline, clomipramine (refer to note g), dothiepin, doxepin, imipramine, nortriptyline, trimipramine.
[c] Irreversible nonselective MAOIs (phenelzine or tranylcypromine) should be commenced with caution after all other antidepressants because of the risk of hypertensive crisis and serotonin toxicity. Allowance should be made for the washout period (5 half-lives) and individual patient differences in pharmacokinetics.
[d] Abrupt withdrawal is usually possible, however if patients are likely to experience problems with discontinuation symptoms then a slower withdrawal may be required.
[e] Low Dose- citalopram 10mg/day; escitalopram 5mg/day; paroxetine 10mg/day; sertraline 25mg/day; fluoxetine 20mg on alternate days
[f] If changing from paroxetine or fluoxetine, TCA concentration may be elevated for at least several weeks due to persisting SSRI-induced cytochrome P450 inhibition.
[g] Do not co-administer clomipramine with SSRIs or venlafaxine.
[h] Care is required when changing from fluoxetine to another antidepressant as it has a longer half-life than other SSRIs, leading to significant concentrations of fluoxetine or its active metabolite being present for about five weeks after cessation.

Monitoring

1. Sodium levels, U&Es with SSRIs
2. ECG prior to TCA initiation

Depression/Major Depressive Disorder (MDD)

NZF: https://nzf.org.nz/nzf_70682

Description

MDD is a mental condition characterised by feelings of severe despondency and dejection.

Depression	Dysthymia	Normal	Hypomania	Mania
Major Depression				

TYPES OF MDD	
Seasonal Affective Disorder (SAD)	MDD that occurs during winter months where there is less sunlights. • Light therapy for 15-30 minutes a day can help
Psychotic Depression	MDD with psychotic symptoms such as hallucinators, delusions and paranoia. • Antipsychotics and ECT help
Postpartum Depression (PPD)	MDD in the weeks/months following childbirth, can affect both men and women. • Citalopram is the recommended antidepressant due to its compatibility with breastfeeding.
Premenstrual Dysphoric Disorder (PMDD)	MDD occurs at the start of their period. • Oral contraceptives or HRT can help.
Atypical Depression	MDD with features that vary from the traditional criteria for depression — particularly mood improvement in response to actual/potential positive events, over-eating and sleeping.

Signs & Symptoms

Loss of interest, sadness, anhedonia, fatigue, hopeless, guilt/worthlessness. Residual symptoms may occur in non-remitters.

- Most common: insomnia, fatigue/pain, concentration/interest
- Least common: depressed mood, suicidal ideation, psychomotor retardation

Social complications of depression

1. Substance use and abuse
2. Social/family withdrawal
3. Decreased performance at work/school
4. Suicide (highest risk in young men, recently widowed men, anyone < 30 recently prescribed anti-depressants in the last 2 weeks)

Diagnosis

For depression to be diagnosed, patients experience ≥ 5 of the following symptoms during the same 2-week period. These symptoms tend to cause clinically significant distress or impairment in social, occupational, or other important areas of function.

Must include ONE of these:	...and must include at least FOUR from the following:
Depressed Mood	Weight/appetite changes
Apathy/Loss of Interest (anhedonia)	Sleep disturbances
	Psychomotor agitation/retardation
	Fatigue
	Worthlessness/guilt
	Executive dysfunction
	Suicidal ideation

Staging

STAGES OF MDD	
Stage	Description
Mild depressive episode	Two or three of the above symptoms are usually present. The patient is usually distressed by these but will probably be able to continue with most activities.
Moderate depressive episode	Four or more of the above symptoms are usually present and the patient is likely to have great difficulty in continuing with ordinary activities.
Severe depressive episode without psychotic symptoms	An episode of depression in which several of the above symptoms are marked and distressing, typically loss of self-esteem, and ideas of worthlessness or guilt. Suicidal thoughts and acts are common and a number of "somatic" symptoms are usually present.

Pharmacological Treatment

See Antidepressant Prescribing Guidelines



Treatment Duration

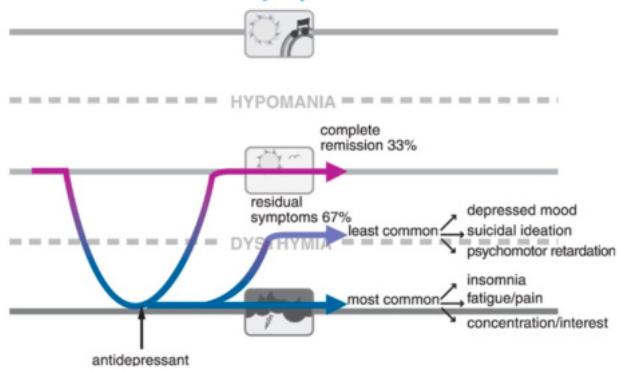
How long someone should be given an antidepressant depends on how many episodes they've had. Failure to meet the total duration can result in relapse.

- *1st episode:* 6 months once well (symptoms totally resolved) i.e. 9 months treatment in total
- *2nd episode:* 2 years
- *3rd episode:* 5 years to life-long

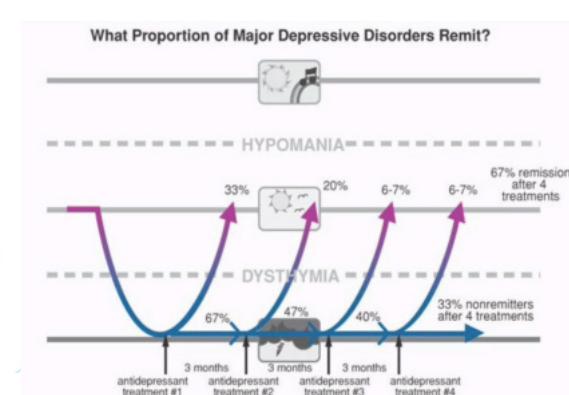
Remission Rates — STAR-D Trial

- Approximately a two-thirds of patients do not respond to the first antidepressant that is prescribed. Options include: **dose escalation, switching to a different drug, and a number of augmentation strategies.**
- After 12 months with four sequential antidepressants taken for 12 weeks each, a cumulative 2/3 of patients will achieve remission.

Common residual symptoms in non-remitters



Remission rates - STAR-D trial



Treatment-Resistant Depression (TRD)

Description

About 1/3 of people treated for depression try several treatment methods without success — this is known as treatment-resistant depression.

Diagnosis & Recommended Treatments

STAGING OF TDD		
Staging	Definition	Recommendation
STAR*D level 3	Failure of 2 adequate dose-duration antidepressants or psychotherapy from different classes (either in combination or succession) in the current episode	Less-invasive novel treatments: rTMS, ketamine, buprenorphine or ECT in some cases
STAR*D level 4	Failure of 3 or more adequate antidepressant or psychotherapy trials from different classes (either in combination or succession) in the current episode	Invasive or higher-risk treatments: surgical interventions [vagus nerve stimulation or deep brain stimulation], ECT
Psychotherapy “failure”	Failed response to adequate course of 8 attended sessions of a form of psychotherapy with demonstrated MDD effectiveness (e.g. CBT or interpersonal therapy)	Electroconvulsive therapy (ECT) is supported in severe treatment resistant depression

Persistent Depressive Disorder (PDD; Dysthymia)

Description

Persistent depressive disorder, also called dysthymia, is a continuous long-term (chronic) form of depression.

Signs & Symptoms

PDD involves fewer symptoms. But they last longer, at least 2 years (1 year in children and adolescents). You can be diagnosed with MDD if you have symptoms for 2 weeks.

Non-Pharmacological Treatment

CBT

Pharmacological Treatment

[See Antidepressant Prescribing Guidelines](#)

Bipolar Disorder (Manic Depression)

NZF Drugs for Bipolar Disorder

Description

Also known as manic depression, bipolar disorder is a psychiatric illness associated with episodes of mood swings ranging from depressive lows to manic highs.

Living with bipolar disorder can be extremely challenging. The mood changes can be swift, or each episode can linger for several days. Episodes of mania and hypomania (less severe mania) are prevalent features of bipolar disorder. While the signs of mania may at first be a pleasant diversion from the dark depressive episodes, the manic phase can also be destabilising and self-destructive.

There are generally 4 types of episodes in bipolar disorder:

DIAGNOSIS OF BIPOLAR DISORDERS	
Episode	Definition
Manic	Abnormal elevated/irritable mood + 3/4 symptoms
Major depressive	Depressed mood + 4 other symptoms
Hypomanic	Less severe/shorter version of the manic episode + 3/4 other symptoms
Mixed	Meets criteria for both manic/major depressive episode

Signs & Symptoms

Characteristics of Mood Episodes

- Length and severity of mood episodes and interval between episodes varies between patients
- Manic episodes often shorter and end more abruptly than major depressive episodes. Average length of an untreated manic episode is **4 - 13 months**
- Episodes can occur regularly (same time/season of year) and often cluster at 12-month intervals
- Women have more depressive episodes than manic episodes, whereas men have a more even distribution
- Rapid cycling (>4 mood episodes/year) are more common in women and are associated with a poor prognosis

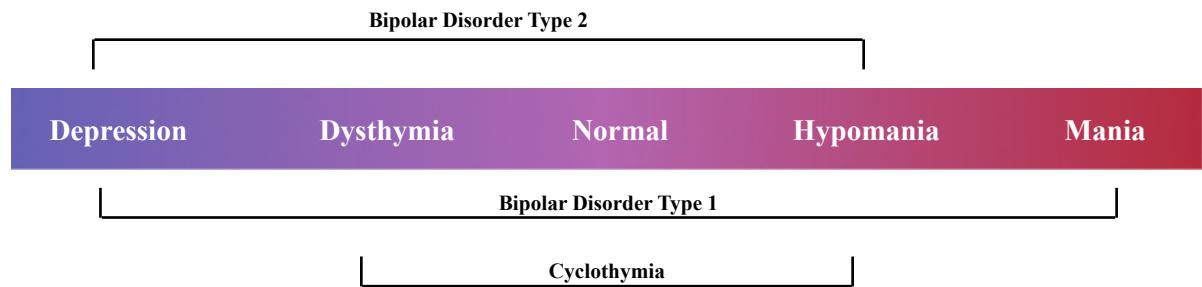


Bipolar Episodes

Possible combinations during the course of illness might also occur, which do not meet diagnostic criteria for an episode. e.g. sub-syndromal manic, depressive episodes

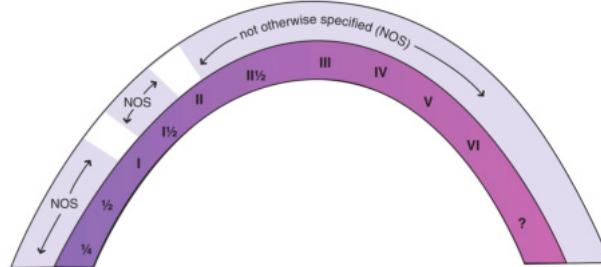
Staging (DSM-V & Spectrum Version)

DSM-V Staging suggests that there are 5 types of Bipolar Disorders that exist.



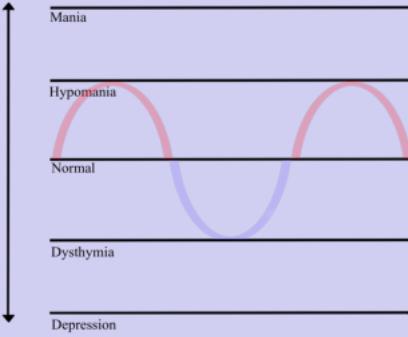
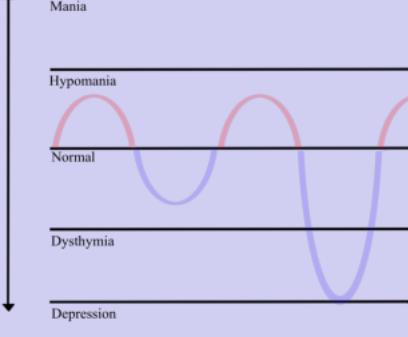
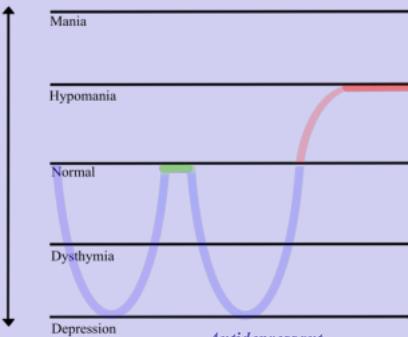
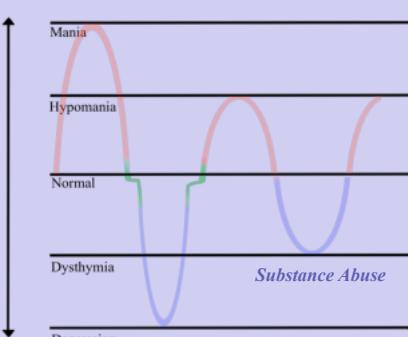
STAGING of BIPOLAR DISORDERS	
DMS-V Staging	Definition
Bipolar Disorder Type 1	Manic + major depressive episode
Bipolar Disorder Type 2	Hypomanic + major depressive episode
Cyclothymic/Sub-Threshold Bipolar Disorder	Chronic fluctuations between subsyndromal depressive and hypomanic (2 years for adults, 1 year for children/adolescents)
Unspecified bipolar and related disorder	Mood states do not meet full criteria for any specific disorder in the bipolar and related disorder class
Rapid Cycling	>4 mood episodes/year, associated with poor prognosis (more common in women)

Moving away from the DSM-V, another approach is to see the bipolar disorders as a spectrum rather than discrete categories.



STAGING of BIPOLAR DISORDERS	
DMS-V Staging	Definition
Bipolar ½ (Schizobipolar disorder)	Positive symptoms of psychosis + [(Hypo)Manic + Normal + Depressive]
Bipolar Disorder Type 1	Manic + Mixed (+/- Major depressive)
Bipolar 1 ½	Protracted hypomania + Normal — without depression
Bipolar Disorder Type 2	Hypomanic + Major depressive
Bipolar Type 2 ½	Depressive + Cyclothymia
Bipolar Type 3 (Antidepressant induced hypomania)	Depressive + Normal + Hypomania
Bipolar Type 3 ½ (Substance abuse-induced)	Mania + Depression + Hypomania + Dysthymia

TYPES OF BIPOLAR DISORDERS		
Bipolar Disorder	Description	Graph
Type 1	<p>Manic or Mixed Episode +/- Major Depressive Episode (Most common bipolar disorder)</p> <p>This type of bipolar disorder is defined as the occurrence of at least 1 manic episode and/or a major depressive episode, or mixed episode. The depressive episode usually occurs after the manic/mixed episode. The mania must be severe enough that hospitalisation is required and/or lasts a week or longer. The depressive episode must last at least 2 weeks.</p>	<p>The graph shows two red bell-shaped curves above a horizontal black line labeled 'Normal'. The top curve is labeled 'Mania' and the lower one is labeled 'Hypomania'. Below the 'Normal' line, there are two blue bell-shaped curves: a larger one labeled 'Dysthymia' and a smaller one labeled 'Depression'.</p>
Type 1/2 Schizoaffective Disorder	<p>Psychosis + [(Hypo)manic + Normal + Depressive]</p> <p>Patient experiences a blend of symptoms between schizophrenia and bipolar disorders — the primary distinguishing factor being psychosis, which is present regardless whether the patient is manic, normal, depressive or hypomanic.</p>	<p>The graph is similar to the Type 1 graph but includes green shaded rectangular areas under the 'Normal', 'Dysthymia', and 'Depression' lines, representing periods of psychosis.</p>
Type 1 1/2 Protracted hypomania without depression	<p>Hypomania + Normal (NO DEPRESSION)</p> <p>Unlike Bipolar Disorder Type 2, episodes of hypomania here are not accompanied by depressive episodes. These patients are at risk of developing Type II.</p>	<p>The graph shows red bell-shaped curves above the 'Normal' line, with no curves below it, indicating no depressive episodes.</p>
Type 2	<p>Hypomanic Episodes + Depressive Episode Any manic episode rules out a diagnosis of bipolar Type II.</p> <p>Bipolar II disorder is characterised by the shifting between the less severe hypomanic episodes and depressive episodes. Usually, a major depressive episode is experienced before and after the manic break. Hypomanic episodes must last at least 4 days.</p>	<p>The graph shows red bell-shaped curves above the 'Normal' line and a large blue bell-shaped curve below the 'Normal' line, indicating a depressive episode.</p>

Cyclothymic Disorder Cyclothymia	<p>Hypomanic Episodes + Dysthymic Episodes In a traditional diagnosis of bipolar I or bipolar II, a person will experience long-term mood cycles of mania and deep depression (1 year in children/adolescents and at least 2 years in adults). When a person experiences cyclothymia, these shifts happen on a smaller scale. They oscillate between hypomania (a slightly manic state) and low-grade depression. There may be periods of normal mood as well, but those periods last less than eight weeks.</p> <p>There is a risk of developing bipolar I or II later on.</p>	 <p>A vertical stack of five horizontal lines representing mood levels. From top to bottom: Mania (red), Hypomania (pink), Normal (light blue), Dysthymia (purple), and Depression (dark blue). A red arc above the Hypomania line and a purple arc below the Dysthymia line represent the range of mood fluctuations for a person with cyclothymia.</p>
Type 2 1/2 Depressive Episodes with Cyclothymia	<p>Cyclothymia + Occasional Major Depressive Episode These patients have episodes of less severe cycles of mania and depression with the occasional major depressive episode.</p>	 <p>A vertical stack of five horizontal lines representing mood levels. From top to bottom: Mania (red), Hypomania (pink), Normal (light blue), Dysthymia (purple), and Depression (dark blue). The mood fluctuates between hypomania and dysthymia, with occasional deep dips into depression.</p>
Type 3 Antidepressant Induced Hypomania	<p>Depression + Normal + Depression + Hypomania Antidepressants given in the treatment of depression can induce hypomania, which creates significant issues for the management of depressive phases for all types of BD.</p>	 <p>A vertical stack of five horizontal lines representing mood levels. From top to bottom: Mania (red), Hypomania (pink), Normal (light blue), Dysthymia (purple), and Depression (dark blue). The mood fluctuates between depression and hypomania, with a brief period of normal mood indicated by a green bar during treatment with antidepressants.</p>
Type 3 1/2 Substance Abuse Induced	<p>Mania + Depression + Hypomania + Dysthymia Meth, cocaine, alcohol all can induce a bipolar disorder.</p>	 <p>A vertical stack of five horizontal lines representing mood levels. From top to bottom: Mania (red), Hypomania (pink), Normal (light blue), Dysthymia (purple), and Depression (dark blue). The mood exhibits extreme and rapid fluctuations between all four states (mania, hypomania, depression, dysthymia) due to substance abuse.</p>

Signs & Symptoms

SIGNS & SYMPTOMS OF BIPOLAR DISORDER	
Extreme Lows Major Depressive Episodes	Extreme Highs (Hypo)manic Episodes
Hopeless & Discouraged	Overly happy/optimistic, euphoric, high self esteem
Lack of energy & focus	Energetic, feels inspired to conquer the world
Physical symptoms e.g. eating too little or sleeping too much	Delusions of grandeur e.g. mission from god, supernatural powers Poor decision making e.g. no regard for consequences Little sleep, hallucinations, psychosis

Diagnosis

At least 1 week of:	...and must include 3+ of these (4 if mood is only irritable):
Abnormally/persistent elevated/expansive mood	Inflated self-esteem/grandiosity
+/- + irritable mood	Increased goal-directed activity or agitation
	Risk taking
	Decreased need for sleep
	Distractible concentration
	More talkative pressure speech
	Flight of ideas/racing thoughts

Prognosis

Alcohol/substance abuse and suicidal attempts occurs in up to 50% of patients and has a significant impact on the age of onset, course of illness, and response to treatment.

Non-Pharmacological Treatment

Psychological Interventions (first line)

- Interpersonal psychotherapy
- Cognitive behavioural therapy (CBT)
- Behavioural couples therapy



Psychological Interventions for Manic Episodes

Psychological interventions are not typically useful in manic episodes but are excellent in preventing them.

Pharmacological Treatment — no cure

Different drugs classes are effective for different phases of BD. Long-term treatment of bipolar disorder should continue for **at least two years** from the last manic episode and should then be reviewed giving consideration to the number of previous episodes and other risk factors for relapse.

First Line

- *Atypical antipsychotics*: quetiapine, aripiprazole, olanzapine, risperidone

Second Line

- *To control mania*: mood stabiliser (Sodium valproate, **lithium**)
- *To control depression*: lamotrigine
- *For Bipolar depression*: Antidepressants

Supportive Care

- *Benzodiazepines*: agitation
- *Topiramate/Zonisamide*: weight loss
- *Gabapentin/Pregabalin*: anxiety, sleep or pain



Antidepressants in Bipolar Disorders

If bipolar depression is mistaken for major depression and the patient is treated with antidepressants, they may either not work and/or worsen symptoms for some by de-stabilising mood and inducing mania or hypomania, rapid cycling or mixed states and possibly suicidality (see Type 3 bipolar disorder). However, that being said, they may be helpful in treating bipolar depression.

Thus, if they are to be used:

1. They must be given **with** a mood stabiliser
2. Patient must be closely monitored and not have a rapid-cycling bipolar disorder or mixed affective states
3. Cease the anti-depressant immediately if the patient experiences an acute manic episode.

PHARMACOLOGICAL TREATMENT OF BIPOLAR DISORDER			
Drug		Description	Side Effects
1st Line Atypical Antipsychotics	Atypicals Quetiapine, aripiprazole, olanzapine, risperidone	Psychotic & Non-Psychotic Mania + Depression Do NOT use quetiapine and olanzapine together — QT prolongation, seizures Improve mood by blocking NA and 5-HT receptors	Careful of metabolic syndrome with olanzapine
2nd Line Mood Stabilisers	Lithium	More effective for Mania than Depression Effective in the treatment of mania and decreases suicide risk possibly by decreasing impulsive aggressive behaviour. However it has a narrow therapeutic range of 0.6-0.75mmol/L which can cause renal toxicity. Aim for the highest tolerable lithium plasma level (within range) to achieve complete remission of both manic and depressive episodes. Avoid concomitant use with NSAIDs — however if this has to be done, use regular NSAIDs and not prn (narrow therapeutic range)	GI effects (weight gain, nausea) alopecia, tremor , sedation and ↓ cognition, renal and thyroid function
	Anti-Epileptics Valproic Acid Carbamazepine Lamotrigine	Valproate — Manic phase + may prevent recurrence Interferes with voltage-sensitive sodium channels (VSSC) by increasing inhibitory effects of GABA and regulating downstream signal transduction cascades. Lamotrigine — Bipolar Depression Blocks α-subunit of VSSC. Also decreases glutamate release. Useful if patient is of child bearing age Carbamazepine — Bipolar Depression Binds to α subunit of VSSCs, may have effects at calcium and potassium ion channels, may enhance inhibitory effects of GABA. Generally used 2nd or 3rd line as it is a potent CYP3A4 inducer.	Weight gain, sedation, many drug interactions

PSYCHOTIC DISORDERS

Introduction

Psychotic disorders are severe mental disorders that cause abnormal thinking and perceptions. People with psychoses lose touch with reality. Two of the main symptoms are delusions and hallucinations

Both depression and bipolar disorder can cause psychosis in some cases — however the most common psychiatric illness that causes psychosis is schizophrenia.

Psychosis also exists in:

- Substance-induced psychotic disorder
- Schizophreniform disorder (psychosis not otherwise specified)
- Schizoaffective disorder
- Delusional disorder



Did You Know?

Dual diagnosis = patient has intellectual disability + mental illness

The duration of untreated psychosis (DUP) has major impact on patient outcomes - thus prompt treatment and management is crucial!

Schizophrenia

Description

Schizophrenia is a chronic, and severe psychotic illness that affects how a person thinks, feels, and behaves. It may result in some combination of hallucinations, delusions, and extremely disordered thinking and behaviour that impairs daily functioning, and can be disabling. The burden of illness of schizophrenia is concerning — most patients affected attempt suicide and are at higher risks of CVD.

Pathophysiology

Integrated Dopamine Hypothesis: Dopamine, Glutamate & Serotonergic System

While the exact cause of schizophrenia is unknown, it is hypothesised that it occurs due to a dysregulation in the dopaminergic pathways as most symptoms can be explained by the hyperactive neurotransmission of dopamine. It is possible other chemicals are involved such as NA, 5-HT and GABA.

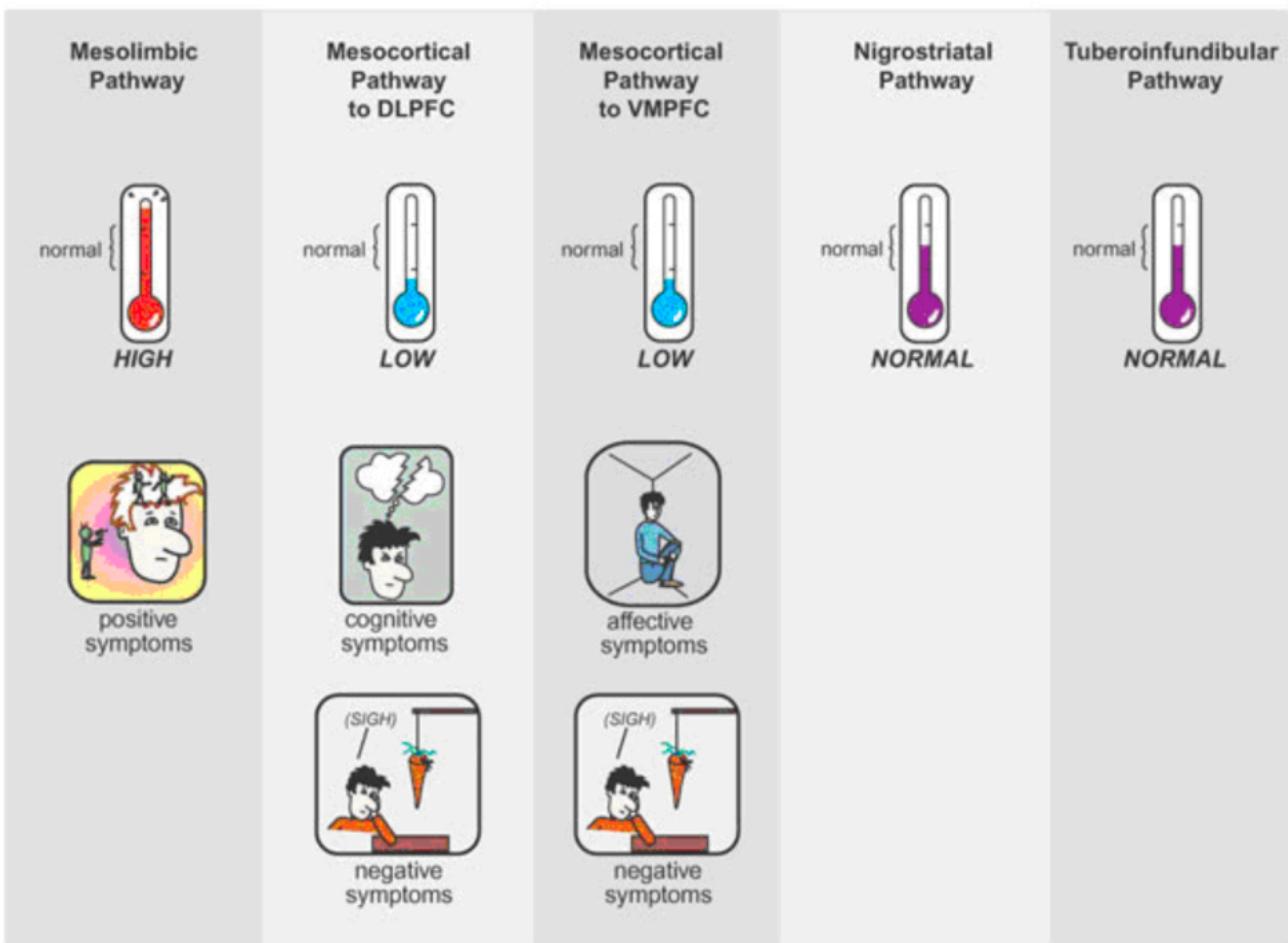


Do You See A Pattern?

In Parkinson's, we saw there was a deficiency of dopamine - causing issues with motor movement. In Schizophrenia, there is an excess of dopamine (in some pathways) - causing hallucinations and other symptoms. Thus, it is possible that when treating Schizophrenia (which uses Dopamine Antagonists) - we may see symptoms of Parkinson's.

So let's see how does the dysregulation dopamine produce schizophrenia. There are 5 pathways in the body by which the release of dopamine will convey a certain action.

THE FIVE DOPAMINERGIC PATHWAYS			
	Function	DA Activity in Schizophrenia	Effect of Treatment (Dopamine Antagonists)
1 Nigrostriatal Pathway (SN to striatum)	This pathway controls <i>motor function/movement</i>	Normal	Dopamine Deficiency Blockage of dopamine here is what causes extrapyramidal side effects
2 Mesolimbic Pathway (VITA to NAc)	This pathway regulates <i>pleasurable sensations, euphoria, delusions/hallucinations</i>	Hyperactive (as uninhibited by GLU) Causes <i>positive</i> symptoms	Normal Dopamine Levels D2 Receptor Antagonism in Mesolimbic Pathway treats positive psychotic symptoms
3 Mesocortical Pathway (to DLPFC)	This pathway mediates <i>cognition</i>	Hypoactive (as unactivated by GLU) Causes <i>negative</i> and <i>cognitive</i> symptom	Dopamine Deficiency Typical Antipsychotics usually worsen these but Atypicals improve them.
4 Mesocortical Pathway (to VMPFC)	This pathway mediates <i>emotions/affective symptoms</i>	Hypoactive (as unactivated by GLU) Causes <i>negative</i> and <i>affective</i> symptoms	
5 Tuberoinfundibular Pathway (Hypothalamus to anterior pituitary)	This pathway controls <i>prolactin secretion</i>	Normal	Dopamine Deficiency Blockage of dopamine here is what causes extrapyramidal side effects
Orbitofrontal Cortex/ Amygdala Pathway	This pathway regulates <i>aggressive symptoms</i>	-	-



NMDA Receptor Hypofunction Hypothesis

You would've noticed from the above table, that in Schizophrenics, 3 out of the 5 dopamine pathways experience a dysregulation in dopamine activity while the rest are normal. So what causes the mesolimbic and the mesocortical pathway to experience this? This is where the NMDA Receptor Hypofunction Hypothesis comes in.

It is believed that NMDA (glutamate) receptor projections normally function to **inhibit** the mesolimbic pathway and **excite** the mesocortical pathway —but in schizophrenia, these projections become **hypoaactive**:

Mesolimbic Pathway

Normally inhibited

When tonic inhibition is lost, this causes hyperactivity = positive symptoms

Mesocortical Pathway

Normally excited

When tonic excitation is lost, this causes hypoactivity = cognitive/negative/affective symptoms



How To Remember?

You can remember this using: HyPOactive MesoCORTical causes COgnitive Symptoms

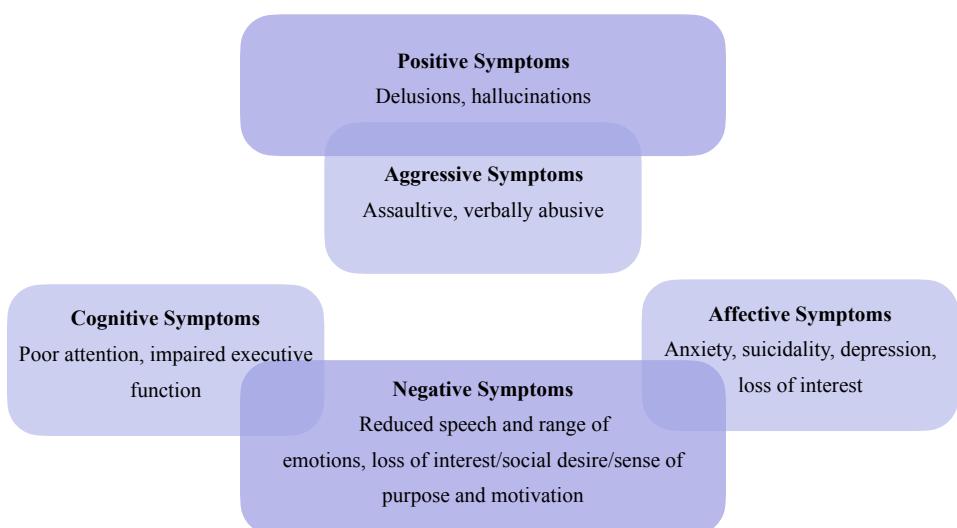
Signs & Symptoms

Symptoms of Schizophrenia can be broken down into three phases (prodromal, active, residual). These phases tend to occur in order and cycle throughout the course of the illness. People who develop schizophrenia may have one or many psychotic episodes during their lifetime.

Clinical Presentation of Schizophrenia			
	Description	Pathophysiology	Examples
Prodromal Phase	<p>Negative Symptoms mainly</p> <p>During the initial onset, warning signs, also known as negative symptoms, occur that indicate an episode is about to occur. They may occur months to years before someone presents with acute symptoms.</p>	<p>Negative Symptoms = Deficit</p> <p>Negative symptoms are deficit symptoms that result due to the loss of a normal body function. These are symptoms that take away a thought, feeling or behaviour.</p> <p>These signs often manifest themselves as barely noticeable changes.</p>	<p><i>Examples</i></p> <ul style="list-style-type: none"> • Flattened emotional response, social withdrawal, apathy, anhedonia • <u>Affective symptoms</u>: anxiety, suicidality, depression, loss of interest • <u>Cognitive symptoms</u>: executive dysfunction e.g. drop in grades or job performance, confused speech or trouble communication
Active Phase	<p>Positive Symptoms mainly</p> <p>The person here experiences a full-blown episode.</p>	<p>Positive Symptoms = Psychotic</p> <p>Positive symptoms are psychotic symptoms. They are symptoms that adds a behaviour, thought or feeling and therefore are symptoms that should be absent and indicate that patient has lost touch with reality</p>	<p><i>Examples</i></p> <ul style="list-style-type: none"> • <u>Aggressive symptoms</u>: assaults, verbally abusive • Life long delusions (paranoid), • Hallucinations (tactile, auditory, visual) • Thought disordered e.g. word salad
Residual Phase	<p>Cognitive Symptoms mainly</p> <p>Best predictor of outcome</p> <p>This is the recovery phase where the person experiences cognitive symptoms</p>	<p>Cognitive Symptoms = Executive Dysfunction</p> <p>Cognitive symptoms are symptoms that affects memory, learning and understanding. They are very subtle and difficult to notice.</p>	<p><i>Examples</i></p> <ul style="list-style-type: none"> • Difficulty representing and maintaining goals • Allocating attention • Evaluating/monitoring performance, • Impaired verbal fluency • Utilising skills to solve problems

Symptoms are divided into five demotions with great overlap:

- Negative, Positive, Cognitive, Aggressive, Affective



Positive symptoms in schizophrenia are associated with aggressive symptoms while negative symptoms are associated with both cognitive and affective symptoms.

Diagnosis

- Patient and family interviews following the presentation of a first psychotic episode
- Psychiatric examination from Diagnostics and Statistics Manual (DSM-V) or ICD-10: Positive & Negative Symptom Score (PANSS), Clinical Global Impressions scale (CGI)
- At Risk Mental State (ARMS) Brief Psychiatric Scale (BPS)

DIAGNOSIS	
Assessment	Description
Symptom Assessment	Two of the following are required: <ul style="list-style-type: none"> • At least one of these: delusions, hallucinations, disorganized speech • At least one of these: disorganized/catatonic behaviour, negative symptoms
Duration Assessment	Ongoing for at least 6 months <ul style="list-style-type: none"> • Prodromal, Active (must be at least 1 month), Residual
Differential Diagnosis	Not due to another condition e.g. drug-induced psychosis



Psychosis Not Otherwise Specified

Patient notes will often read 'psychosis not otherwise specified' due to stigma associated with schizophrenia

Pharmacological Treatment

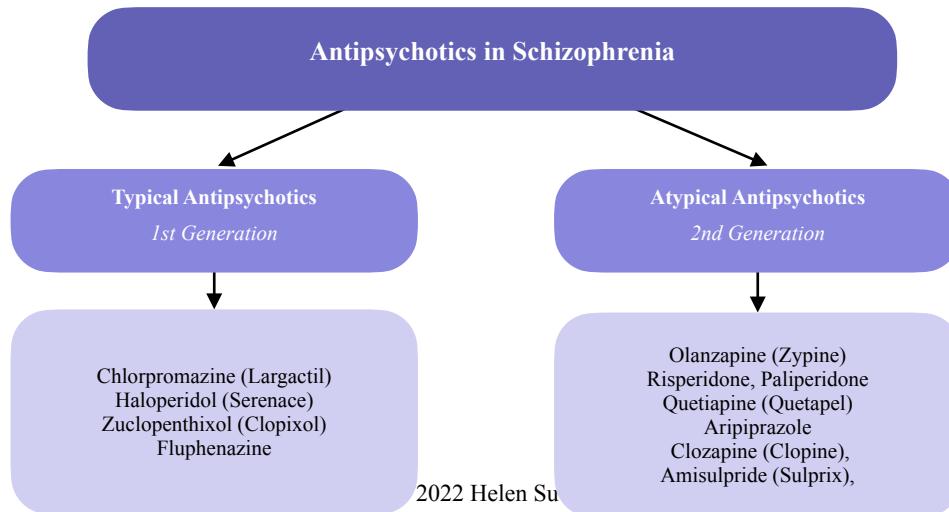
[Antipsychotic Deprescribing Guidelines](#)

Schizophrenia is treated with class of medications called antipsychotics.

Holding the dopamine overactivity hypothesis is true:

- DA agonists (e.g. methamphetamine, amphetamines, cocaine) can produce behavioural phenomenon indistinguishable from acute schizophrenia
- D2 antagonists (antipsychotics) are therefore used for the treatment of schizophrenia

Nearly all antipsychotics are DA antagonists which block 5-HT_{2A} to varying degrees; they can be divided into two generations (typical, atypical). Potency correlates with activity at D2 receptors (not effectiveness).



CLINICAL PRESENTATION OF SCHIZOPHRENIA		
Antipsychotic	Description	Side Effects
First Generation (Typical) Antipsychotics <i>Chlorpromazine (Largactil)</i> <i>Haloperidol (Serenace)</i> <i>Zuclopentixol (Clopixol)</i> <i>Fluphenazine</i>	<p>D₂ Antagonists</p> <ol style="list-style-type: none"> Decrease hyperactivity of the mesolimbic pathway to improve positive symptoms Decrease normal activity in Nigrostriatal/Tuberofundibular pathway, therefore rendering them hypoactive with treatment and creating extrapyramidal side effects (EPSE) Block activity in the mesocortical pathway, worsening its hypo-activity and thus negative & cognitive symptoms 	<p>Schizophrenia Management Not selective for dopaminergic pathways i.e. may improve positive symptoms but worsen negative symptoms</p> <p>Extrapyramidal Side Effects</p> <ul style="list-style-type: none"> Dystonia (muscle spasms) Akathisia (restlessness) Pseudo-Parkinsonism Tardive Dyskinesia (repetitive movements) <p>Other</p> <ul style="list-style-type: none"> Anticholinergic effects Elevated prolactin Sexual dysfunction Blood dyscrasias, QT-Prolongation, postural hypotension
Second Generation (Atypical) Antipsychotics <i>Olanzapine (Zypine)</i> <i>Risperidone, Paliperidone</i> <i>Quetiapine (Quetipal)</i> <i>Aripiprazole</i> <i>Clozapine (Clopine), Amisulpride (Sulpirix),</i>	<p>D₂ Antagonists + 5-HT_{2A} Antagonists</p> <ol style="list-style-type: none"> Decrease hyperactivity of the mesolimbic pathway to improve positive symptoms Block serotonin in mesocortical pathway <p>Take days/weeks/months to work which suggests secondary effects e.g. ↑ D₂ receptors in limbic structures</p>	<p>Metabolic Syndrome (antagonism of 5-HT, H1, M3)</p> <ul style="list-style-type: none"> Weight gain, elevated lipids, insulin resistance, diabetes Less effect on prolactin (EXCEPT risperidone due to high D₂ selectivity) <p>Other</p> <ul style="list-style-type: none"> Sexual dysfunction Less likely to induce EPSE

Treatment Guidelines

First Line: start with an atypical antipsychotic (less side effects)

- Choice depends on side effect profile. Last line: clozapine
- Titrate as necessary to minimum effective dose, adjust per therapeutic response/tolerability/safety

Assess over 2-3 weeks

- If effective:* continue dose, consider switching to depot/long-acting injection before discharge
- If not effective:* change drug and repeat process.
- If not tolerated/poor adherence:* change drug to a favourable side effect profile. Consider early use of depot/long-acting injection

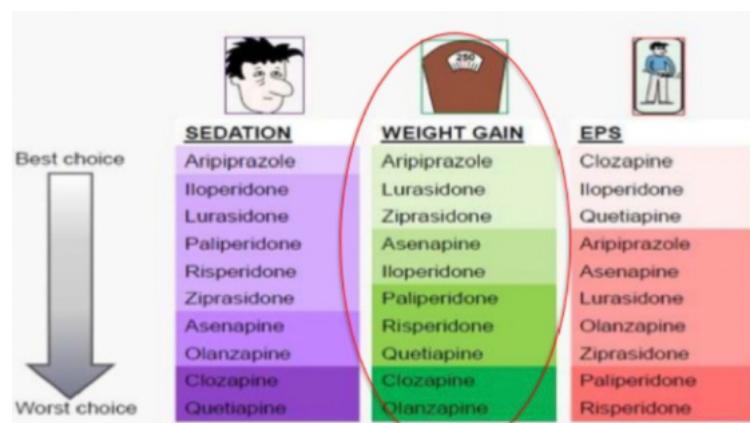
TREATMENT RECOMMENDATIONS BASED ON SIDE EFFECTS					
 Most recommended	Sedation	Weight Gain	EPSE	Hypotension	Anti-Muscarinic
	Aripiprazole	Aripiprazole, Lurasidone, Ziprasidone	Clozapine, Iloperidone, Quetiapine		Clozapine
	Iloperidone, Lurasidone, Paliperidone, Risperidone, Ziprasidone	Asenapine, Iloperidone	Aripiprazole, Asenapine, Lurasidone, Olanzapine, Ziprasidone	Haloperidol, Zuclopentixol, Risperidone, Clozapine, Quetiapine	Zuclopentixole
	Asenapine, Olanzapine	Paliperidone, Risperidone, Quetiapine	Paliperidone, Risperidone		Haloperidol, Olanzapine, Quetiapine
	Clozapine, Quetiapine	Clozapine, Olanzapine	-		

Table 1.8 Relative adverse effects of antipsychotic drugs

Drug	Sedation	Weight gain	Akathisia	Parkinsonism	Anti cholinergic	Hypotension	Prolactin elevation
Amisulpride*	-	+	+	+	-	-	+++
Aripiprazole	-	-	+	-	-	-	-
Asenapine*	+	+	+	-	-	-	+
Benperidol*	+	+	+	+++	+	+	+++
Brexpiprazole*	-	+	+	-	-	-	-
Cariprazine*	-	+	+	-	-	-	-
Chlorpromazine	+++	++	+	++	++	+++	+++
Clozapine	+++	+++	-	-	+++	+++	-
Flupentixol	+	++	++	++	++	+	+++
Fluphenazine*	+	+	++	+++	+	+	+++
Haloperidol	+	+	+++	+++	+	+	++
Iloperidone*	-	++	+	+	-	+	-
Loxapine*	++	+	+	+++	+	++	+++
Lurasidone	+	-	+	+	-	-	-
Olanzapine	++	+++	-	-	+	+	+
Paliperidone	+	++	+	+	+	++	+++
Perphenazine	+	+	++	+++	+	+	+++
Pimozide*	+	+	+	+	+	+	+++
Pipotiazine*	++	++	+	++	++	++	+++
Promazine*	+++	++	+	+	++	++	++
Quetiapine	++	++	-	-	+	++	-
Risperidone	+	++	+	+	+	++	+++
Sertindole*	-	+	+	-	-	+++	-
Sulpiride*	-	+	+	+	-	-	+++
Trifluoperazine	+	+	+	+++	+	+	+++
Ziprasidone*	+	-	+	-	-	+	+
Zuclopentixol*	++	++	++	++	++	+	+++

*Availability varies from country to country.

+++ high incidence/severity; ++ moderate; + low; - very low.



Switching Antipsychotics

If one option becomes intolerable, we can always switch to another! See the below recommendations for alternatives depending on the reason the switching is needed in the first place.

Table 1.38 General recommendations for switching antipsychotic drugs

Adverse effect	Suggested drugs	Alternatives
Acute EPS ^{1–8} – dystonia, parkinsonism, bradykinesia	Aripiprazole Olanzapine Quetiapine	Brexpiprazole* Cariprazine* Clozapine Lurasidone Ziprasidone
Akathisia ^{2,9}	Olanzapine Quetiapine	Clozapine
Dyslipidaemia ^{7,8,10–15}	Amisulpride Aripiprazole [†] Lurasidone Ziprasidone*	Asenapine Brexpiprazole* Cariprazine*
Impaired glucose tolerance ^{7,8,14,16–19}	Amisulpride Aripiprazole [†] Lurasidone Ziprasidone*	Brexpiprazole* Cariprazine* Haloperidol
Hyperprolactinaemia ^{7,8,14,20–25}	Aripiprazole [†] Brexpiprazole* Cariprazine* Lurasidone Quetiapine	Clozapine Olanzapine Ziprasidone*
Postural hypotension ^{8,14,26}	Amisulpride Aripiprazole Lurasidone	Brexpiprazole* Cariprazine* Haloperidol Sulpiride Trifluoperazine
QT prolongation ^{25,27–33}	Brexpiprazole* Cariprazine* Lurasidone Paliperidone (all with ECG monitoring)	Low-dose monotherapy of any drug not formally contraindicated in QT prolongation (with ECG monitoring)
Sedation ^{7,8,25}	Amisulpride Aripiprazole Brexpiprazole* Cariprazine* Risperidone Sulpiride	Haloperidol Trifluoperazine Ziprasidone*
Sexual dysfunction ^{8,34–40}	Aripiprazole Lurasidone Quetiapine	Brexpiprazole* Cariprazine* Clozapine
Tardive dyskinesia ^{41–44}	Clozapine	Aripiprazole Olanzapine Quetiapine
Weight gain ^{15,32,45–52}	Amisulpride Aripiprazole [†] Haloperidol Lurasidone Ziprasidone*	Asenapine Brexpiprazole* Cariprazine* Trifluoperazine

OSCE Points

- Antipsychotics take time to work. Over the first few weeks, you may find you sleep better or your mood is better. Over the next 2 to 8 weeks, the hallucinations or delusions fade away and your thoughts should become clearer.
- ADRs:
 - Feeling sleepy, drowsy or tired. May occur for some. Usually improves with time. Avoid driving or operating machinery until you know how it affects you.
 - Dizziness. May lower blood pressure for some. Usually improves with time. Try not to stand up too quickly. Do not drive.
- Encourages follow-up with prescriber and getting bloodwork done.

Treatment Resistant Schizophrenia (TRS)

[Clozapine NZF](#) [Clozapine SafeRx](#) [Clozapine Monitoring Medsafe](#) [Additional monitoring for clozapine](#)

Description

Treatment resistant schizophrenia occurs when treatment with a minimum of **2 antipsychotics** for at least **6 weeks at maximum tolerated dose** (not necessarily maximum licensed dose) fails to treat the condition. About ~30% of patients with schizophrenia will experience this.

Pharmacological Treatment

Clozapine is the drug of choice in TRS and induces remission in ~30 - 50% of patients affected by it. It is easily the most effective anti-psychotic that exists and the only one to show ↓ suicide rates, ↑ rate of independent living, have marked ↓ re-hospitalisation, and have additional benefits for aggression.

However treatment initiation constitutes of an average wait time of 9 years post-first psychotic episode in NZ due to its severe side effects. Thus patients afflicted with TRS will typically have a very poor quality of life during this period.

CLOZAPINE MONITORING	
	Description
Initiation of Clozapine	<ul style="list-style-type: none">Physical examination, FBC, liver function tests, U&Es, lipids, glucose/HbA1cConsider troponin, CPR, ESR, beta-natriuretic peptideECG – particularly to screen for evidence of past myocardial infarction or ventricular abnormalityEchocardiogram if clinically indicated
Monitoring of ADR	<ol style="list-style-type: none">Agranulocytosis (neutropenia/leukopenia): increased susceptibility to infection — <i>Clopine connect</i><ul style="list-style-type: none">Blood test (WCC): weekly for the first 18 weeks, then every 4 weeks thereafterStop treatment if neutrophil count is $0.5\text{--}1.5 \times 10^9/\text{L}$.Intestinal Obstruction: can cause toxic megacolon<ul style="list-style-type: none">Prophylaxis: regular laxativesOther: Sedation, hypersalivation, tachycardia (pulse), hypotension (BP), myocarditis, fever, headache, seizures, constipation, N/V, weight gain, raised lipids, glucose impairment, blurred vision, urinary incontinence, eosinophilia, thrombocytopenia
Interactions	<ul style="list-style-type: none">Clozapine is metabolised by CYP450, CYP1A2, and less so by CYP2D6<ul style="list-style-type: none">CYP inducers ↓ clozapine levels: high levels of caffeine, valproate, carbamazepine, cigarette smokingCYP inhibitors ↑ clozapine levels: clarithromycin, rifampicin, erythromycin, fluoxetine, paroxetineLithium may exacerbate ADRs but is still used to raise low baseline WCC to then be eligible for clozapine

Note: Permanent discontinuation of clozapine treatment is recommended for patients showing evidence of agranulocytosis or myocarditis — **Do NOT re-challenge**.

Ultra-Treatment Resistant Schizophrenia (UTRS)

Description

Defined by clozapine resistance and occurs in ~ 1/3 of patients. Symptoms vary from partial resolution of psychosis and associated symptoms to a complete absence of response.

PERSONALITY DISORDERS

Introduction

APA Personality Disorders

A personality disorder is a way of thinking, feeling, and behaving that deviates from the expectations of the culture, causes distress or problems functioning, and lasts over time.

All personality disorders share the following 4 core symptoms, which combine in various ways to form ten specific personality disorders identified in DSM-5:

1. Distorted thinking patterns
2. Problematic emotional responses
3. Over/under-regulated impulse control
4. Interpersonal difficulties

PERSONALITY DISORDERS	
Cluster	Description
Cluster A: Odd or Eccentric	<ul style="list-style-type: none">• Paranoid• Schizoid• Schizotypal
Cluster B: Dramatic, emotional, erratic	<ul style="list-style-type: none">• Antisocial• Borderline• Histrionic• Narcissistic
Cluster C: Anxious, fearful	<ul style="list-style-type: none">• Avoidant• Dependent• Obsessive-compulsive (different from OCD)

Diagnosis

In order to be diagnosed with a specific personality disorder, a person must meet the minimum number of criteria established for that disorder. Furthermore, to meet the diagnostic requirements for a psychiatric disorder, the symptoms must cause **functional impairment and/or subjective distress**. This means the symptoms are distressing to the person with the disorder and/or the symptoms make it difficult for them to function well in society.

Cluster A: Odd or Eccentric

DSM-5: The Ten Personality Disorders: Cluster A

Introduction

Cluster A is called the *odd, eccentric* cluster. It includes:

- Paranoid Personality Disorder
- Schizoid Personality Disorder
- Schizotypal Personality Disorder

The common features of the personality disorders in this cluster are *social awkwardness and social withdrawal*. These disorders are *dominated by distorted thinking*.

Paranoid Personality Disorder

Description

Paranoid Personality Disorder is characterised by a pervasive distrust and suspiciousness of other people. People with this disorder assume that others are out to harm them, take advantage of them, or humiliate them in some way.

Signs & Symptoms

- They put a lot of effort into protecting themselves and keeping their distance from others
- They are known to preemptively attack others whom they feel threatened by
- They tend to hold grudges, are litigious, and display pathological jealousy
- Distorted thinking is evident. Their perception of the environment includes reading malevolent intentions into genuinely harmless, innocuous comments or behaviour, and dwelling on past slights
- For these reasons, they do not confide in others and do not allow themselves to develop close relationships
- Their emotional life tends to be dominated by distrust and hostility

Schizoid Personality Disorder

Description

Schizoid Personality Disorder is characterised by a pervasive pattern of social detachment and restricted range of emotional expression. For these reasons, people with this disorder tend to be socially isolated.

Signs & Symptoms

Schizoid is (conceptually) linked to **negative** symptoms of schizophrenia

- They don't seem to seek out or enjoy close relationships and appear indifferent to both criticism and praise/
- They almost always chose solitary activities, and seem to take little pleasure in life
- Emotionally, they seem aloof, detached, and cold.
- They may be oblivious to social nuance and social cues causing them to appear socially inept & superficial
- Their restricted emotional range and failure to reciprocate gestures or facial expressions (such as smiles or nods of agreement) cause them to appear rather dull, bland, or inattentive

Schizotypal Personality Disorder

Description

Schizotypal Personality Disorder is characterised by a pervasive pattern of social and interpersonal limitations. They experience acute discomfort in social settings and have a reduced capacity for close relationships. For these reasons they tend to be socially isolated, reserved, and distant. Unlike the Schizoid PD, they **also** experience perceptual and cognitive distortions and/or eccentric behaviour.

Signs & Symptoms

Schizotypal is (conceptually) linked to (less severe) **positive** symptoms of schizophrenia

- These perceptual abnormalities may include noticing flashes of light no one else can see, or seeing objects or shadows in the corner of their eyes and then realising that nothing is there
- They have odd beliefs, for instance, they may believe they can read other people's thoughts, or that their own thoughts have been stolen from their heads
- These odd or superstitious beliefs and fantasies are inconsistent with cultural norms

Risk Factors

Schizotypal Personality Disorder tends to be found more frequently in families where someone has been diagnosed with Schizophrenia. There is some indication that these two distinct disorders share genetic commonalities.

Cluster B: Dramatic, Emotional, Erratic

DSM-5: The Ten Personality Disorders: Cluster B

Introduction

Cluster B is called the *dramatic, emotional, and erratic cluster*. It includes:

- Antisocial Personality Disorder
- Borderline Personality Disorder
- Narcissistic Personality Disorder
- Histrionic Personality Disorder

Disorders in this cluster share problems with *impulse control* and *emotional regulation*.

Antisocial Personality Disorder

Description

Antisocial Personality Disorder is characterised by a pervasive pattern of disregard for the rights of other people that often manifests as hostility and/or aggression. Deceit and manipulation are also central features.

Signs & Symptoms

In many cases, hostile-aggressive and deceitful behaviours may first appear during **childhood**.

- These children may hurt or torment animals or people
- They may engage in hostile acts such as bullying or intimidating others
- They may have a reckless disregard for property such as setting fires and often place themselves in dangerous or risky situations
- They often engage in deceit, theft, and other serious violations of standard rules of conduct
- This difficulty with impulse control results in loss of employment, accidents, legal difficulties, and incarceration

People with Antisocial PD typically do not experience genuine remorse for the harm they cause others

- However, they can become quite adept at feigning remorse when it is in their best interest to do so (such as when standing before a judge)
- They *take little to no responsibility* for their actions. In fact, they will often blame their victims for "causing" their wrong actions, or deserving of their fate
- The aggressive features of this personality disorder make it stand out among other personality disorders as individuals with this disorder take a unique toll on society

Borderline Personality Disorder

Description

Borderline Personality Disorder is one of the most widely studied personality disorders. People with this disorder tend to experience intense and unstable emotions and moods that can shift fairly quickly. They generally have a hard time calming down once they have become upset. As a result, they frequently have angry outbursts and engage in impulsive behaviours such as substance abuse, risky sexual liaisons, self-injury, overspending, or binge eating. These behaviours often function to soothe them in the short-term, but harm them in the longer term.

Signs & Symptoms

People with Borderline PD tend to see the world in polarised, over-simplified, all-or-nothing terms

- They apply their harsh either/or judgments to others and to themselves and their perceptions of themselves and others may quickly vacillate back and forth between "all good" and "all bad"
- This tendency leads to an unstable sense of self, so that persons with this disorder tend to have a hard time being consistent
- They can frequently change careers, relationships, life goals, or residences. Quite often these radical changes occur without any warning or advance preparation

Black-and-White or All or Nothing Thinking

Their tendency to see the world in black-or-white (polarised) terms makes it easy for them to misinterpret the actions and motivations of others. Suppose the partner of a woman with Borderline PD fails to remember their anniversary. Black-and-white thinking causes her to conclude, "He doesn't love me anymore" and all-or-nothing thinking leads her to (falsely) conclude, "If he does not love me, then he must hate me."

Emotion Dysregulation

- These polarised thoughts about their relationships with others lead them to experience intense emotional reactions, which in turn interacts with their difficulties in regulating these intense emotions
- The result is that they will characteristically experience great distress which they cannot easily control and may subsequently engage in self-destructive behaviours as they do their best to cope
- The intensity of their emotions, coupled with their difficulty regulating these emotions, leads them to act impulsively

Clearly, the Borderline Personality Disorder with its combination of distorted thought patterns, intense and under-regulated emotions, and poor impulse control is practically designed to wreak havoc on any interpersonal relationship.

Histrionic Personality Disorder

Description

Persons with *Histrionic Personality Disorder* are characterised by a *pattern* of excessive emotionality and attention seeking. Their lives are full of drama (so-called "drama queens"). They are *uncomfortable* in situations where they are *not the centre of attention*.

Signs & Symptoms

People with this disorder are often quite *flirtatious* or *seductive*, and like to dress in a manner that draws attention to them

- They can be flamboyant and theatrical, exhibiting an exaggerated degree of emotional expression
- Yet simultaneously, their emotional expression is vague, shallow, and lacking in detail. This gives them the appearance of being disingenuous and insincere
- Moreover, the drama and exaggerated emotional expression often embarrasses friends and acquaintances as they may embrace even casual acquaintances with excessive ardor, or may sob uncontrollably over some minor sentimentality

People with this disorder can also *appear flighty* and *fickle*. Their behavioural style often gets in the way of truly intimate relationships, but it is also the case that they are uncomfortable being alone

- They tend to feel depressed when they are not the centre of attention. When they are in relationships, they often imagine relationships to be more intimate in nature than they actually are
- They tend to be *suggestible*; that is, they are *easily influenced by other people's suggestions and opinions*.

Narcissistic Personality Disorder

Description

People with *Narcissistic Personality Disorder* have significant problems with their sense of self-worth stemming from a powerful sense of entitlement. This leads them to believe they deserve special treatment, and to assume they have special powers, are uniquely talented, or that they are especially brilliant or attractive. Their sense of entitlement can lead them to act in ways that fundamentally disregard and disrespect the worth of those around them.

Signs & Symptoms

People with Narcissistic PD are preoccupied with fantasies of unlimited success and power, so much so that they might end up getting lost in their daydreams while they fantasise about their superior intelligence or stunning beauty

- These people can get so caught up in their fantasies that they don't put any effort into their daily life and don't direct their energies toward accomplishing their goals
- They may believe that they are special and deserve special treatment, and may display an attitude that is arrogant and haughty
- This can create a lot of conflict with other people who feel exploited and who dislike being treated in a condescending fashion

People with this disorder also often feel devastated when they realise that they have normal, average human limitations; that they are not as special as they think, or others don't admire them as much as they would like

- These realisations are often accompanied by feelings of intense anger or shame that they sometimes take out on other people
- Their need to be powerful, and admired, coupled with a lack of empathy for others, makes for conflictual relationships that are often superficial and devoid of real intimacy and caring
- Status is very important to these people i.e. associating with famous and special people provides them a sense of importance
- These individuals can quickly shift from over-idealising others to devaluing them

However, the same is true of their self-judgments

- They tend to vacillate between feeling like they have unlimited abilities, and then feeling deflated, worthless, and devastated when they encounter their normal, average human limitations
- Despite their bravado, they require a lot of admiration from other people in order to bolster their own fragile self-esteem
- They can be quite manipulative in extracting the necessary attention from those people around them

Cluster C: Anxious, Fearful

DSM-5: The Ten Personality Disorders: Cluster C

Introduction

Cluster C is called the *anxious, fearful* cluster. It includes:

- Avoidant Personality Disorders
- Dependent Personality Disorders
- Obsessive-Compulsive Personality Disorders

These three personality disorders share a *high level of anxiety*.

Avoidant Personality Disorder

Description

The *Avoidant Personality Disorder* is characterised by a pervasive pattern of social inhibition, feelings of inadequacy, and a hypersensitivity to negative evaluation.

Signs & Symptoms

People with this disorder are intensely afraid that others will ridicule them, reject them, or criticise them

- This leads them to avoid social situations and to avoid interactions with others. This further limits their ability to develop social skills
- They often have a very limited social world with a small circle of confidants. Their social life is otherwise rather limited

Dependent Personality Disorder

Description

The core feature of the *Dependent Personality Disorder* is a strong need to be taken care of by other people. This need to be taken care of, and the associated fear of losing the support of others, often leads people with Dependent PD to behave in a "clingy" manner; to submit to the desires of other people.

Signs & Symptoms

- In order to avoid conflict, they may have great difficulty standing up for themselves
- The intense fear of losing a relationship makes them vulnerable to manipulation and abuse
- They find it difficult to express disagreement or make independent decisions, and are challenged to begin a task when nobody is available to assist them
- Being alone is extremely hard for them
- When someone with Dependent PD finds that a relationship they depend on has ended, they will immediately seek another source of support

Obsessive-Compulsive Personality Disorder

Description

Persons with *Obsessive-Compulsive Personality Disorder* are preoccupied with rules, regulations, and orderliness. This preoccupation with perfectionism and control is at the expense of flexibility, openness, and efficiency. They are great makers of lists and schedules, and are often devoted to work to such an extent that they often neglect social relationships. Please note this **personality** disorder is not the same as OCD.

Signs & Symptoms

- They have perfectionist tendencies, and are so driven in their work to "get it right" that they become unable to complete projects or specific tasks because they get lost in the details, and fail to see the "forest for the trees"
- They tend to be rigid and inflexible in their approach to things. It simply isn't an option for them to do a "sub-standard" job just to get something done. Often, they are unable to delegate tasks for fear that another person will not "get it right"
- Sometimes they adopt a miserly style with both themselves and others
- Money is regarded as something that must be rigidly controlled in order to ward off future catastrophe
- People with this disorder are often experienced as rigid, controlling, and stubborn

SUBSTANCE-USE DISORDERS (ADDICTION)

Introduction

Over the years there has been a change in the terms we use to describe drug addiction due to stigma; they are now referred to as substance use disorders. These include: drug addiction, gambling, internet addiction, food addiction, compulsive shopping.

There are three levels of abuse that exist:

1. *Experimental*: people trying it for the first time to see what it is like. Peer pressure?
2. *Recreational*: people start using it to have fun
3. *Habitual*: the usage is so frequent it has now become a habit

Definitions

Definition	Description
Dependence	<ul style="list-style-type: none">• A person's need to take a substance to feel 'normal'. It is characterised by the symptoms of tolerance and withdrawal• While it differs from addiction, it can lead to it
Tolerance	<ul style="list-style-type: none">• Reduced response after repeated administration of the drug (usually due to receptor/secondary messenger desensitisation and down-regulation)• Can occur in the absence of dependence <p>Types of tolerance</p> <ol style="list-style-type: none">1. Acute/chronic2. Cross-tolerance: repeated use of a drug in a given category confers tolerance to the drug being used AND others within the same pharmacological category3. Metabolic/PK tolerance: increased metabolism requires increasing doses to produce the same pharmacological effect4. PD tolerance: increasing doses required to produce the same effect (learned behaviour) e.g. alcohol
Addiction	<ul style="list-style-type: none">• A disease (unlike dependence and tolerance) marked by a change in behaviour caused by the biochemical changes in the brain after continued substance abuse• Substance use becomes the main priority of the addict, regardless of the harm they may cause to themselves or others• Causes people to act irrationally when they don't have the substance they are addicted to in their system
Withdrawal	<ul style="list-style-type: none">• The reversal of "abnormal" homeostatic state in the presence of a drug to the normal state

Recreational Drugs

Drug (WHO): A chemical entity used, non-medically, self-administered for its psychoactive effect

Drug Class		CD Class	Other Names
CNS Depressants	Alcohol		
	Benzodiazepines	Class C	Xanax, Roofies
	Barbiturates		
CNS Stimulants	Amphetamines	Class B	Amphetamine (Adderall): Speed, billy
			Methamphetamine: Meth, P, Ice
			Methylphenidate (Ritalin): Vitamin R, ritz, Posh
	MDMA (3,4-Methylenedioxymethamphetamine)	Class A	Ecstasy (XTC), E, Brownies, Molly, MD, Mandy, Pinglers
	BZP (Benzylpiperazine)	Class C	Party Pills, Happy pills, blast
	Cocaine	Class A	Coke, crack, snow, white
	Oxycodone	Class B	
	Morphine	Class B	

Opioids	Codeine	Class C	
	Methadone	Class B	
	Heroin	Class A	Gear
Hallucinogens	LSD (Lysergic acid diethylamide)	Class A	Acid, Lucy, Flash, Trips
	Psilocybin		
	Ketamine	Class B	Ket, K, Vitamin K, Special K, Green
Cannabinoids	Cannabis	Class B	Weed, marijuana, pot, grass, kush
Anaesthetic	Nangs (nitric oxide)		Laughing gas, NOS

Pathophysiology

Drugs induce addiction/dependence by activating the following two systems for the dopaminergic (reward) pathways e.g. nicotine, alcohol, amphetamines, THC.

1. *Mesolimbic* system (euphoria, delusions, pleasure) &
2. *Mesocortical* system (cognition, emotion)

The VTA is the origin of dopaminergic cell bodies of the mesocorticolimbic dopamine system and other dopamine pathways; it is widely implicated in the drug and natural reward circuitry of the brain.

- GABAergic interneuron feedback projections provide tonic inhibition of VTA dopaminergic neurons
- However, naturally occurring neurotransmitters (e.g. ACh, enkephalins, DA) that reinforce adaptive behaviours (such as eating, drinking, sex) can activate it

Psychotropics often bypass neurotransmitters and directly stimulate receptors causing DA release and the “artificial high”. The speed a drug enters the brain dictates 2 factors:

1. Degree of the ‘subjective high’ — the faster it enters your system the ‘higher you get’
2. Speed with which addiction can be induced

Impulsivity → Addiction → Compulsivity

Substance and behavioural addictions are disorders that manifest as deficits in impulse control and/or compulsive control. Both of these are natural and essential behaviours controlled by brain mechanisms and both types share the inability to inhibit or delay repetitive behaviours.

	Impulsivity	Compulsivity
Description	Impulsivity describes action without forethought and/or a lack of reflection about the consequences of one's behaviour	Compulsivity describes a persisting action that is inappropriate and often results in undesirable consequence
Drive	Impulsivity is driven by the desire to obtain pleasure, arousal, or gratification . Inability to postpone immediate reward for a more beneficial but delayed reward	Compulsivity is driven by an attempt to alleviate anxiety or discomfort . Inability to adapt behaviour after negative feedback.
Structure	Mediated by the Ventral Striatum (NAc)	Mediated by the Dorsal Striatum
Neuro-Circuitry	Hypothetically speaking, impulsive-compulsive behaviours are neuro-biologically driven ‘bottoms up’ — they are caused by the relaxation of the circuit and suppressed by the prefrontal cortex	
Examples	Pyromania, kleptomania, impulsive violence, antisocial behaviour, mania, ADHD	Obsessive-Compulsive Spectrum Disorders, hair pulling, skin picking, body dysmorphic disorder, hoarding, Tourette's, autism spectrum disorder

Over time, compulsive behaviours may become impulsive (reinforced habits) and impulsive behaviours may become compulsive (driven behaviours without arousal). **Addiction, specifically, causes the latter shift.**



Understanding Impulsivity vs Compulsivity

When the person first takes a drug, it is usually impulsive to receive the pleasure/satisfaction ("high"). When the behaviour is infrequent, it is viewed as bad but doesn't necessarily lead to compulsiveness. However, the impulsiveness may lead to the person becoming addicted. As the drug use becomes more chronic, compulsivity develops as the drive changes from seeking pleasure to seeking relief from the withdrawal symptoms and anticipation of obtaining/consuming the drug.

Risk Factors

Factors	Description
Iatrogenic cause	The use of medically prescribed drugs for a chronic medical condition (e.g. insomnia, headache, anxiety, pain) can be influenced by social and environmental factors, with potential to lead to addiction. <ul style="list-style-type: none">• Iatrogenic addictions, in contrast to illicit drug addictions, are commonly maintained for years before being brought to the attention of mental health professionals• By the time treatment is sought, both the physiological addiction and its related psychological problems may have encapsulated the patient's lifestyle — there is usually a progressive constriction of social and occupational functioning
Genetic Pre-disposition	There are a number of genes associated with dependence. Thus, addiction can run in families, making certain people genetically pre-disposed to being addicted/dependent to a drug.
Medical Conditions	Depression, ADHD, PTSD
Other	Difficult childhood, peer pressure, use of drugs while the brain is still developing (early use)

Diagnosis

DSM-V Criteria For Substance Use Disorders

The person must meet **2 or more criteria** from the list within the last 12-month period

1. Impaired Control
2. Social Impairment
3. Risky Use
4. Pharmacological Dependence

Assessment

- A&D History
- Physical Examination
- Laboratory Tests
- Other investigations as indicated e.g. checking for malnutrition

Alcohol Dependence & Withdrawal

[Maudsley's Prescribing Guidelines in Psychiatry p. 387](#) [NICE Guidelines UK](#)

Description

Drinking alcohol is an integral part of the social culture in New Zealand - however the prevalence of hazardous drinking in this country is also high.

A stylized illustration of a doctor wearing blue scrubs and a stethoscope, holding a clipboard in their left hand.

Alcohol Drinking Guidelines

Females

- Daily limit: 2 standard drinks AND
- Weekly limit: 10 standard drinks (with at least two days with no drinking)

Males

- Daily limit: 3 standard drinks AND
- Weekly limit: 15 standard drinks (with at least two days with no drinking)

Alcohol Addiction/Dependence

Alcohol addiction and dependence describes the most serious form of high-risk drinking, often characterised by a strong, often uncontrollable desire, to drink. This level of drinking is capable of causing harm to your health and the decision to stop the vicious cycle is not easy.

Alcohol Withdrawal

Alcohol withdrawal can occur when alcohol use has been heavy and prolonged and is then stopped or greatly reduced. It presents with many symptoms which vary in severity and can be life-threatening.

Pathophysiology

Alcohol is believed to mimic GABA, the main inhibitory neurotransmitter in the brain resulting in dampening of activity. However, constant supply in alcohol-dependent drinkers causes the CNS to adjust in response to the overstimulation by decreasing GABA receptors (neuroadaptation). Thus, when blood-alcohol concentration (BAC) falls, fewer GABA receptors result in the brain remaining in a hyper-excited state, resulting in the withdrawal syndrome.

Alcohol either acts directly on opioid μ receptors or releases endogenous opiates (encephalin, endocannabinoids), leading to increased DA release in NAc. Reinforcing effects are theoretically mediated by enhancing GABA inhibition and reducing glutamatergic excitation.

Risk Factors

A person may fall into the loop of heavy alcohol use due to a number of different reasons:

Societal Factors

- Economic development, culture, social norms, availability of alcohol
- Implementation and enforcement of alcohol policies

Individual Factors

- Age, gender, family circumstances, SES

Signs & Symptoms

Alcohol Dependence

- Person often places drinking above other obligations i.e. gives increasing priority to alcohol
- Develops physical tolerance (drinks more for a similar effect)
- Impaired control over alcohol use
- Unwanted physical or mental effects from drinking (e.g. suicide, malnutrition)

Diagnosis - Alcohol Dependence

[Alcohol Use Disorder Identification Test \(AUDIT-C\)](#): Identifies potentially hazardous drinking

- Females ≥ 3 and males ≥ 4 proceed to full AUDIT (as hazardous drinking identified)

[Full AUDIT tool](#): Identifies level of hazardous drinking

People who score **≥ 20 on AUDIT** are likely to be dependent on alcohol

- Low risk: ≤ 5 points for females, ≤ 6 points for males
- Medium risk: 6–12 points for females, 7–14 points for males
- High risk: ≥ 13 points for females, ≥ 15 points for males

[Severity of Alcohol Dependence Questionnaire \(SADQ\)](#)

Diagnosis - Alcohol Withdrawal

- [Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised \(CIWA-Ar\)](#)
- [PAWSS Score for Predicting Risk of Severe Alcohol Withdrawal](#)

Goal of Treatment

To curb the strong, often uncontrollable desire to drink

Monitoring

Laboratory Investigations

- Full Blood Count (FBC)
- Urea & Electrolytes (U&E)
- Liver Function Tests (LFTs)

- International Normalised Ratio (INR)
- Pro-Thrombin (PT)
- Urinary Drug Screen

Non-Pharmacological Treatment

- Counselling, Self-Help, Talk therapy, Group Therapy, CBT

A Note on ABC Approach

- The ABC approach is recommended at every opportunity to identify patients who may benefit from reducing their alcohol intake:
- Ask about alcohol
- Brief advice
- Counselling



Alcohol & Cold Turkey

While this method can be useful/safe for certain addictions such as smoking or those that do not have addiction treatment e.g. amphetamines, it can be extremely dangerous for severe alcohol dependence.

There are two particular concerns:

1. An overdose can occur if the person relapses as cold turkey can quickly drop the body's tolerance to the substance
2. Withdrawal can be fatal and life-threatening

Pharmacological Treatment

BPAC Alcohol Misuse Treatment Guidelines

All pharmacological interventions are to be used as an adjunct to psychological approaches and aim to reduce alcohol consumption. Pharmacologically assisted withdrawal is likely to be needed when:

1. Regular consumption of >15 units/day
2. AUDIT score >20
3. There is a history of significant withdrawal symptoms

ACUTE TREATMENT <i>Alcohol Withdrawal Symptoms</i>			
Severity	Timing After Last Drink	Withdrawal Symptoms	Recommended Treatment
Mild Withdrawal Symptoms	Onset 3-12 hours	Irritability, Agitation, Restlessness, Tremors.	Long acting benzodiazepine (Diazepam): <ul style="list-style-type: none"> • Short term treatment — <i>do not ingest alcohol as combination can cause respiratory depression</i>
		Skin Itching	Oral Antihistamines
		Dehydration	IV Fluids
	Peak at 24-48 hours	Nausea	<ul style="list-style-type: none"> • Metoclopramide 10mg • Prochlorperazine 5mg 4-6 hourly — <i>may decrease absorption of vitamin B1 (thiamine)</i>
		Diarrhoea	Loperamide
		Headache	Paracetamol
		Sweating	N/A
		Generalised Seizures	<i>First Line:</i> Long acting benzodiazepine (Diazepam) <i>Second Line:</i> Carbamazepine
Complications of Withdrawal	-	Wernicke's Encephalopathy (Thiamine (vitamin B1) Deficiency)	Thiamine (Vitamin B1): during the first week of cessation <ul style="list-style-type: none"> • Pabrinex: At least 2 pairs (4 ampoules) TDS for 3-5 days, followed by 1 pair (2 ampoules) OD for 3-5 days or longer. • If allergy symptoms (but not anaphylactic): administer oral antihistamine prior to Pabrinex
		Problems sleeping (insomnia)	Long acting benzodiazepine (Diazepam)
	Onset 3-4 days	Hallucinations (Tactile & Visual)	Haloperidol
	Duration up to 14 days	Fever, tachycardia, systolic HTN, general malaise	Tachycardia: β-blockers

LONG TERM TREATMENT Prevention of Drinking			
Medicine	MoA	Dose	ADR
[PRESCRIPTION] <i>Naltrexone</i> (Naltraccord)	<p>Strongly Recommended (initiated in secondary care)</p> <ul style="list-style-type: none"> Opioid receptor antagonist which prevents increased dopaminergic activity after drinking, therefore reducing its rewarding effects <p>Treatment should be stopped for those who continue to drink 4-6 weeks after starting.</p>	<p>Max 3 months treatment 50mg OD</p> <ul style="list-style-type: none"> Do not take with opioids as this is an opioid antagonist. If opioids are necessary, use 48–72 hours after cessation of naltrexone. 	<p>Nausea, headache, abdominal pain, reduced appetite, tiredness</p> <p>Do not start if not opioid free for 7-10 days.</p>
[PRESCRIPTION] <i>Acamprosate</i> (Campral)	<p>Strongly Recommended</p> <ul style="list-style-type: none"> NMDA antagonist Increase GABA-ergic function <p>Treatment should be stopped for those who continue to drink 4-6 weeks after starting.</p>	<p>Treatment for approx. 6 months</p> <ul style="list-style-type: none"> Adult (16 - 65y + ≥ 60kg): 666mg TDS Adult (16 - 65y + < 60kg): 666mg OD, 333mg BD 	<p>N/V/D, abdominal pain, pruritus Avoid in pregnancy and breastfeeding</p>
[PRESCRIPTION] <i>Disulfiram</i> (Antabuse)	<p>Moderate Recommendation (can be initiated in primary care with funding and without restrictions)</p> <ul style="list-style-type: none"> Inhibits aldehyde dehydrogenase (ALDH), therefore preventing complete metabolism of alcohol in the liver. This results in an accumulation of the toxic product which causes the alcohol-disulfiram reaction for alcohol aversion i.e. produces an acute sensitivity to ethanol. Note: Metronidazole also has a “disulfiram-alcohol reaction” 	<p>Start treatment 24 hours after the last drink (use if acamprosate or naltrexone is not suitable).</p> <ul style="list-style-type: none"> 800mg for the first dose, reducing to 100-200mg OD for maintenance No immediate benefit, often family support determines effectiveness 	<p>Mild alcohol-disulfiram reaction:</p> <ul style="list-style-type: none"> Facial flushing, Sweating Nausea, Hyperventilation Dyspnoea, Tachycardia Hypotension <p>Severe alcohol-disulfiram reaction:</p> <ul style="list-style-type: none"> Acute heart failure, MI, Arrhythmias, Bradycardia Respiratory depression Severe hypotension <p>Contraindications:</p> <ul style="list-style-type: none"> Ingestion of alcohol within the previous 24 hours Cardiac failure, CAD, HTN Cerebrovascular disease Pregnancy, Breastfeeding Liver disease, Peripheral neuropathy Severe mental illness
[PRESCRIPTION] <i>Topiramate</i> (Topamax) (Unlicensed)	<p>Weak Recommendation</p> <ul style="list-style-type: none"> Reduce dopamine activity in the reward pathway of alcohol ingestion 	25mg OD, increasing to 300mg OD	<p>Paraesthesia, dizziness, taste perversion, anorexia and weight loss, memory and concentration difficulties</p>
[PRESCRIPTION] <i>Baclofen</i> (Pacifen) (Unlicensed)	<p>Weak Recommendation</p> <ul style="list-style-type: none"> GABA_A agonist 	10-20mg TDS	

Monitoring

Long-term follow up is essential - recovery from alcohol misuse can be a lifelong process for those who are severely affected. These people require an ongoing commitment to sobriety with regular support and monitoring for relapse. Health professionals in primary care are well-placed to help, however, continued backing from family and friends and support organisations are essential for people who are committing to a life free of alcohol.

Generally

- Alcohol Interactions — see [BPAC Alcohol Misuse Treatment Guidelines](#)
- Respiratory depression: if continue drinking, additive effect with benzo's

Helplines

All services are free and available 24/7 unless otherwise specified.

For counselling and support

- Lifeline: Call 0800 543 354 or text 4357 (HELP)
- Suicide Crisis Helpline: Call 0508 828 865 (0508 TAUTOKO)
- Need to talk? Call or text 1737
- Depression helpline: Call 0800 111 757 or text 4202

For children and young people

- Youthline: Call 0800 376 633 or text 234
- What's Up: Call 0800 942 8787 (11am to 11pm) or webchat (11am to 10.30pm)
- The Lowdown: Text 5626 or webchat

For help with specific issues

- Alcohol and Drug Helpline: Call 0800 787 797
- Anxiety Helpline: Call 0800 269 4389 (0800 ANXIETY)
- OutLine: Call 0800 688 5463 (0800 OUTLINE) (6pm-9pm)
- Safe to talk (sexual harm): Call 0800 044 334 or text 4334

Opioid (Narcotics) Addiction — OST

Please visit *Chapter 20 - Fever, Pain & Infection* for more information on Opioids.

Description

Opioids are commonly prescribed for moderate to severe pain relief. With prolonged use, pain-relieving effects may lessen and pain can become worse. In addition, the body can develop dependence.

Opioid dependence causes withdrawal symptoms, which makes it difficult for people to stop taking them. Addiction occurs when dependence interferes with daily life. Taking more than the prescribed amount or using illegal opioids such as heroin may result in death.

Signs & Symptoms

Symptoms of addiction include uncontrollable cravings and inability to control opioid use even though it is having negative effects on personal relationships or finances.

Pathophysiology

Opioids act on opioid neurons which arise in the arcuate nucleus and project to the VTA and NAc. They bypass enkephalins to directly stimulate receptors causing dopamine release and therefore the ‘artificial high’. With abuse, dependence readily occurs. Chronic administration will lead to neuroadaptation, receptor desensitisation and eventual tolerance (which decreases after 3-4 days).

Non-Pharmacological Treatment

- Cold Turkey

Pharmacological Treatment

1. Dependence: Opioid Substitution Therapy (OST)
2. Withdrawal: Clonidine (Autonomic symptoms) + Loperamide (GI symptoms)

Opioid Substitution Treatment (OST)

OST Supply Guidelines

OPIOID SUBSTITUTION TREATMENT (OST)				
	Description	Prescribing & Paperwork	Cautions	ADRs
Methadone (Biodone) 2mg/ml (pink) 5mg/ml (Forte - clear) 10mg/ml (Extra Forte - orange)	Class B3 - Liquid Methadone is an opioid agonist used for moderate to severe pain treatment as well as opioid dependence. • It takes 5-6 days to reach a steady state and may need thereafter dose adjustments.	Prescribing <ul style="list-style-type: none"> Can only be prescribed by prescribers in authorised methadone maintenance treatment clinic e.g. Specialist Addiction Services or permitted individual GPs. Prescription quantity: 28 days Exemption permitting emergency treatment for dependence in hospital and not exceeding 3 days. Maximum Takeaway doses: 5 Paperwork <ul style="list-style-type: none"> Must be prescribed on a controlled drug prescription form, written in register and kept in locked safe Patient cannot be given an extra dose. 	<ul style="list-style-type: none"> This medicine can be dangerous if you have taken alcohol or other medicines that can make you sleepy, if you exceed your recommended dose, or if you are particularly sensitive to its effects. 	Dry mouth, constipation, drowsiness, dizziness, nausea, vomiting, dental problems. Interaction Warning <ul style="list-style-type: none"> Urinary alkalinisers Sedating Anti-histamines
Buprenorphine + Naloxone (Suboxone)	Class C4 - Sublingual Tablet Buprenorphine is a mu agonist and kappa antagonist while Naloxone is a mu, delta and kappa antagonist. Its purpose is to enhance the opioid blocking properties of buprenorphine and discourages misuse. For example, naloxone has no effect if taken orally. However it is active if injected intravenously, therefore the component of naloxone in the Suboxone tablet is to prevent misuse by patients i.e. IUD Note: In some cases, the dose can be doubled to extend its half life	Prescribing <ul style="list-style-type: none"> Prescription quantity: 84 days (12 weeks) Must be kept in safe Maximum Takeaway doses: 6 Paperwork <ul style="list-style-type: none"> Must be prescribed on a controlled drug prescription form 	<ul style="list-style-type: none"> This medicine may make you sleepy. If this happens, do not drive or use tools or machines. Do not drink alcohol. Dissolve this medicine under your tongue, it will not be absorbed if swallowed. Tablets may be broken into a few pieces to speed up absorption (but care should be taken not to crush into powder). 	Can induce mild withdrawal symptoms in patients dependent on opioids; also diarrhoea, abdominal pain, anorexia, dyspepsia; vasodilation; dyspnoea; paraesthesia, asthenia, fatigue, agitation, anxiety

A Note on Specialist Addiction Services (SAS)

- They are very firm towards patient enrolled in the program as there is a long waiting list
- Fully funded program
- Carry out routine and random: calls, urine & blood tests
- May grant takeaway doses but retract this if the patient misbehaves

GP Prescribing of OST

- GPs can be authorised to prescribe by SAS, but they need to review this every 3 months
- GPs in hospital can prescribe for 3 days, which gives them time to hear back from SAS

Missed doses of OST

- If 1 dose is missed: Report to SAS
- If 3 doses are missed: Report to SAS and do not administer any more doses (as the dose may be too high for them — may be fatal)

Needle Exchange Programme

- Safe space which offers clean needles and return of used needles to stop infections from spreading, else patients may use the same needles.

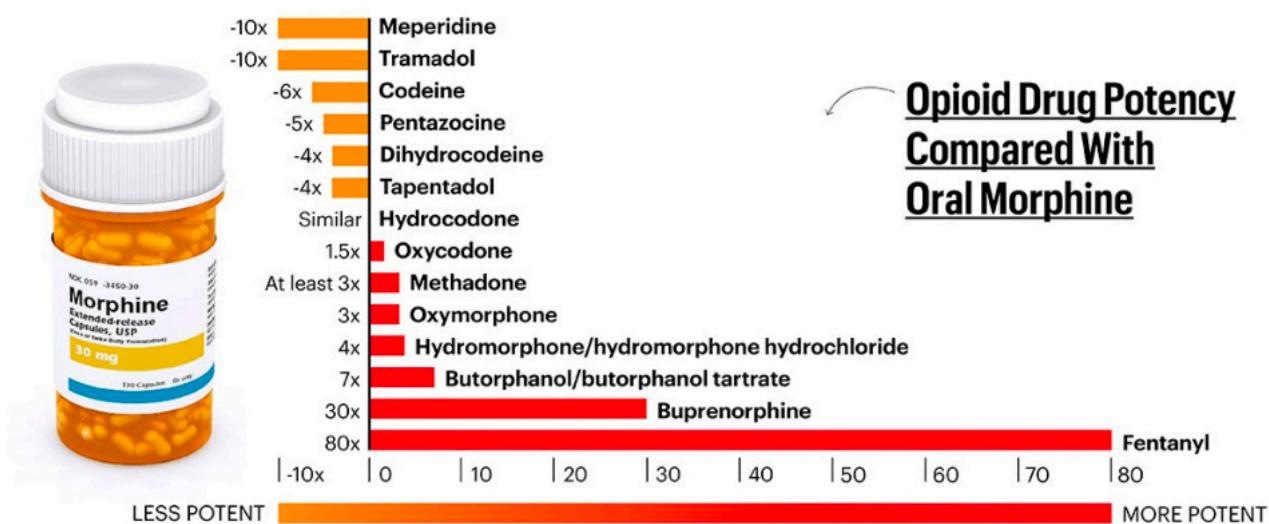
Methadone or Buprenorphine are used to treat dependence — not induce abstinence

Opioid Equivalent to Methadone		
Drug	Total Daily Dose (mg)	Equivalent Methadone Dose (mg)
Buprenorphine S/L	0.2	5
Codeine Phosphate	15	1
Dihydrocodeine	30	2.5
Fentanyl Patches (mcg/h)	25	2
Gee's Linetus	100	10
Oral Morphine	15	10
Morphine Injection BP	10	10
LA Morph Tablets	10	3.25
Pethidine Injection/Tablets	50	4.25
Tramadol	50	1.6

THE DRUGS

THE FDA HAS APPROVED 18 OPIOID DRUGS

The generic names are listed here. Drugs primarily used in surgery (such as alfentanil and remifentanil) were not included.



Cannabis THC (Marijuana) Addiction

Description

The cannabis plant makes 2 natural compounds; cannabidiol (CBD) and tetrahydrocannabinol (THC). While CBD can treat addiction, THC can cause it as it is an analogue of the endogenous neurotransmitter anandamide.

BENEFIT/RISK EVALUATION OF CANNABIS		
	Benefit	Risk
Substantial Evidence	<ul style="list-style-type: none">• Chronic Pain• Chemo-Induced Nausea• MS Spasticity	<ul style="list-style-type: none">• Respiratory symptoms• Motor vehicle crashes• Low birth weight• Psychosis
Moderate Evidence	<ul style="list-style-type: none">• Obstructive Sleep Apnoea• Fibromyalgia• Chronic Pain• MS• Psychosis Cognition	<ul style="list-style-type: none">• Paediatric overdose• Impaired learning, memory, attention• Increased (hypomania) in bipolar• Depression/suicidality• Social Anxiety Disorder (SAD)• Substance use disorder development towards other drugs
Limited Evidence	<ul style="list-style-type: none">• Decreasing weight loss• HIV• Tourette's• Anxiety• PTSD	<ul style="list-style-type: none">• Testicular cancer• CVD: MI, IHD, Pre-diabetes• Respiratory: COPD• Pregnancy complications• Increased unemployment,• Impaired social functioning, academic achievement• Increased schizophrenia positive symptoms• Bipolar disorder• Anxiety disorders (other than social anxiety)

Currently, synthetic THC is only approved for severe and rare forms of epilepsy.

Pathophysiology

Cannabinoids in the mesolimbic pathway

Anandamine is a retrograde neurotransmitter and shares most, but not all the properties of THC. CB₁ receptors mediate marijuana's reinforcing properties.

Pharmacological Treatment

- No dependence treatment exists
- Withdrawal treatment exists: methadone, buprenorphine

Nicotine Addiction — NRT

Description

Nicotine addiction occurs when a person becomes addicted to nicotine, which is a chemical found in tobacco. In addition to its many health risks, smoking induces CYP enzymes — causing many interactions with many medicines.

Pathophysiology

Nicotine is a N-cholinergic agonist that activates DA release in VTA. It is both a CNS stimulant and depressant. Tolerance can be acute or chronic. Nicotine is easily the most dependence-inducing drug that exists due to rapid brain entry and place conditioning. Withdrawal can also be difficult.

Signs & Symptoms

Withdrawal

- Irritability, impatience, hostility, anxiety, dysphoria
- Difficulty concentrating, restlessness
- Decreased HR, increased appetite/weight gain

Non-Pharmacological Treatment

- Cold Turkey

Pharmacological Treatment

Guide to Prescribing Nicotine Replacement Therapy (NRT)

- Nicotinic partial agonist: Varenicline
- Anti-craving medication: Bupropion (Zyban)
- Nicotine Replacement Therapy (NRT)

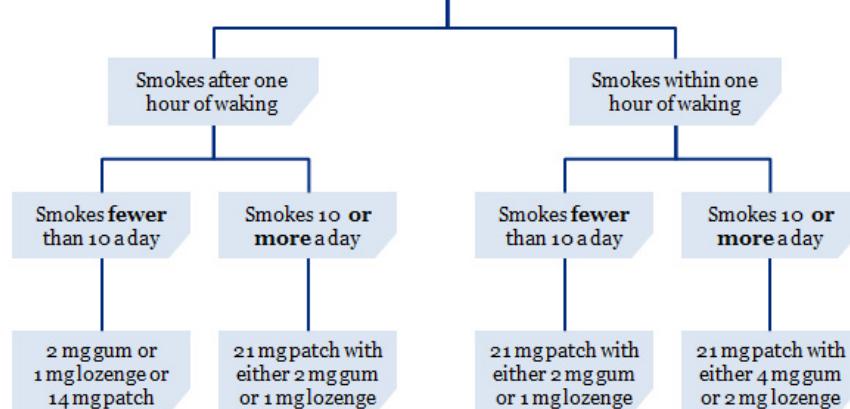
Step 1: Explain how NRT works and the products available

NRT provides some of the nicotine that a person gets from smoking. Nicotine is the addictive part of cigarettes but does not cause the harm associated with smoking. NRT works to reduce craving and other withdrawal symptoms associated with stopping smoking.

Step 2: Assess the time when the first cigarette is smoked (see note 1)

Step 3: Assess how many cigarettes are smoked (see note 2)

Step 4: Recommend which product and dose to use and explain how to use the product (see below)



Subsidised NRT products				Unsubsidised NRT	
Product information	Patch*	Gum*	Lozenge*	Inhalator	Mouth spray
Instructions for correct use	Three strengths (21 mg, 14 mg, and 7 mg) Apply patch to clean, dry and hairless skin. Remove the old and apply new patch daily, alternating sites. Some redness under the patch may occur – this is normal. The patch can be removed overnight if sleep is disturbed.	Two strengths (4 mg and 2 mg) Recommend regular use. Bite to release the peppery taste and then rest in the side of the mouth (between cheek and gum). Chew again when the taste starts to fade. Chew for about 30 minutes then discard.	Two strengths (2 mg and 1 mg) Recommend regular use. Suck to release the peppery taste, and then rest in the side of the mouth (between cheek and gum). Suck again when the taste starts to fade. Chew for about 30 minutes then discard.	15 mg cartridge Recommend regular use. Puff for 20 minutes each hour and replace the cartridge every 3 hours. People tend to under-dose (1 cigarette puff = 10 inhalator puffs).	1 mg nicotine/spray dose Recommend regular use, but it can also be used when craving occurs. Prime the spray and point nozzle into the mouth, spraying towards the side of the mouth. For best results, do not swallow for a few seconds after spraying.

- * Patches, gum and lozenges are subsidised if supplied on prescription or via the Quit Card programme. Otherwise, all NRT products (including the inhalator and mouth spray) can be purchased over the counter from supermarkets for the normal retail price. Community pharmacies can also provide subsidised NRT without a prescription and many stop-smoking providers supply NRT at no cost to clients.

Amphetamine Addiction

Description

Amphetamines e.g. ecstasy are stimulant drugs, which means they speed up the messages travelling between the brain.

Pathophysiology

Amphetamines are competitive inhibitors of DA and NA at their respective transporters as well as at vesicular monoamine transporter (VMAT). In high levels, they will displace DA from their vesicles into the axon terminal — when a critical threshold of DA is reached, it is expelled from the terminal by opening channels. This allows a large scale release of DA into the synapse, causing euphoria.

Amphetamines can induce significant damage to both serotonin and dopamine neurons.

Pharmacological Treatment

Treatment for amphetamine addiction does not exist, instead it is for overdose:

1. *Preventing CVD ADRs*: β -blockers or DHP-CCBs
2. *Seizures*: diazepam
3. *Psychosis*: anti-psychotics
4. *Other*: acidification of urine, physical lowering of body temperature

Hallucinogen Addiction

Description

Hallucinogens e.g. LSD mescaline, DMT typically do not cause dependence. Instead, intoxication is associated with ‘bad trips’ or panic attacks. Hallucinogens are currently used to treat depression, GAD (especially in cancer patients) and PTSD

Pathophysiology

Hallucinogens are all 5-HT_{2A} agonists that also affect NA and DA release and reuptake to varying degrees.

4 classes of hallucinogens:

- Indoleamines
- Phenethylamines
- NMDA antagonists
- Kappa opioid agonists

Pharmacological Treatment

- Benzodiazepines

EATING DISORDERS

Description

MARSIPAN Guidelines

An eating disorder is a condition that involves eating in a disordered way, such as eating very little or very large amounts of food, or purging (getting rid of) food you have eaten. The most common eating disorders include anaemia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED) — which arises from a focus on weight and body shape. A new category of eating difficulties is avoidant restrictive food intake disorder (ARFID) which involves a disinterest in food for other reasons. Eating disorders can affect any age or gender; however, women are more often affected, particularly younger women.

Food is the only thing that can cure eating disorders! However, the reintroduction of food must be carefully administered due to the possibility of re-feeding syndrome. This can be defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving artificial re-feeding (whether enterally or parenterally). These shifts result from hormonal and metabolic changes and may cause serious clinical complications

Risk Factors

- Societal factors and environments associated with body image
- Personal events

Signs & Symptoms

Eating Disorders

- Muscle wasting
- Electrolyte abnormalities, cardiovascular complications
- Absence of periods
- Osteoporosis
- Purge through vomiting: loss of tooth enamel, GI erosion, dehydration
- Purge through: laxative/insulin/thyroxine abuse (increase metabolism)

Complication of Re-feeding Syndrome

- Neurological disability (Wernicke-Korsakoff's syndrome)
- Electrolyte and metabolic complications
- Acute anaemia
- Potential death

Non-Pharmacological Treatment

- Behavioural therapy: Counselling
- Re-feeding by nasogastric tube

Pharmacological Treatment

1. Olanzapine (unlicensed): 1.25mg | Anorexia Nervosa & Weight Restoration

- Olanzapine is “used to reduce extreme beliefs regarding body image and eating-related disturbed thoughts such as intense ruminations about food, pseudo-hallucinations as well as the hyper-arousal and agitation found when people are confronted with weight gain

2. Prevention of Re-Feeding Syndrome

From Starship guidelines: inpatient administration

- Phosphate Sandoz*: 1 tablet BD for 2 weeks (start on day of admission before feeding starts)
- Multivitamin* (must contain: 400iu Vitamin D daily, thiamine): 1 tablet BD for ≥ 3 months
- Other Supplements* (e.g. potassium, zinc) in accordance with blood levels

Indication	Drug	Mechanism of Action	Side Effects
Weight restoration	[PRESCRIPTION] <i>Olanzapine (unapproved use)</i>	Block DA and 5-HT3 receptors Block receptors involved in the neurobiology of eating disorders This antipsychotic was also found to reduce the high levels of anxiety associated with anorexia nervosa.	Hunger, QTC prolongation
Prevention of Re-Feeding Syndrome	[PRESCRIPTION] <i>Phosphate Sandoz</i> <i>Phosphate Phebra</i>	For the treatment of hypophosphataemia In anorexia, loss of phosphate occurs through starvation, low food intake and excretion (stool, urine).	Diarrhoea
	[PRESCRIPTION] <i>Multivitamin (with 400 units Vitamin D daily & thiamine)</i> MVite	Nutritional supplementation	B vitamins may colour urine bright yellow
	[PRESCRIPTION] <i>Potassium & Zinc</i>	Nutritional supplementation To be given in accordance with blood levels	Hyperkalaemia

Anorexia Nervosa (AN)

Description

Anorexia is an eating disorder characterised by an abnormally low body weight, an intense fear of gaining weight and a distorted perception of weight. People with anorexia place a high value on controlling their weight and shape, using extreme efforts that tend to significantly interfere with their lives.

The important distinction is that AN isn't about food - it is an unhealthy, life-threatening coping mechanisms for emotional problems e.g. equating thinness with self worth. No matter how much weight is lost, the person continues to fear weight gain.

Bulimia Nervosa (BN)

Description

Bulimia Nervosa is a serious, potentially life-threatening eating disorder. People with bulimia may secretly binge - eat large amounts of food with a loss of control over the eating and then purge, trying to get rid of the extra calories in an unhealthy way.

Binge Eating Disorder (BED)

Description

Binge eating disorder is characterised by recurrent episodes of binging, or extreme overeating. Binging occurs when a person eats a large amount of food in a short amount of time, and is usually marked by a lack of control. On average, Binge Eating Disorder is diagnosed when a person has an episode at least once a week for at least three months.

People with binge eating disorder may eat very quickly, even if they're not hungry. They often feel guilt and embarrassment about their eating, which leads to binging alone to hide the behaviour.

The most obvious difference is that people diagnosed with binge eating disorder do not force themselves to throw up (purge) the food they have just eaten. Alternately, people struggling with bulimia nervosa will eat and immediately empty the contents of their stomach.

Avoidant Restrictive Food Intake Disorder (ARFID)

Description

Avoidant Restrictive Food Intake Disorder (ARFID) is a new diagnosis in the DSM-5, and was previously referred to as “Selective Eating Disorder.”

Unlike anorexia nervosa and bulimia nervosa, ARFID is not characterised by preoccupation with body shape and weight or by intentional weight loss behaviours. Instead, patients suffering from ARFID may be disinterested in food and eating with lack of appetite leading to slower rate of eating, eating smaller portions, and greater struggles around food.

There appears to be a genetic predisposition towards picky eating or heightened sensitivity toward internal and external stimuli and patients may avoid foods because of dislike of colour, texture, smell or taste. Picky eating habits tend to appear in early childhood and tend to be relatively stable and persist long term. Some individuals might also develop a fear of choking, gagging or vomiting.

It is quite important to distinguish ARFID from picky eating, which is relatively common among children. Children with ARFID are extremely picky eaters and have little interest in eating food. They eat a limited variety of preferred foods, which can lead to poor growth and poor nutrition.

Re-Feeding Syndrome

Description

Re-feeding syndrome can be defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving artificial re-feeding (whether enterally or parenterally). These shifts result from hormonal and metabolic changes and may cause serious clinical complications.



CHAPTER 18

IMMUNISATIONS & VACCINATIONS

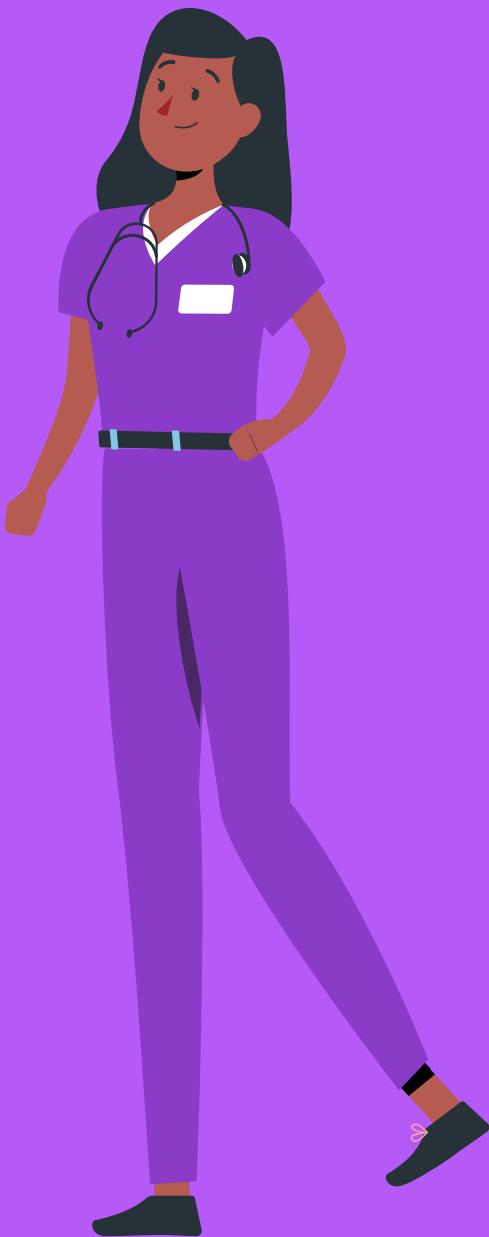


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Chapter 18

Immunisations & Vaccinations

General Overview of Immunology

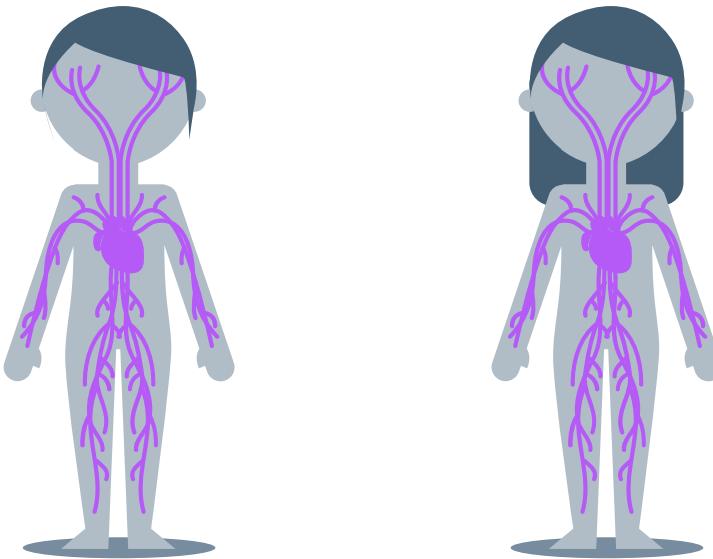
Chapter Resources

Excellent resources for this chapter are:

1. Pharmacy Standard Operating Procedures (SOP)
2. [MOH Immunisation Handbook 2020](#)
3. [New Zealand Immunisation Advisory Centre \(IMAC\)](#)
4. [Pharmaceutical Society of New Zealand \(PSNZ\) — Pharmacist Vaccination Service Guidelines](#)
5. [Medsafe - Database on Medicine Classifications](#)

Introduction

Welcome to the Immunisations Chapter! Here we will look into various vaccine-preventable diseases. But before we look into them, let's first look into how the immune system works.



Note

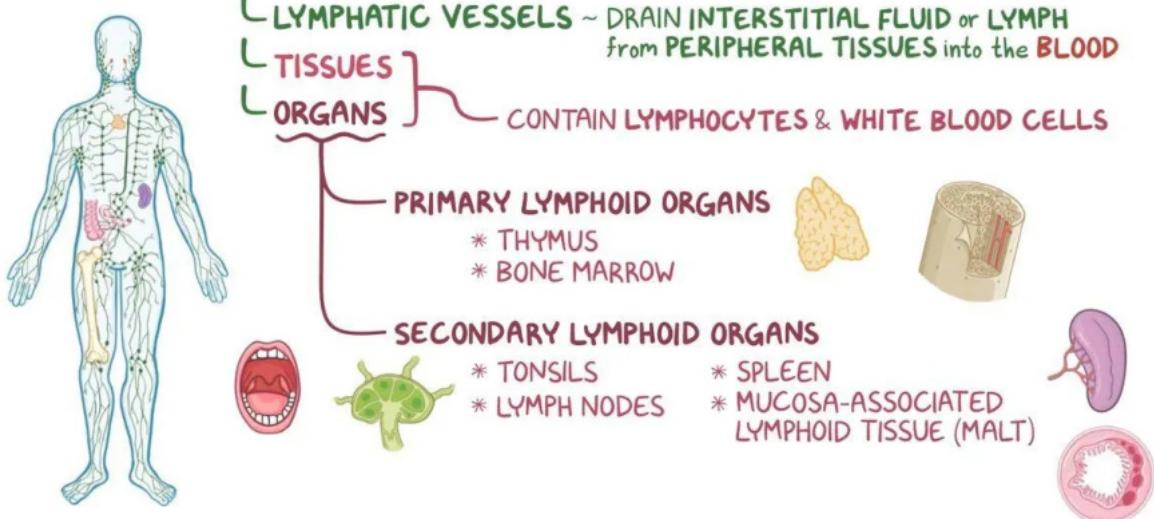
Many of the diseases that we vaccinate against have already been mentioned in the previous chapters. In the event of so, this chapter will serve to re-list the vaccines available to prevent this disease. Please revisit their respective chapters for further information on them.

The Immune System

The immune system is an organised system of organs, cells, and molecules that interact together to defend the body against disease.

IMMUNE SYSTEM

THE LYMPHATIC SYSTEM



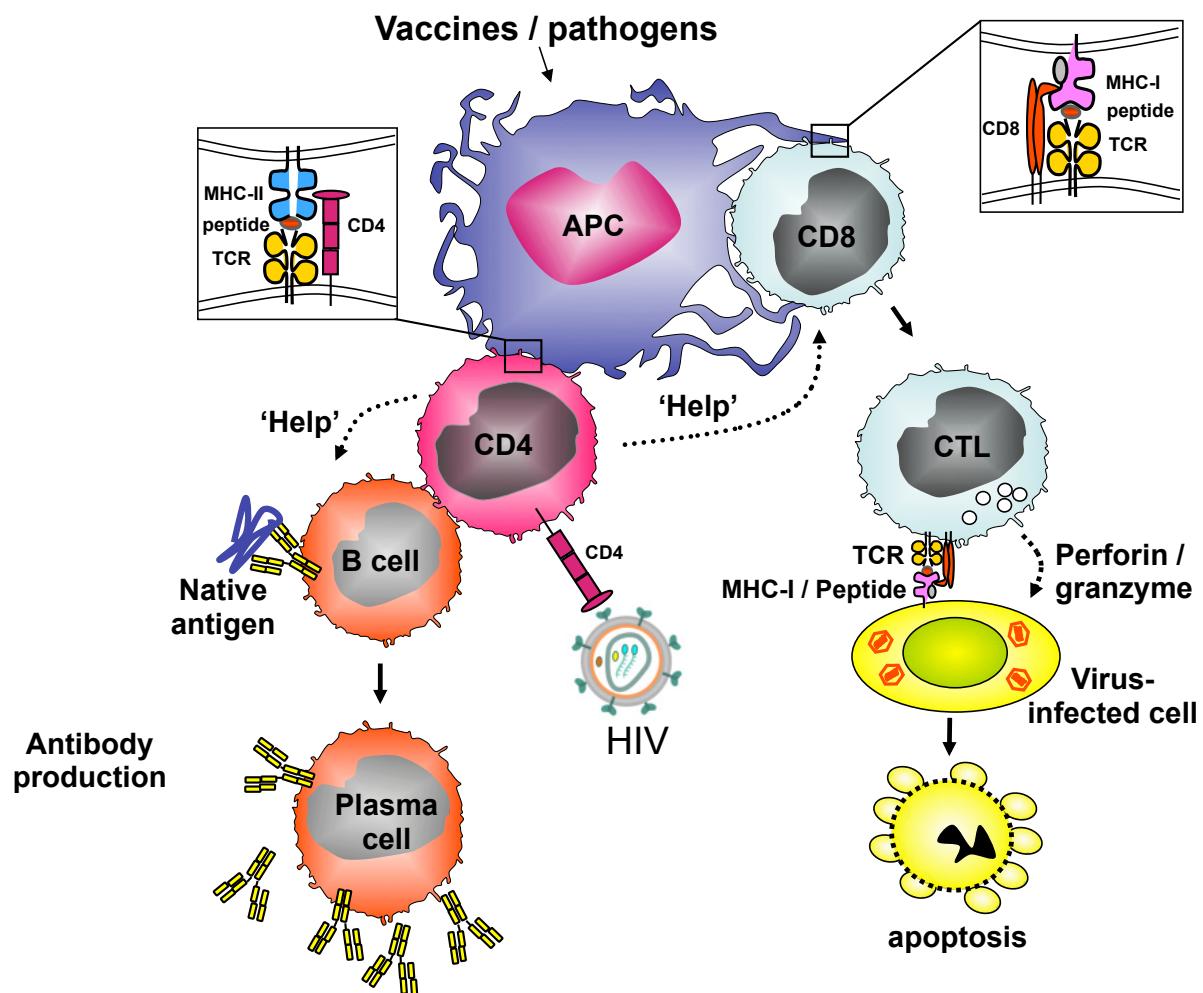
Organs of the immune system are found in the lymphoid organs (the lymphatic system) and can be classified into primary & secondary lymphoid organs.

	Primary Lymphoid Organs	Secondary Lymphoid Organs
Purpose	<i>Primary Lymphoid Organs</i> are involved in the production of white blood cells (lymphocytes.)	<i>Secondary Lymphoid Organs</i> are the sites where the immune response is initiated.
Key Organs	Thymus and the bone marrow. <ul style="list-style-type: none"><i>The thymus</i> is a school for white blood cells (T-Cells). This is where they learn not to react to themselves<i>The bone marrow</i> is a source of stem cells, these are pluripotent cells that will go onto develop into cells of the innate and adaptive immune responses.	Lymph nodes and spleen. <ul style="list-style-type: none"><i>Lymph nodes</i> are located along lymphatic vessels. They filter lymph fluids from blood and tissue and are the site of initiation of immune responses.<i>The spleen</i> is the site of initiation for immune response against blood-borne pathogens.

Immunological Defences

Immunological memory is the ability of the immune system to respond more rapidly and effectively to pathogens that have been encountered previously. The body has three lines of defences against infection which act together to maintain the integrity of our internal environment. The first two lines make up the innate immunity system, and the third line makes up the adaptive immunity system.

Line of Defense	1st Line Innate Immune System	2nd Line Innate Immune System	3rd Line Acquired Immune System
	Body's Physical & Chemical Defences	Non Specific Cellular Responses	Very Specific Immunological Memory
Function	Immediate Response <ul style="list-style-type: none"> Static Response & Activates acquired immune response Memory <ul style="list-style-type: none"> No Memory 		Delayed Response (days) <ul style="list-style-type: none"> Can adapt i.e. expand, differentiate, improve Memory <ul style="list-style-type: none"> Develops over time Infants have no memory
Structures	Skin & Mucous Membranes <p><i>Skin</i></p> <ul style="list-style-type: none"> Shedding, lysozymes, sebaceous glands, sweat glands. <p><i>Mucous Membrane</i></p> <ul style="list-style-type: none"> Epithelium layer, mucociliary escalator, low stomach pH, bile 	Blood Lineages <p><i>Erythroid Lineages</i></p> <ul style="list-style-type: none"> Red Blood Cells <p><i>Myeloid Lineages</i></p> <ul style="list-style-type: none"> Granulocytes (neutrophils, mast cell) Monocytes Dendritic Cells 	Blood Lineages <p><i>Lymphoid Lineages</i></p> <ul style="list-style-type: none"> T & B cells <p>T-Cell CD8</p> <p>Activated by endogenous antigens and presented on MHC-Class I.</p> <ul style="list-style-type: none"> Kill virus infected cells and intracellular bacteria Cells best activated by live attenuated & vector vaccines Non-living genetic vaccines can activate these cells but require boosting. <p>T-Cell CD4</p> <p>Activated by exogenous antigens and presented on MHC-Class II</p> <ul style="list-style-type: none"> Activates B Cells which produce antibody IgG Help CD8 T Cell killing mechanism MHC II pathway default pathway for vaccines as they are exogenous antigens Whole cell killed and toxoid vaccines generate this response Subunit vaccines will need boosting or a strong adjuvant <p>B Cells</p> <ul style="list-style-type: none"> Produce antibody and memory B-Cells alongside memory T-Cells
Cellular Purpose	These cells control the infection in the 7 days that it takes for the immune response to kick in. They have no memory. Not a vaccine target.		



Viral = endogenous (uses host processes) = MHC2 = CD4

Bacterial = exogenous (toxins) = MHC1 = CD8

General Overview of Immunisations

Introduction

As we've seen, when the immune system is first exposed to a germ, we become unwell until the adequate antibodies/responses are produced in order to overcome the infection. The immune system also produces a memory of the infection so that it is able to respond rapidly to destroy the germ the next time we are exposed.

Immunisation, thus, serves to increase the number of people that survive natural infection, reduce side effects associated with natural infections while promoting a protective memory immune response. Not only do vaccines provide individual protection, but for many of the diseases we vaccinate against, there is also a population effect called herd/community immunity.



Herd Immunity

Herd immunity protects individuals unable to be immunised or those unable to develop protective immune responses to the vaccine. Vaccines each have a:

1. Herd Immunity Threshold (no of vaccinated people needed for the disease to stop spreading) +
2. Vaccine Efficacy (how effective it needs to be to achieve herd immunity).

Who Should Get Vaccinated - Special Groups

These are individuals that are at high risk of serious disease and thus vaccination is highly recommended.

1. Preterm & Low Birthweight Infants

- Absence of immunological memory
- Vaccinate per chronological age (see immunisation schedule)
- Cocooning for protection from influenza and pertussis

2. Pregnancy & Breast Feeding

- Vaccines recommended prior to conception: MMR, Varicella, pneumococcal
- Vaccines recommended during pregnancy: TdP booster, Pertussis, Flu
- **Live vaccines are not recommended in pregnant women but are okay in breastfeeding**
- Inactivated vaccines are safe in either cases

3. Immunocompromised

- These groups have an increased risk from infectious diseases and thus vaccination should be prioritised
- Live vaccines are not recommended but Inactivated and subunit vaccines are safe

4. Other

- Immigrants (age-appropriate catch-up)
- Risk occupations and other risk factors (e.g. pharmacy)

Funded vaccines for special groups from 1 October 2020

To determine whether your patient meets the eligibility criteria, please check the specific eligibility details described on the Pharmaceutical Schedule (www.pharmac.govt.nz) for every vaccine listed below. Please refer to the current Immunisation Handbook for vaccine administration schedules.

Adolescents and young people 13–25 years inclusively entering specified close-living situations	immunodeficiency – primary or secondary • Hib, influenza, meningococcal, and pneumococcal vaccines
Asplenia - Functional or Pre- or Post-Splenectomy Immunisation Programme	Influenza Immunisation Programme » Pregnancy » Children aged 6 months to under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness » Individuals aged 6 months to under 65 years with an eligible medical condition » Individuals aged 65 years or older • Influenza vaccine
Chemotherapy - following	Kidney disease • Hepatitis B, Hib, influenza, pneumococcal, Tdap, and varicella vaccines
• Hib, HPV, influenza, pneumococcal, Tdap, and varicella vaccines Also consider immunosuppression for longer than 28 days • Hepatitis B and meningococcal vaccines	Liver disease • Hepatitis A and varicella vaccines
Cochlear implant	Meningococcal disease case - contact with • Meningococcal vaccine
• Hib, influenza, and pneumococcal vaccines	Needle stick injury - following • Hepatitis B vaccine
Error of metabolism at risk of major metabolic decompensation	Non-consensual sexual intercourse - following • Hepatitis B vaccine
• Influenza and varicella vaccines	Neonatal Intensive Care Unit or Specialist Care Baby Unit admission more than 3 days • Tdap for parents/primary caregivers if maternal Tdap not given at least 14 days before birth
Haematopoietic stem cell transplantation (HSCT) - following	Pneumococcal disease - increased risk • Additional pneumococcal vaccines
• Hib, HPV, influenza, meningococcal, pneumococcal, Tdap, and varicella vaccines Also consider immunosuppression for longer than 28 days • Hepatitis B vaccine	Pregnancy • Influenza and Tdap vaccines in every pregnancy
Hepatitis A case - contact with	Solid organ transplantation Prior to solid organ transplantation • Hepatitis A, hepatitis B, Hib, meningococcal, pneumococcal, Tdap, and varicella vaccines
• Hepatitis A vaccine	Following solid organ transplantation • Hepatitis A, hepatitis B, Hib, HPV, influenza, meningococcal, pneumococcal, and Tdap vaccines
Hepatitis B case - contact with	Tuberculosis - infants and children aged under 5 years at risk of tuberculosis (TB) exposure • BCG vaccine
Infants born to mothers who are hepatitis B surface antigen (HBsAg) positive	
• Hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) at birth	
Household and sexual contacts of known acute hepatitis B cases or carriers	
• Hepatitis B vaccine	
Hepatitis C positive	
• Hepatitis B vaccine	
HIV positive	
• Hepatitis B, HPV, influenza, meningococcal, pneumococcal, and varicella vaccines	
Immunosuppression	
Household contacts of children or adults who will be/are immunosuppressed	
• Varicella vaccine	
Prior to elective immunosuppression for longer than 28 days	
• Varicella vaccine	
Following immunosuppression for longer than 28 days	
• Hepatitis B, Hib, influenza, meningococcal, and Tdap vaccines	

VACCINE KEY
BCG: tuberculosis
Hib: *Haemophilus influenzae* type b

HPV: human papillomavirus
IPV: inactivated polio vaccine
Tdap: tetanus, diphtheria, acellular pertussis

For more details, visit immune.org.nz  The Immunisation Advisory Centre

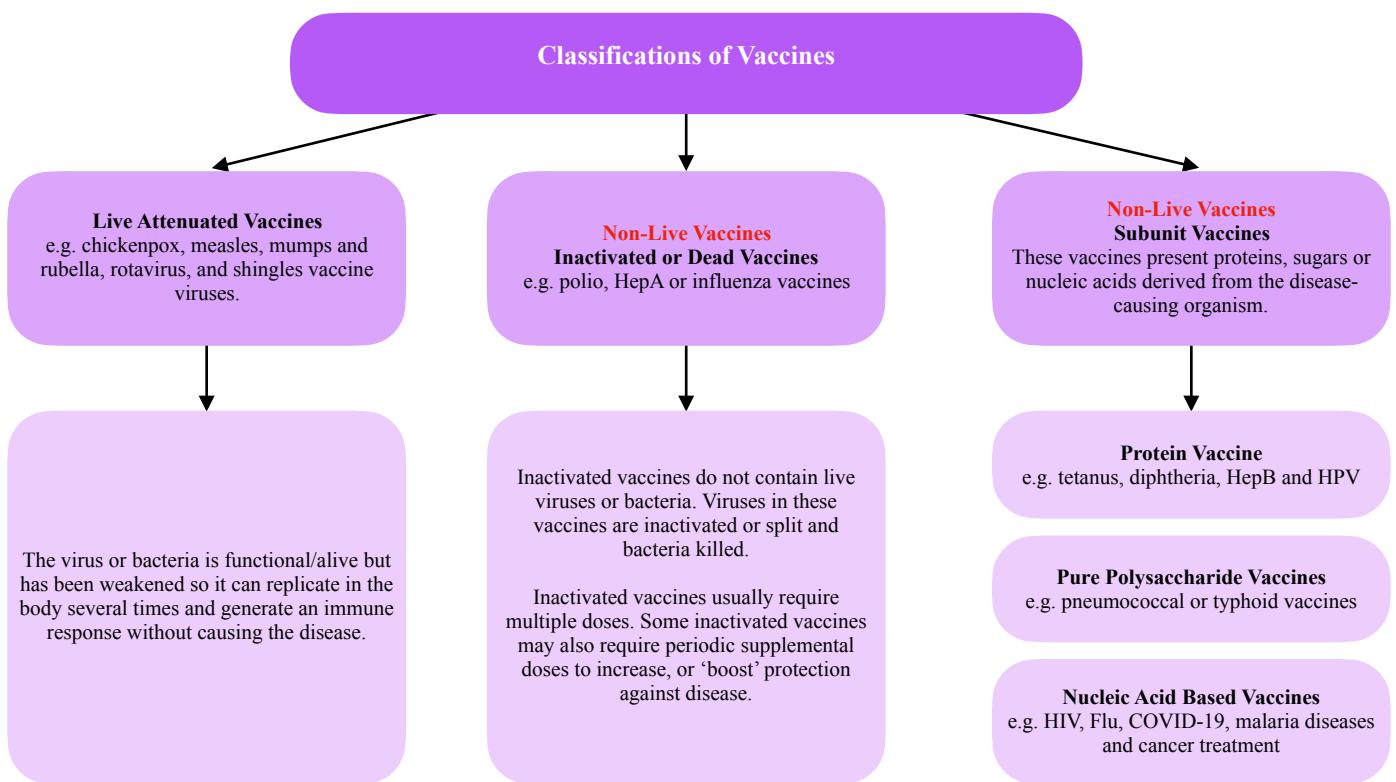
Overview of Available Vaccines in NZ

Available Vaccines	
ADT Booster	Protects against tetanus and diphtheria.
Boostrix	Protects against tetanus, diphtheria and pertussis. -- can be given by a Pharmacist Vaccinator
Infanrix-Hexa	Protects against diphtheria, tetanus, pertussis, polio, hep B and HiB
Infanrix-IPV	Protects against diphtheria, tetanus, pertussis and polio
BCG Vaccine SSI	Protects against severe tuberculosis
Ipol	Protects against polio - can be given by a Pharmacist Vaccinator
Gardasil 9	Protects against the 9 types of HPV
Havrix	Protects against Hepatitis A
Engerix-B	Protects against Hepatitis B
HBvaxPRO	Protects against Hepatitis B
Hiberix	Protects against Hib

Flu Vaccine	Protects against influenza - can be given by a Pharmacist Vaccinator
Bexsero	Protects against Meningitis Group B - can be given by a Pharmacist Vaccinator
Menactra/Nimenrix	Protects against Meningitis A, C, Y, W - can be given by a Pharmacist Vaccinator
NeisVac-C	Protects against Meningitis C - can be given by a Pharmacist Vaccinator
Pneumovax23	Protects against 23 types of Streptococcus Pneumoniae
Prevenar 13	Protects against 13 types of Streptococcus Pneumoniae
Synflorix	Protects against 10 types of Streptococcus Pneumoniae
Priorix	Protects against measles, mumps and rubella
MMR	Protects against measles, mumps and rubella - can be given by a Pharmacist Vaccinator
Rotarix	Protects against rotavirus
Varilrix/Varivax	Protects against chickenpox
Zostavax/Shingrix	Protects against shingles - can be given by a Pharmacist Vaccinator
Comirnaty	Protects against COVID-19

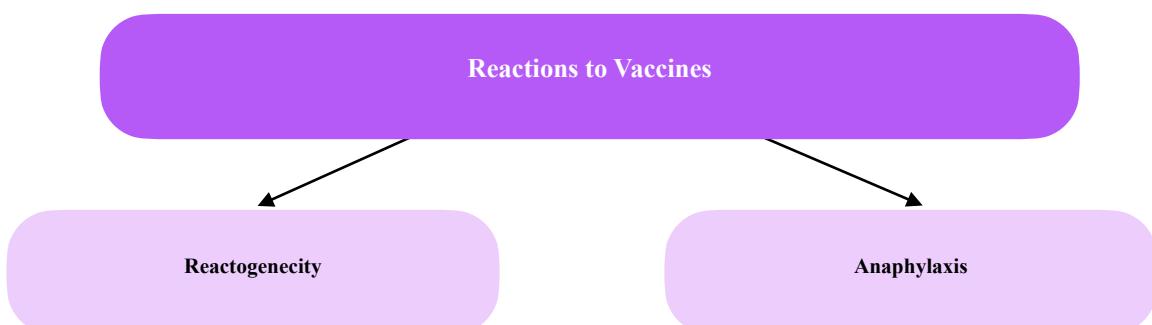
Types of Vaccines

Vaccines can be broadly classified by how the antigen(s), the active component(s) that generate a specific immune response against the disease-causing organism, are prepared.



Reactions to Vaccines

There are two reactions we will look into:



1. Reactogenicity

Reactogenicity is a term that essentially describes the immune response that vaccines cause. Expected examples following a vaccination include:

- a) *Local*: Localised swelling & redness
- b) *Systemic*: Headache, myalgia and fever

While different vaccines cause different levels of responses, reactogenicity is an overall good indicator that they are working. However, this means there is a trade off between tolerability and effectiveness.

For example, live vaccines are extremely effective and thus also, more reactogenic as a by-product. This is because they are a weakened version of the antigen. But despite this, they cannot be given to certain populations e.g. immunocompromised individuals, pregnant women and so forth.

Many factors including intrinsic host factors (age, co-morbidities, birth-weight, infections) contribute to what reaction one may have. A poor/absent response generally indicates a non-functioning immune system while an excessive one can kill a person.

Managing fainting

- If sitting, position with head between knees for 5 minutes
- Lie down with legs elevated
- Take time to change positions e.g. seating to standing

Managing pain/swelling/redness at injection site

- Paracetamol/ice pack or cool cloth at injection site

Managing fever <38°C, malaise or fatigue

- Drink more fluids
- Paracetamol
- Rest

2. Anaphylaxis

Anaphylaxis is a potentially life threatening type of hypersensitive immune response that involves the respiratory and/or cardiovascular system. It is a IgE-mediated response that occurs within minutes and is a medical emergency. Observation periods following vaccination allows such events to be promptly attended to. There are a few vaccine components that have been known to be associated with anaphylaxis:

- a) Gelatine (most common)
- b) Yeast (for culture-grown vaccines - HBV and HPV)
- c) Latex (uncommon, contact type allergy)
- d) Antibiotics (neomycin sulphate - Infanrix Hexa, HAV, MMR, VV, ZV)
- e) Egg protein or albumin (for culture-grown vaccines - MMR)

If individuals indicate allergies to the above and have been able to receive vaccines containing that allergen with no issues in the past — vaccine may be administered safely with **precaution** and a longer observation period (30 instead of 15 minutes) - this also applies to individuals prone to fainting.

Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute **contraindication**.

	Faint (Vasovagal Response)	Anaphylaxis
Onset	Usually before, at the time, or soon after injection	Soon after injection but may delay up to 30 mins
Skin	Pale, sweaty, cold, clammy	Red, raised and itchy rash; swollen eyes and faced, generalised rash
Respiratory	Normal to deep breaths	Noisy breath due to airway obstruction (wheeze/stridor); respiratory arrest
Cardiovascular	Bradycardia, transient hypotension	Tachycardia, hypotension, dysrrhythmias, circulatory arrest
Gastrointestinal	N/V	Abdominal cramps
Neurological	Transient loss of consciousness, good response once supine/flat	Loss of consciousness, little response once supine/flat

Management of Anaphylaxis

Acute onset of life-threatening airway and/or breathing and/or circulation problems and usually skin and/or mucosal changes.

ASSESS

- Airway: swelling, hoarseness, noisy breathing (stridor)
- Breathing: fast, wheeze, cyanosis, fatigue, confusion
- Circulation: pale, clammy, slow capillary refill, low BP, faintness, drowsy/coma
- Skin and mucosal changes: urticaria, flushing, angioedema

1. CALL FOR HELP

Send for emergency medical assistance (ambulance, doctor).

2. POSITION PATIENT SAFELY

Do not allow them to stand and never leave them alone.



3. ADMINISTER ADRENALINE

By deep IM injection into outer thigh.

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

AGE	12 years and over	DOSE	500 mcg (0.5 mL)
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Expect to see some response to the adrenaline within 1–2 minutes.

If necessary, adrenaline can be repeated at 5–15 minute intervals, while waiting for assistance.

4. BE PREPARED TO COMMENCE AGE APPROPRIATE CPR*

If needed.

5. ADMINISTER OXYGEN

If available.

If there is respiratory distress, stridor, or wheeze, use high flow rates.

6. RECORD VITAL SIGNS EVERY 5–10 MINUTES

All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

7. ADMIT PATIENT TO HOSPITAL

All cases of anaphylaxis should be admitted to hospital for observation.

Rebound anaphylaxis can occur 12–24 hours after the initial episode.

*Note, a current Resuscitation certificate is required covering the skills outlined in Appendix 4.2 Immunisation Handbook.

Vaccine Storage & Transportation

The Cold Chain Process

We will now look into how to store vaccines. All immunisation providers are required to follow to the Ministry of Health [National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 \(2nd Edition\)](#)

The cold chain is a process used to maintain vaccines within the required temperature range. This is because vaccines are temperature sensitive so we need to ensure potency/stability has not been compromised. All vaccines in New Zealand must be stored between **+2°C to +8°C (5°C is recommended)**, at all times during storage and transport.

Cold Chain Accreditation

Cold chain management of an immunisation provider is assessed through the use of the audit tool Cold Chain Accreditation (CCA). In order to achieve CCA, an immunisation provider is required to demonstrate it has appropriate cold chain management practices and processes in place to meet the standards' requirements.

Vaccine Fridge

Just like there is a storage requirement for controlled drugs - there is one for vaccines.

- Pharmaceutic or general fridge — needs to meet criteria
- Requires annual servicing, maximum 10 year replacement
- Usually store **4 weeks'** worth of vaccines
- Can only store products >25mm from the walls and back of fridge

Temperature Recording

Each refrigerator must have two forms of temperature monitoring equipment, as follows. Records are kept for 10 years and are decked during audits.

1. The daily check device using a minimum/maximum thermometer with externally visible display
 - Staff should take minimum and maximum temperature readings and record them once a day – ideally first thing in the morning – and then reset the monitoring device.
2. The weekly check device using an electronic temperature recording device

Maintaining Cold Chain for Offsite Immunisation Clinics

Immunisation providers must use temperature-monitored chilly bins to store vaccines when transporting vaccines.

- For each chilly bin, there should be enough frozen ice packs, approved insulated material along bottom of container
- Stabilise chilly bins between 2°C to 8°C **before** vaccines are added
- Volume of vaccines not to exceed 1/3 of container's capacity
- Each chilly bin must have the ability to be temperature monitored without needing to open them:
 - Primary device: data logger, external display, alarm
 - Secondary back-up device: min/max thermometer

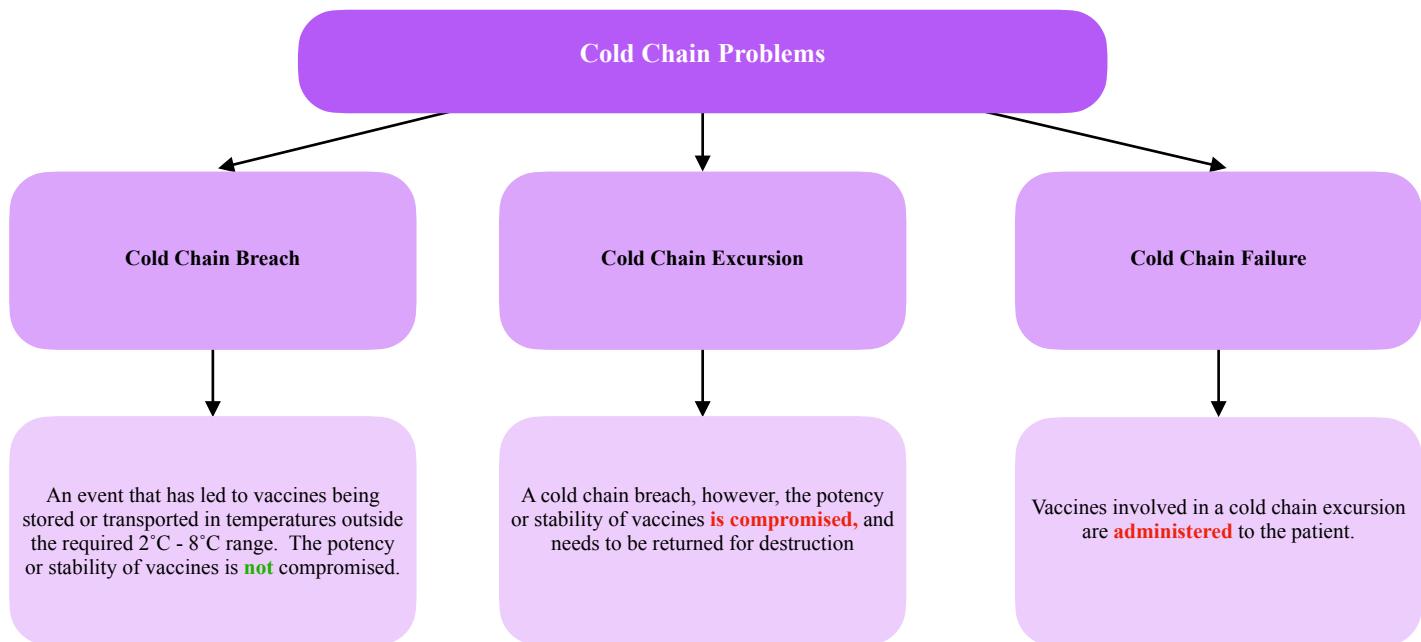
- Record min, max, current temperatures reviewed every **30 minutes** while offsite — download data
- Providers must keep documentation associated with monitoring the temperature of vaccines in chilly bins for 10 years, along with the rest of the cold chain documentation.

Challenges of Off-Site Vaccine Administration

- Maintaining privacy (e.g. health information)
- Incorrect number of vaccines prepared
- Paperwork
- Availability and clashes
- Sterility of environment
- Informed consent
- Appropriate clothing (need to vaccinate arm)
- Maintaining cold-chain

Cold Chain Breaches, Excursions & Failure

However that being said, mistakes happen - so let's look into problems that can occur with cold chain. If one has occurred, it is recommended to contact your Cold Chain Co-Ordinator with this [form filled](#) so that they can advise what kind of problem has occurred and how to proceed.



Cold Chain Failures are associated with:

- Public health consequences: need to revaccinate
- Loss of money: vaccines need to be replaced
- Loss of time: need to contact all patients involved
- Loss of public trust in healthcare professionals

What to do in a Cold Chain Problem?

1. Check for reason of breach
2. Quarantine vaccines and do not use (i.e. isolate vaccines or put in chilly bin and label “not for use”)
3. Download data logger. Review temperatures and duration of breach
 - Immunisation Handbook: Breaches of less than 30 minutes, under 12°C with a known cause can be documented but you do not need to report to local immunisation coordinator.
4. Seek alternative storage if fridge temperature is not between 2-8° C
5. Contact local immunisation/cold chain co-ordinator for advice
6. Only until advised would vaccines be removed from quarantine
7. Document steps and actions you have taken

Processes for Safe Vaccine Administration

Introduction

Now let's look into how to safely administer vaccines. In a community pharmacy, vaccines can only be administered by approved pharmacist vaccinators and provisional vaccinators such as Intern Pharmacists or Pharmacy Students.

Appendix 4: Authorisation and criteria of vaccinators

Pharmacist vaccinator	Pharmacists are enabled to vaccinate pursuant to the Medicines Regulations classifications on completion of full vaccinator training.	Registered Pharmacists Pharmacist interns	Influenza MMR COVID-19 ^c HPV Meningococcal Tdap Zoster	Ages 13 years and over Ages 16–49 years Ages 9–27 years Ages 16 years and over Ages 18 years and over. Pregnant women aged 13 years and over Ages 50 years and over	Deltoid only ^b	Yes
<p>It is then recommended that they inform the Pharmaceutical Society of New Zealand to be added to the vaccinator database.</p>						

Step 1 - Physical Setup Considerations/Privacy

You should consider the organisation of your ‘vaccinating space’.

1. Can you access the adrenaline and emergency equipment quickly?
2. Do you have a sharps bin close by?
3. Do you require/have computer access in the room?
4. Are patient leaflets and any forms required, hand sanitiser, swabs, plasters etc. accessible?

Step 2 - Obtain Informed Consent

To facilitate a conversation that provides for ‘informed’ consent you should have at least two chairs available. Having this conversation while the client and/or you are standing is not good practice. It implies you are in a hurry and is not comfortable for many people.

Regardless of age, an individual and/or their parent/guardian must be able to understand:

- that they have a choice
- why they are being offered the treatment/procedure
- what is involved in what they are being offered
- the probable benefits, risks, side-effects, failure rates and alternatives, and the risks and benefits of not receiving the treatment or procedure.

Step 3 - Pre - Vaccination Screening

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccine recipient (child or adult) has a condition or circumstance which may influence whether a vaccine is:

1. Given
2. Deferred or
3. Contraindicated.



Spacing Doses

There are no known contraindications to administering registered vaccines at the same visit, provided they are administered in separate syringes at separate sites. Live injected vaccines either need to be given on same day or with a minimum gap of 4 weeks (exception 7 days between COVID and shingles).

Potential screening outcomes:

- **There are no contraindications to vaccination.** Follow your usual informed consent process, ensure that you fully document this in the patient notes.
- **Vaccination is deferred.** Advise the patient of the outcome and why they the vaccination has been deferred. Let them know when to come back for vaccination and make an appointment if possible.
- **Vaccination is contraindicated.** Advise the patient of the outcome and why they cannot receive the vaccine.
- **Specialist opinion is required.** Let the patient know, discuss how the advice from the specialist will be sought and approximately when you will tell them whether they can have the vaccination or not.

All Vaccines: Questions	Rationale
Are you/your child feeling well today?	General screening for acute moderate/severe illness.
Have you/your child ever had a serious allergic reaction (to anything)?	Screening for history of anaphylaxis to a vaccine or vaccine component e.g. neomycin or gelatin.
Have you/your child ever had a serious reaction to any vaccine? Have you ever been told you/your child should not receive certain vaccines?	Screening for any other serious reaction e.g., HHE or Arthus reaction Screening for possible medical contraindications
What other vaccinations have you/your child received? <ul style="list-style-type: none">• What vaccines did you receive?• When did you receive the vaccination?• Who gave you your last vaccination?	To ensure appropriate spacing between vaccines with same antigens and avoid repeating vaccines already administered. This information should be confirmed with NIR status query and/or review of information held in medical records. A gap of seven days is recommended between the mRNA-CV, and ZV. Live injected vaccines either need to be given on same day or with a minimum gap of 4 weeks between the live vaccine doses.
Do you/your child have a bleeding problems or blood disorders?	Screening for prolonged bleeding/haematoma risk post vaccination. Consider administering via subcutaneous route if appropriate. Patients who are stable on blood thinning medications, can usually receive vaccines via the intramuscular route. After vaccination, apply firm pressure to the site without rubbing for 10 minutes.
Do you/your child have any medical conditions or take any regular medications? Have you/your child had any medical conditions in the past?	Some patients may be eligible for more vaccinations because of medical conditions or certain medications. Check practice management system for any medications that are listed. For live vaccines see over the page for more detail.
Do you/your child have any immune system problems you know of?	The effectiveness of some vaccines may be compromised and protection may be suboptimal. For live vaccines see over the page for more detail.
Are you/your child taking any medications that were not prescribed at this practice?	Screening for medications that are not recorded in the practice management system.
Do you/your child have an undiagnosed or evolving neurological condition? Relevant for pertussis containing vaccines only.	Specialist advice should be sought before vaccinating, as any post vaccination response may confuse the clinical picture in an unstable illness.
Are you pregnant or trying to get pregnant?	Inactivated vaccines can usually be given during pregnancy and some are recommended (Influenza and Tdap), however the risk and benefit of this must be discussed with the vaccinee. Live vaccines should not be given to pregnant women. Women should be advised to avoid getting pregnant for 4 weeks after the administration of a live vaccine.

See over for additional questions for live vaccines.

Page 1 of 2

This document was reviewed in October 2021.

Live Vaccines only: Additional Questions	Rationale
Do you/your child have or have ever had cancer, leukaemia, lymphoma, a transplant, stem cell therapy, TB or any condition that effects your immune system (including HIV/AIDS) or any blood disorders or live with someone who does?	Screening for diseases or medical conditions that could cause immune system compromise such as cancer, leukaemia, lymphoma, organ transplant, stem cell transplant, HIV/AIDS or any blood disorders. Live vaccines may be contraindicated or a specialist opinion required. Refer to Chapter 4 of the Immunisation Handbook.
Do you/your child live with someone who has a condition or is receiving treatment that affects their immune system?	If the vaccinee lives with someone who is immunocompromised, additional precautions maybe required for example covering any rash from varicella vaccine.
In the past 12 months have you/your child taken any medications that affect the immune system such as oral steroids for asthma , COPD, sarcoidosis, other steroids, or anticancer drugs; drugs for the treatment of rheumatoid arthritis, Crohn's disease, ulcerative colitis or psoriasis or similar conditions.	Screening for medications that could cause immune system compromise because vaccination with a live vaccine may be contraindicated or a specialist opinion required. For further information refer to Chapter 4 of the Immunisation Handbook section 4.3.2, 4.3.5 and 4.3.6 For children you can also refer to: https://www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/i/immunosuppression-infection-and-immunisation-in-rheumatology/
For infants under 12mths of age: did the mother take immunosuppressive therapy during pregnancy?	For infants aged under 12 months, please discuss immunosuppressive therapies taken during pregnancy with infant's mother or specialist, or contact IMAC (on 0800 IMMUNE /0800 466 863) before administration of rotavirus, BCG, MMR or VV vaccines.
Have you/your child received any blood products in last 12 months and when did you receive them? Are you/your child due to receive any blood products, for example immunoglobulin or a blood transfusion?	Administration of MMR and/or VV may need to be deferred due to receipt of a blood product. Refer to Table A6.1 in the Immunisation Handbook to identify the blood product received and the recommended interval before MMR and/or VV can be given. MMR and/or VV vaccines should be given at least 3 weeks before the administration of blood products. No set interval required between blood products and rotavirus or zoster vaccine administration.
Are you/your child taking any medication to prevent cold sores, herpes or shingles? Relevant for Varicella and Zoster vaccines only.	Antiviral medication can interfere with ZV and VV and needs to be stopped for 24 hours prior to ZV or VV vaccination and for 14 days after vaccination. Patients on long-term antiviral medication should discuss the possible risk of disease flare-up from stopping the antiviral medication and risks and benefits of ZV vaccination with their health professional.

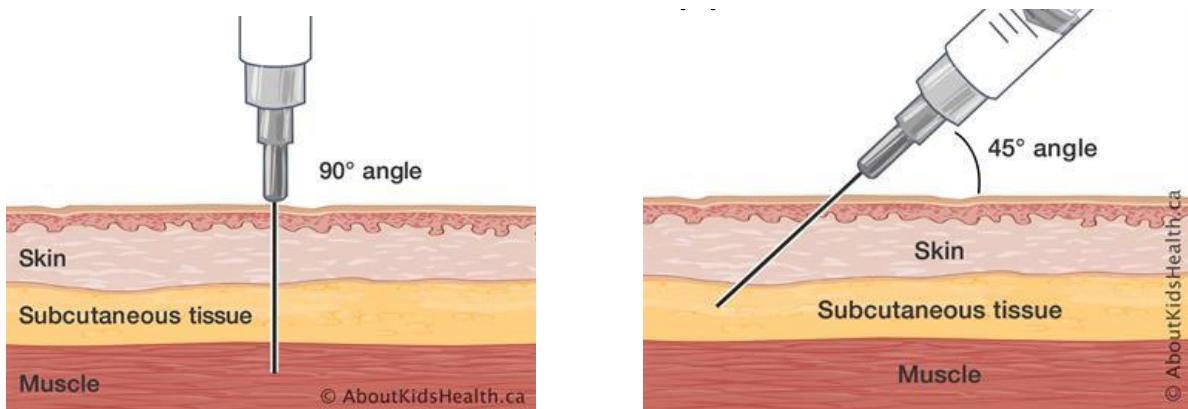
Step 4 - Vaccine Preparation

Different vaccines are prepared differently - please see Immunisations Handbook for instructions.

Step 5 - Vaccine Administration

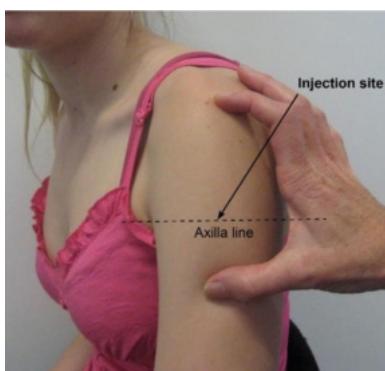
Most schedule vaccines are administered by intramuscular injection. The exceptions are IPV (IPOL; subcutaneously), BCG (intradermally) and rotavirus (oral).

Intramuscular injections should be administered at a **90-degree angle** to the skin plane usually in **the deltoid muscle**. The volume injected into the deltoid should not exceed 0.5 mL in children and 1.0 mL in adults. The needle length used will be determined by the size of the limb and muscle bulk, whether the tissue is bunched or stretched and the vaccinator's professional judgement. **Subcutaneous injections** should be given at a **45-degree angle**.



Locating the Deltoid Muscle

The deltoid muscle is located in the lateral aspect of the upper arm.



1. The vaccine recipient should be seated with their arm removed from the garment sleeve and hanging relaxed at their side.
2. The vaccinator places their index finger on the vaccine recipient's acromion process (the highest point on the shoulder) and their thumb on the vaccine recipient's deltoid tuberosity
3. The injection site is at the axilla line, between these anatomical landmarks. The vaccine should be deposited at the bulkiest part of the muscle

Administering the Vaccine

- Push the plunger at a consistent speed to inject the medicine into the muscle
- Remove the needle and immediately discard into the sharps container (do not recap)
- Using a piece of gauze or cotton ball, apply light pressure to the injection site.
- Use a bandage if necessary
- If you hit bone, you will hear a bit of a thud, just retract needle back a bit and inject vaccine

Minimising Pain

Vaccines can be painful, here are some tips for minimising pain and distress at the time of vaccination:

- do not aspirate (draw back) when giving vaccines
- Ensure proper administration technique - poor administration can result in SIRVA
- administer vaccines from the least to the most painful for all ages
- breastfeed before and during vaccine injection
- Skin preparation or cleansing is not necessary



Pain Relief During Immunisations

Routine use of paracetamol and/or ibuprofen are not recommended before or after vaccination (with the exception of **Bexsero** — Mens B vaccine) as it may reduce the immune response and impact long-term immunity.

Step 6 - Discard Sharps

The syringe and needle are placed in the sharps bin immediately after removing from the client's arm.

Step 7 - Post Vaccination Advice

Post-vaccination advice should be given both verbally and in writing. The advice should cover:

- which vaccines have been given and the injection sites, and whether the injections were IM or SC
- potential vaccine responses following immunisation and what to do if these occur
- when the individual or parent/guardian should contact the vaccinator if they are worried or concerned
- contact phone numbers (including after-hours phone numbers).

Step 8 - Send Patient To Observation Area

- Patient needs to wait 20 minutes post-immunisation - remind them of this.
- This may be extended to 30 minutes if they have a known allergy to a component to the vaccine or are prone to fainting.

Step 7 - Documentation

Accurate documentation, including information on the National Immunisation Register (NIR) and the Aotearoa Immunisation Register (AIR), COVID-19 immunisation register (CIR) is essential to keep up accurate clinical records.

VACCINE-PREVENTABLE DISEASES ON SCHEDULE

The National Immunisation Schedule

The New Zealand National Immunisation Schedule is a series of immunisations (including boosters) given at specific times between the ages of six weeks and twelve years. To get the best possible protection, have the immunisations on time, every time. See the schedule below.

New Zealand National Immunisation Schedule from 1 October 2020

	RV	DTaP-IPV-HepB/Hib	PCV	MMR	Hib	VV	DTaP-IPV	Tdap	HPV	Influenza	HZV
Every pregnancy										Boostrix® from 2nd trimester	Afluria Quad® any trimester
6 weeks	Rotarix®	Infanrix®-hexa	Synflorix®								
3 months	Rotarix®	Infanrix®-hexa									
5 months		Infanrix®-hexa	Synflorix®								
12 months			Synflorix®	Priorix®							
15 months				Priorix®	Hiberix®	Varivax®					
4 years							Infanrix®-IPV				
School year 7 (11 years)								Boostrix®			
School year 8 (12 years)									Gardasil® 9 two doses		
45 years								Boostrix®			
65 years								Boostrix®	Afluria Quad®	Zostavax®	



From 1 October 2020

The National Immunisation Schedule
immunise
our best protection

Age	Disease to protect against	Vaccine
Pregnancy	Tetanus + diphtheria + whooping cough (pertussis) Influenza	Boostrix® Brand varies.
6 Weeks	Rotavirus (first dose must be given before 15 weeks) Diphtheria + tetanus + whooping cough (pertussis) + polio + hepatitis B + Haemophilus influenzae type b (Hib) Pneumococcal disease	Rotarix® (oral) Infanrix® hexa Synflorix®
3 Months	Rotavirus (second dose must be given before 25 weeks) Diphtheria + tetanus + whooping cough + polio + hepatitis B + Haemophilus influenzae type b (Hib)	Rotarix® (oral) Infanrix® hexa
5 Months	Diphtheria + tetanus + whooping cough + polio + hepatitis B + Haemophilus influenzae type b (Hib) Pneumococcal disease	Infanrix® hexa Synflorix®
12 Months	Measles + mumps + rubella Pneumococcal disease	Priorix® Synflorix®
15 Months	Haemophilus influenzae type b (Hib) Measles + mumps + rubella Chickenpox (varicella)	Hiberix® Priorix® Varivax®
4 Years	Diphtheria + tetanus + whooping cough + polio	Infanrix® IPV
11-12 Years	Tetanus + diphtheria + whooping cough Human papillomavirus (HPV)	Boostrix® Gardasil® 9 (2 doses, 6 months apart)
45 Years	Tetanus + diphtheria + whooping cough	Boostrix®
65 Years	Tetanus + diphtheria + whooping cough Influenza Shingles	Boostrix® Brand varies. Zostavax®

This resource is available from healthed.govt.nz or the Authorised Provider at your local DHB. Revised June 2020. 05/2020. Code HE1308

Rotavirus

Revisit *Chapter 4 - Gastrointestinal System* for information on this condition.

Prevention

- Rotarix

Vaccine	Vaccine Type	When
Rotarix	Live Oral Vaccine	6 weeks, 3 months

Diphtheria, Tetanus & Whooping Cough (Acellular Pertussis)

Revisit *Chapter 7 - Respiratory System* for information on Whooping Cough.

Diphtheria

Diphtheria is a rare but serious disease caused by toxin-producing strains of *Corynebacterium diphtheriae*. The bacteria usually cause infection of the **throat**, but can also cause **skin** infections. The infection has a gradual onset over 2 - 5 days, and is transmissible up to 4 weeks.

Signs & Symptoms

Sore throat, enlarged cervical lymph nodes, low grade fever, grey mucous on tonsils, headache.

Complications: Nerve damage, heart & kidney failure.

Pharmacological Treatment

- Diphtheria anti-toxin
- Antibiotics

Prevention of DTaP

Whooping cough & Poliomyelitis: **Cocooning**

- Infanrix-hexa (DTaP-IPV-HepB/Hib)
- Infanrix-IPV booster (DTaP, polio)
- Boostrix booster (DTaP)

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Infanrix-IPV booster (DTaP, polio)	IPV is inactivated or whole killed	4 years
Boostrix booster (DTaP)	Booster	11 or 12 years Unfunded at 45y, 65y, pregnant

Poliomyelitis (Polio)

Revisit *Chapter 4 - Gastrointestinal System* for information on this condition.

Prevention: Cocconing

- Infanrix-hexa (DTaP-IPV-HepB/Hib)
- Infanrix-IPV (DTaP, polio) booster

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Infanrix-IPV booster (DTaP, polio)	IPV is inactivated or whole killed	4 years

Haemophilus Influenzae B (HiB)

Description

Hib is a bacteria which causes serious illness, often causing pneumonia and meningitis in young children under 5 years old. The bacteria is found in the nose and throat, usually without causing symptoms, and is spread through the air by droplets.

Signs & Symptoms

- **Haemophilus meningitis does NOT cause rash**
- Epiglottitis (infection and swelling in throat that blocks breathing passages)

Complications: Mental retardation, cerebral palsy, deafness, epilepsy, partial blindness

Prevention

- Infanrix-hexa (DTaP-IPV-HepB/Hib)
- Hiberix (Hib-PRP-T) booster

Vaccine	Vaccine Type	When
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months
Hiberix (Hib-PRP-T) booster	Conjugate vaccine	15 months

Hepatitis A & B

Revisit *Chapter 5 - Hepatic System* for information on this condition.

Prevention

- Passive immunisation: IG
- Active immunisation: heat killed vaccines
 - Avaxim (HAV)
 - Twinrix (HAV & HBV)
 - Infanrix-hexa (DTaP-IPV-HepB/Hib)

Vaccine	Vaccine Type	When
Avaxim (HAV)	Inactivated	
Twinrix (HAV & HBV)	Inactivated	Risk groups only
Infanrix-hexa (DTaP-IPV-HepB/Hib)	Toxoid vaccine inactivated with formaldehyde + adjuvanted with alum	6 weeks, 3 months, 5 months

Measles (MeV), Mumps (MuV), Rubella (German Measles)

Revisit *Chapter 7 - Respiratory System* for information on this condition.

Prevention

- MMR (Priorix)

Vaccine	Vaccine Type	When
MMR (Priorix)	Live Attenuated Contraindicated if neomycin anaphylaxis, immunocompromised, pregnancy.	12 and 15 months. Give to contacts within 72 hours.

Influenza (Flu)

Revisit *Chapter 7 - Respiratory System* for information on this condition.

Prevention

- FLUAD-QUAD (inactivated quadrivalent subunit vaccine)

Vaccine	Vaccine Type	When
Afluria Quad Afluria Quad Junior Flaud Quad Fluquadri	Inactivated quadrivalent subunit vaccine	Influenza immunisation programme: 1st April - 31st December Funded for: 1. >65 years old 2. Māori/Pacifica 55-64 years old 3. Pregnant 4. Children ≤4 with respiratory illness 5. CVD, chronic respiratory disease, diabetes, CKD, cancer, immunocompromised

Varicella-Zoster Virus (VZV)

Revisit Chapter 1 - Dermatology for information on these conditions

Description

Chicken Pox & Shingle

Prevention

- Varicella: Varilrix
- Herpes Zoster: Shingrix

Vaccine	Vaccine Type	When
Varicella (Varilrix)	Live attenuated vaccine (contraindicated if neomycin anaphylaxis, immunocompromised, pregnant)	15 months
Herpes Zoster (Shingrix)	Live attenuated vaccine (contraindicated if neomycin anaphylaxis, immunocompromised, pregnant)	65 years (recommended at 50y) (If infected, wait 12 months before vaccination)

Recommended and funded
1 dose of VV for: <ul style="list-style-type: none">• children at age 15 months (who were born on or after 1 April 2016); or• previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.
2 doses of VV, at least 6 weeks apart, for the following special groups: ^a <ul style="list-style-type: none">• non-immune patients:<ul style="list-style-type: none">- with chronic liver disease who may in future be candidates for transplantation^b- with deteriorating renal function before transplantation^b- prior to solid organ transplant- prior to any elective immunosuppression^c- for post-exposure prophylaxis of immune-competent in-patients• patients at least 2 years after bone marrow transplantation, on the advice of their specialist• patients at least 6 months after completion of chemotherapy, on the advice of their specialist• HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression, on the advice of an HIV specialist• patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella• household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella• household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.
Recommended, not funded
1 dose for all susceptible healthy children aged under 13 years who do not meet the eligibility criteria for the funded dose.
2 doses, at least 6 weeks apart, for all susceptible adolescents and adults.

Recommended and funded
1 dose of HZV is recommended and funded for: <ul style="list-style-type: none">• individuals at age 65 years, or• catch-up^a of individuals aged 66–80 years, inclusive.
For consideration, but not funded
1 dose of HZV may be considered, but is not funded, for individuals aged 50–64 years: <ul style="list-style-type: none">• who are at increased risk of zoster^{24, 25, 26, 27} and who may benefit from being vaccinated earlier than the routine schedule:<ul style="list-style-type: none">- with asymptomatic HIV^b (if CD4+ lymphocyte count is ≥ 200 cells/mm³)- with end-stage kidney disease^b (CKD stages 4–5)- at least 4 weeks prior to commencing high-dose immunosuppressive therapy^{b,c} and/or solid organ transplantation^{b,c}- after ceasing high-dose immunosuppressive therapy^{b,c}- at least 2 years post-HSCT^{b,c}- with autoimmune disease^{b,c} (eg, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis)- with a first generation family history of zoster- with depression- with diabetes- with psychiatric disorders- with chronic obstructive pulmonary disease.• who are household contacts of immunocompromised individuals.

Human Papillomavirus (HPV)

Revisit Chapter 1 - Dermatology & Communicable Diseases for information on this condition

Prevention

- Gardasil 9 (9-valent HPV vaccine)

Vaccine	Vaccine Type	When
Gardasil 9 (9-valent HPV vaccine)	Non-infectious recombinant vaccine	11 or 12 years Those beginning vaccination at >15 years will need three doses

MENINGITIS

Description

Meningitis is an inflammatory disease of the meninges (dura mater, arachnoid mater, pia mater layers that line the brain and spinal cord) — it occurs when the fluid surrounding the meninges become infected.

Causative Agents

Although it is caused by different kinds of infections it is most commonly caused by viruses. However bacterial meningitis is the most problematic infection and thus the one we vaccinate against. Bacterial Meningitis will thus be the focus of this sub-section.



Note

These pathogens can exist in the nose/throat of healthy people without causing illness.

1. *Bacteria*: **life threatening** illness, spread through extended contact with infected person
 - Meningococcal Meningitis (*Neisseria Meningitidis*)
 - Pneumococcal Meningitis (*Streptococcus Pneumoniae*)
 - Haemophilus Influenzae B (HiB)
 - Others - GBS, E.Coli, Listeria, Mycobacteria
2. *Viruses*: **most common**, immunocompromised, spread through direct contact with infected body fluids
3. *Fungi*: rare disease in immunocompromised individuals
4. *Other*: cancer, chemical irritation, drug allergies

The infective agent will spread through the bloodstream until it reaches the brain or the spinal cord via BBB penetration where it can develop into a more advanced infection in the CSF. The resulting inflammatory response is known as meningitis.

Complications

- *Morbidity* ~ 15 - 30 % | *Mortality* ~ 20 - 25 %
- *Systemic* - vascular, respiratory (pneumonia), arthritis
- *CNS* - inflammation causes hearing loss, language disorders, cognitive and motor abnormalities, seizures; cerebral oedema, hydrocephalus or haemorrhage; visual disturbances; behavioural problems
- *Spread* - A meningitis infection may release bacteria in the bloodstream, which produce toxins that can cause blood vessel damage and the k of blood into skin or organs. The blood infection can lead into gangrene - which can result in amputation.

Signs & Symptoms

Often: headache, lethargy, confusion, vomiting, irritability, fever, **stiff neck, photophobia**.

Sometimes – non-blanching rash (not always present with all types of bacterial meningitis, but if this appears, you want to get to hospital quickly — not present in *haemophilus influenzae* meningitis)

Diagnosis

- *Antibiotics*
- *Lumbar Puncture* - CSF examination

However, this is rarely done due to the many complications that can occur. Thus doctors often go straight for antibiotics

Prevention

1. Surveillance
2. Education for symptom recognition (public & health care providers)
3. Public health measures (health housing, smoking, crowding)
4. Vaccination (only for bacterial - all are subunit vaccines!)

Vaccination

- Safe for pregnancy and breast feeding
- Only contraindication is previous anaphylaxis
- May cause pain, irritability, headache, fatigue and fever.

Non-Pharmacological Treatment

- Isolation
- Avoid overcrowded living conditions, if possible
- Avoid sharing food, drinks and eating utensils
- Limit close physical contact when coughing and sneezing
- Remember to cover your mouth and wash hands thoroughly after coughing or sneezing

Pharmacological Treatment (to reduce complications)

[BPAC Meningitis Antibiotic Guidelines](#)

- Antimicrobials (depends on the strain)

Bacterial Meningitis

BACTERIAL MENINGITIS		
Bacteria	Disease	Epidemiology
Neisseria Meningitis	Meningococcal Meningitis	Causes epidemics, septicaemia , rash
Streptococcus Pneumoniae	Pneumococcal Meningitis	Common in adults and immunocompromised, causes pneumonia
Haemophilus Influenzae B	Haemophilus Influenzae B	Common in kids, causes brain damage

Meningococcal Meningitis (*Neisseria Meningitidis*)

*Please note this vaccination is not on schedule.

Description

Meningococcal disease is a bacterial infection that causes two very serious illnesses (meningitis and/or septicaemia), and is transmitted via droplets. 13 serotypes (disease mostly caused by A, B, C, W, Y). *Neisseria meningitidis* is carried in the nasopharynx in some people (commensal bacteria).

At-Risk Populations

Meningococcal disease can affect anyone but it is more common in children under 5, teenagers, and young adults. Students in their first year of tertiary education living in student accommodation may also be at higher risk.

Signs & Symptoms

Rash (septicaemia), stiff neck, headache, fever, sleepiness, joint and muscle pain

Pharmacological Treatment

- *Antibiotics*: Ceftriaxone, ciprofloxacin, rifampicin
- *Supportive Care*: pain relief, fluid replacement
- *Prevention of Complications*: corticosteroids (dexamethasone), decrease intracranial pressure, anti-epileptics (midazolam, levetiracetam, phenytoin)

Prevention

There are 4 different meningococcal vaccines in NZ to cover the different groups:

	Vaccine	Groups Covered	Vaccine Type	When	How
Group B Vaccines	Bexsero 4CMenB Meningococcal B Vaccine	B	Recombinant protein-based vaccine	Funded in 9 months - 55 years old of high risk Recommended but not funded for people of all ages in communal accomodation	2 doses at least 8 weeks apart Bexsero - IMAC
Non Group B Vaccines (ACWY)	Menactra Quadrivalent MCV4-D	(A, C, Y, W)	Conjugate vaccine	Funded for 13 - 25 years old in close-living situations Also funded in high risk groups	Menactra - IMAC
	NeisVac-C MenCCV	C	Conjugate vaccine	Funded in < 9 months of high risk	NeisVac-C - IMAC
	Nimenrix MCV4-T	(A, C, Y, W)	Conjugate vaccine	Unfunded. 12 months - 55 years	Nimenrix - IMAC

Table 13.4: Meningococcal vaccine recommendations

Note: Funded circumstances are in the shaded rows. See the [Pharmaceutical Schedule](#) for any changes to the funding decisions.

Recommended and funded

MenC or MenACWY-D and 4CMenB are recommended and funded for:

- patients pre- or post-splenectomy or with functional or anatomical asplenia^{a,b}
- patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited)
- patients who are pre- or post-solid organ transplant^b
- HSCT (bone marrow transplant) patients^b
- patients prior to planned immunosuppression^{b,c}
- patients following immunosuppression^{b,c}
- close contacts of meningococcal cases of any group^d
- individuals who have previously had meningococcal disease of any group^e

MenACWY-D is recommended and funded for:

- individuals aged 13–25 years inclusively who are entering within three months or are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks or prisons.

Pneumococcal Meningitis (*Streptococcus Pneumoniae*)

Description

Pneumococcal disease is an infection caused by pneumococcal bacteria, causing severe disease such as meningitis and septicaemia. The bacteria can also cause pneumonia usually of **ONE** lobe (CAP), ear, and sinus infections.

At Risk Populations

It is the most common cause of **adult meningitis**.

Young, Elderly, Immune Compromised

Complication: Influenza

Signs & Symptoms

- Pneumococcal meningitis is not contagious (although strep itself is) and does **NOT** cause a rash

Pathophysiology

- Congestion/Consolidation (1 -2 days)*: acute inflammatory response, decreased air entry, cough
- Red hepatisation (2 -3 days)*: bacterial replication (fever, general malaise), influx of erythrocytes, more leukocytes, accumulation of fibrin (clotting)
- Grey hepatisation (3 - 7 days)*: adaptive immune response, purulent exudate (broken down erythrocytes, leukocytes, fibrin, dying bacteria)
- Resolution (< 2 weeks)* OR systemic spread

Pharmacological Treatment

- Antimicrobials (penicillin)

Prevention

- PCV10 vaccine (Synflorix)

Vaccine	Vaccine Type	When
Synflorix PCV10	Vaccine covers most common streptococcus serotypes but not all.	Usual childhood schedule at 6 weeks, 3/5 and 15 months

Haemophilus Influenzae Meningitis (HiB)

Description

Before we had a vaccine, it was the main cause of bacterial meningitis in the under 5 age group. (95%). Since its availability, this type occurs much less.

Signs & Symptoms

- No rash
- Fever, loss of appetite, vomiting
- Drowsiness, headache, sensitivity to bright light, neck stiffness
- Signs may be vague and non-specific in young infants; they may have a bulging fontanelle

At Risk Populations

Immune Compromised

Treatment

- Dexamethasone (only for children >6 weeks)
- Anti-epileptics (midazolam, levetiracetam, phenytoin)

Vaccine

Funded vaccine part of childhood schedule.

Vaccine	When
HiB Vaccine <i>DTaP-IPV-HepB/HiB</i>	Usual childhood schedule at 6 weeks, 3/5 and 15 months

Viral Meningitis

Viral Meningitis

Please note that there is no vaccine available yet for viral meningitis.

Description

Viral infection affecting the meninges. Causative viral agents include poliovirus, enterovirus, paramyxovirus (mumps), HSV

Signs & Symptoms

Non-blanching petechial rash (blood leaking into tissue), stiff neck, headache, pyrexia, chills, malaise, N/V, photophobia

Pharmacological Treatment

- No cure, self-resolving in 2 weeks
- Symptomatic relief (paracetamol, aciclovir if **HSV**)

VACCINE-PREVENTABLE DISEASES NOT ON SCHEDULE

Introduction

We will look into TB and COVID-19.

Tuberculosis (TB)

Description

Tuberculosis is an infectious disease caused by infection with the bacterium *Mycobacterium tuberculosis*. TB most commonly affects the lungs, but can also affect the lymph nodes, bones, joints, and kidneys. It can also cause meningitis. Transmitted via airborne transmission. Identified using **Ziehl-Nielsen stain**.

Pathogenesis

Inhalation of mycobacteria, activation of macrophages, spread to lymph node, activation of acquired immune response, granuloma formulation (stable, exudative, breakdown), +/- **extra-pulmonary spread**

Risk Factors

1. *Socioeconomic*: poverty, malnutrition, wars
2. *Immunosuppression*: HIV, AIDS immunosuppressive therapy
3. *Occupation*: mining, construction workers, ect...

Diagnosis

1. Chest X Ray & Microbiological Diagnosis
2. Blood/Sputum Tests
3. Tuberculin skin test (Mantoux, Heaf)
 - *False negative*: poor immune function (failure of body to respond to test)
 - *False positive*: environmental mycobacteria

Note: MMR/PRIORIX may affect the tuberculin skin test. Tuberculin testing may be done before or at the same time that PRIORIX is given. Test may be affected if 4-6w after vaccine.

Signs & Symptoms

Asymptomatic, fatigue, malaise, loss of appetite, fever, night sweats, painful and productive cough (sputum is mucoid, purulent, bloody), bacteraemia (spleen, liver, CNS disease)

Pharmacological Treatment

Eliminate fast and slow growing bacteria and reduce Multi Drug Resistant/Extensively Drug Resistant Tb

- Intensive phase (2 months): isoniazid, rifampicin, pyrazinamide, ethambutol
- Continuation phase (4-10 months): isoniazid, rifampicin

Prevention: *Eligibility criteria apply*

- *Public Health Measures* (improved nutrition, housing, co-morbidities)
- *Vaccination*: Bacille Calmette-Guerin (BCG) vaccine

Vaccine	Vaccine Type	When
Bacille Calmette-Guerin (BCG)	Live attenuated intradermal vaccine	At birth or < 5 years if high risk

Treatment

1. *Intensive Phase (2 months)* - isoniazid, rifampicin, pyrazinamide (+ ethambutol)
2. *Continuation (4-10 months)* - isoniazid, rifampicin

Table 20.1: Neonatal BCG eligibility criteria

Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:

- will be living in a house or family/whānau with a person with either current TB or a history of TB
- have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥ 40 per 100,000*
- during their first five years will be living for three months or longer in a country with a TB rate ≥ 40 per 100,000.*

Funded BCG may be offered to the following at-risk people if they are tuberculin skin test- or interferon gamma release assay-negative:

- contacts of active TB cases aged under 5 years (note that a contact exposed to TB in the preceding three months will need two negative tuberculin skin tests, 8 to 12 weeks apart, before vaccination)
- immigrants aged under 5 years from countries with a rate ≥ 40 per 100,000
- health care workers and laboratory staff, depending on their risk of exposure (refer to the *Guidelines for Tuberculosis Control in New Zealand 2010*,¹ or the current edition)
- people exposed to animals that are likely to be infected.

COVID-19

COVID-19 Written Resources (IMAC)

Revisit *Chapter 7 - Respiratory System* for information on this condition.

Prevention — Note wait 7 days between Covid and Shingles vaccine

- Pfizer mRNA vaccine
- Public health measures

Vaccine	Vaccine Type	When
Pfizer-BioNTech (Comirnaty)	mRNA	2 doses (3-8 weeks apart) Booster (5 months after 2nd dose) 2nd Booster for > 50 years (4 months after 1st booster)
Moderna	mRNA	
Janssen/Johnson & Johnson	Vector	
AstraZeneca	Vector	
Novavax	Protein subunit	

Vaccine Storage Conditions

Storage conditions - mRNA-CV (10 mcg) and mRNA-CV (30 mcg)

Storage conditions	mRNA-CV (10 mcg) 5–11-year-olds	mRNA-CV (30 mcg) 12+ year olds
Vial cap colour	Orange	Purple
Ultra-cold freezer (-90°C to -60°C)	Up to 6 months	Up to 9 months
Freezer (-25°C to -15°C)	n/a	2 weeks
Fridge (2°C to 8°C)	Up to 10 weeks	Up to 1 month
Diluted vaccine (in vial) (2°C to 30°C)	12 hours	6 hours
Drawn up vaccine (2°C to 30°C)	6 hours	6 hours

Vaccine specifications - mRNA-CV (10 mcg) and mRNA-CV (30 mcg)

Description	mRNA-CV (10 mcg) 5–11-year-olds	mRNA-CV (30 mcg) 12+ year olds
	Dilution required (0.9% saline)	Dilution required (0.9% saline)
Age group	5–11-year-olds	12 years and older
Vial cap colour	Orange	Purple
Dose	10 mcg (10 µg)	30 mcg (30 µg)
Dose volume	0.2 mL	0.3 mL
Fill volume (before dilution)	1.3 mL	0.45 mL
Volume of diluent (0.9% saline) per vial	1.3 mL	1.8 mL
Doses per vial	10–12 doses per vial (after dilution)	6–7 doses per vial (after dilution)
Route; site	IM; deltoid	IM; deltoid

VACCINE LONG-TERM STORAGE IN FREEZER



Undiluted vaccine stored for up to **31 days** at **+2°C to +8°C**
(includes maximum of 12 hours distribution time).

Box containing vials has expiry printed on outer sticker.
This is 31 days from when removed from freezer storage.
Monitor temperature as per cold chain policy. If temperature varies from **+2°C to +8°C**, follow cold chain breach process.

Additional **2 hours** allowed to prepare vaccine for dilution.
Purpose is to bring vial to **room temperature** (up to max **+30°C**)
before adding diluent ie, not cold to touch.

Once diluent added to vial, now have
6 hours for administration. This 6 hours
is to be spent between **+2°C to +30°C**.

DISCARD ANY UNUSED VACCINE 6 HOURS AFTER DILUTION

Stable for up to 31 days at +2°C to +8°C

Up to 2 hours

Up to 6 hours

Once removed from freezer, timer starts

Once removed from fridge, timer starts

Once diluent added, timer starts

Paediatric Pfizer/BioNTech mRNA-CV-10ug vaccine VACCINE STORAGE SUMMARY



Long-term storage in freezer for up to 6 months.
Stored at **-90°C to -60°C**.

Undiluted vaccine stored for up to **10 weeks** at **+2°C to +8°C**
(includes maximum of 12 hours distribution + transport time).
Box containing vials has expiry printed on outer sticker. This is 10 weeks from when removed from freezer storage.
Monitor temperature as per cold chain policy. If temperature varies from **+2°C to +8°C**, follow cold chain breach process.

Additional **2 hours** allowed to prepare vaccine for dilution.
Purpose is to bring vial to **room temperature** (up to max **+30°C**)
before adding diluent ie, not cold to touch.

Once diluted the vial can be stored for up to 12 hours
at **+2°C to +30°C**. Mark vial with USE BY time.

Label syringe with USE BY time of 6 hours from when dose was drawn up or USE BY time on vial, whichever is soonest.
Store at **+2°C to +30°C**.

Stable for up to 10 weeks at +2°C to +8°C

Up to 2 hours

Up to 12 hours

Up to 6 hours

Once removed from freezer, timer starts

Once removed from fridge, timer starts

Once diluent added to vial, now have 12 hours

Once in syringe, USE BY time applies

DISCARD ANY UNUSED VACCINE IN SYRINGES AFTER 6 HOURS, IN VIALS AFTER 12 HOURS

mRNA COVID-19 vaccine Pfizer/BioNTech [mRNA-CV]

Screening and guidance form

Pre-vaccination screening, guidance for regulated vaccinators

SCREENING QUESTIONS	RATIONALE FOR QUESTIONS AND ADVICE ON ACTIONS REQUIRED
Please tell me your full name and date of birth.	To check you have the correct patient records on the CIR. Check '12 years or older'. If any adult, ask them their age. See back page re consent for those under 16.
Are you feeling well today?	Postpone vaccine if: fever >38°C or acute systemic illness. Anyone directed to self-isolate or waiting for test should not attend vaccination appointment. See opt guidelines for the screening questions. Very frail or elderly, with comorbid condition, ensure they are stable as well as possible before vaccination and advise carer, on need for post vaccines observation and hydration.
Have you had a serious allergic reaction to anything including previous Pfizer vaccine?	Contraindications: A history of anaphylaxis to previous dose of the mRNA-CV vaccine or any component of the vaccine. Precaution: Anaphylaxis to reagent polyethylene glycol (PEG) (under specialist guidance). A definite history of anaphylaxis-type reaction to any other product: A slightly increased risk of anaphylaxis has been noted in individuals who have had a previous anaphylaxis-type reaction to any other product. These individuals can still receive mRNA-CV. They should be well observed for at least 30 minutes and be given clear post vaccination advice, it is important that the observation staff are specifically alerted to this history by the vaccinator. This must be a verbal handover as the CIR automates a 15-minute wait timer. All vaccination sites are set up to manage anaphylaxis for those with precautions. Those who have been diagnosed with myocarditis following first COVID-19 vaccine dose should have cardiac review and guidance from IMAC on future doses of vaccine.
Is this your first COVID-19 vaccination?	Check spacing between vaccines: at least 3 weeks between doses. New recommendation, reverting back to 3 weeks between doses. Day 0 is the vaccination day. Vaccination at less than 21 days is off-label use (ie, unapproved by Medsafe). No maximum spacing.
Do you have a bleeding problem or blood disorders?	Vaccines can be administered to people on anticoagulants. For patients with haemophilia, receiving clotting factor replacement or similar, vaccinations should be given as soon as possible after receiving the medicine. It is recommended that the platelet count is kept $30 \times 10^9/L$. Specialist advice is recommended. After vaccination, apply firm pressure over the injection site, without rubbing, for 10 minutes to reduce the risk of bruising.
Do you have any other questions? See responses to medical concerns.	Immunosuppression: The antibody response to the vaccine may be reduced and protection may be suboptimal, but it is still likely to be adequate to protect against severe disease and there are no safety concerns. Patients may have been advised on specific timing of vaccinations to fit into other treatment regimens. Where possible accommodate this. Cardiac patients with heart disease or cardiac abnormalities should be vaccinated. If patients have had bilateral lymph clearance, vaccine can be given in the vastus lateralis, seek help from experienced vaccinator or 0800 if unsure. Other concerns, if you are unsure how to respond, call IMAC for support.
Other vaccines in the last 7 days	Any National Schedule vaccines can be given at the same time as mRNA-CV with any interval spacing. The only exception to this is Zostavax (shingles vaccine). Ideally it is recommended to allow seven days between Zostavax and either dose of Comirnaty.
Our message is 'don't delay'! Before turning anyone away, please consult with your clinical lead or IMAC on 0800 IMMUNE [0800 466 863], 8 am - 8pm 7 days a week	

- Syringes should be given to the vaccinator with a sticker/label stating vaccine and diluent batch numbers and expiry date (date from vaccine box, not from vial), the time of expiry (6 hours post dilution), and initials of who drew up and who checked.
- For more detailed instructions please see related document: *Instructions for multi-dose vial Pfizer/BioNTech vaccine: preparation and administration*.

Post-vaccination advice must include:

- Reminder of need to stay for at least 15 minutes for observation.
- Anyone with a history of anaphylaxis to any product, will still need close observation, a 30-minute wait and given clear post vaccination advice.
- Discussion of potential side effects, advise use of paracetamol or other analgesia for pain, fever, or discomfort, and if unwell rest, drinking fluids and avoid vigorous activities, such as going to the gym. For further advice call GP or Healthline.
- For any unexpected concerns including chest pain, shortness of breath, or palpitations call seek medical advice. If an emergency call 111.
- For those who are insulin dependent diabetics, discuss the need to closely monitor blood sugars for next few days, as high or low sugars can occasionally be a side effect of the vaccine.
- Supply information on how and when to make a second appointment.

Reminder

- It is important that the name of the person administering the vaccine is logged in the CIR.
- If you do need to record an AEF in CIR for CARM please include patient's GP contact phone number.
- Expiry date record in CIR is the sub-batch number from the box NOT the vial.

Incident management

- It is the site clinical and quality lead's responsibility to record, report and investigate vaccine administration incidents.
- IMAC will continue to offer support and guidance in the event of such incidents.
- Please contact: 0800 IMMUNE (466 863) or your IMAC Regional Immunisation Advisor.

CALL 0800 IMMUNE (466 863) FOR CLINICAL ADVICE, 8AM - 8PM, 7 DAYS PER WEEK

Instructions for multi-dose vial Pfizer/BioNTech vaccine: preparation and administration

1. STORAGE

Pfizer vaccine vials will thaw during distribution to clinics. **DO NOT REFREEZE.**
Store undiluted vials at +2°C to +8°C for up to 31 days. This includes distribution time.
For dilution, vials can be stored at room temperature (but less than +30°C) for an additional two hours at most.

Pfizer vaccine comes as a concentrate and MUST be diluted.

Avoid exposure of vaccine to direct sunlight, or UV light at all times.
After dilution, store vials between +2°C and +30°C and use within six hours. **You must monitor room temperature.**

Vaccine preparation should always take place in a well-lit, dust free area, away from distractions.

Two appropriately trained staff need to work together, independently checking each other's work.

2. PRIOR TO DILUTION

- The vaccine should be brought to room temperature. It should not feel cold to touch.
- Check the expiry date & time printed on the box.
- Check the vial stopper is intact.
- Invert the vaccine vial gently 10 times. **DO NOT SHAKE.**
- Inspect the vial. The thawed suspension may contain white to off-white opaque amorphous particles. Do not if discoloured, save the vial and report as an incident.

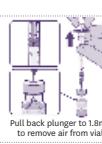

3. DILUTING THE VACCINE

- Remove purple plastic cap/guard on top of vaccine vial carefully using an aseptic technique.
- Cleanse vial/vial stopper with a single-use antiseptic/alcohol swab and leave to dry for 30 seconds.
- Use **suppling diluent** (0.9% sodium chloride for injection). Check expiry date and batch number.
- Open diluent just before use. Diluent that is opened and not used immediately must be discarded. Only prepare saline syringes as needed.
- Using aseptic technique, withdraw **1.8 mL** of diluent into a syringe (using a 25-gauge orange standard needle). Discard the rest of the saline.
- Independently check this volume with an appropriately trained colleague.


4. EQUALIZE

Before withdrawing the needle, equalize vial pressure by keeping the needle above the fluid level and **withdrawing 1.8 mL of air** into the now empty diluent syringe. You may notice a very small amount of liquid in the syringe that had been held inside the needle. This should stay in the syringe.

- Remove the syringe and needle attached to the vaccine vial and discard.
- After dilution, the vial contains 2.25 mL from which 6 or occasionally 7 doses of 0.3 mL can be extracted.


5. AFTER DILUTION

Gently invert vial containing diluted vaccine **10 times** to mix. **DO NOT SHAKE.**
Inspect vaccine in vial. It should be an off-white suspension with no particulates visible.

Do not use if discoloured or contains particulates, save vial and report as incident.

6. LABELLING VACCINE

Label the vaccine doses, one label per dose of vaccine:

- Name of vaccine.
- Diluent name and expiry date.
- Vaccine sub batch number (number on box including the extra 3 digits).
- Expiry date for vaccine sub batch, (this is the expiry date on the box not the vial).
- Time the syringe must be used by (6 hours from time of dilution).
- Who prepared the vaccine and who checked it.

Vaccine must be used within 6 hours of dilution and can be stored at room temperature.

If returned to the fridge, allow to return to room temperature, ie not cold to touch, before administration.

The 6-hour allowance for use is in addition to the 31 days storage, once defrosted.

7. PREPARATION OF INDIVIDUAL 0.3ML DOSES OF PFIZER/BIONTECH

Each dose is drawn up using the needles that will be administered with.

All doses must be drawn up from the vial at the same time so you can confirm dilution was correct. See section on Doses.

Cleanse the vial stopper with a single-use antiseptic swab and allow to dry.

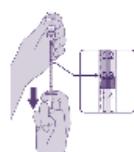
Prepare syringes and needles

Prepare syringes and needles only as required. Always open packets by unpeeling them, do not push needles or syringes out through wrap as this contaminates them. Do not prepare them in advance as this increases risk of contamination.

- Take a 1 mL syringes with either a BD [non-LDS] Orange 25mm (1") needle or LDS Orange Needle 25g x 25mm (1") or a 23-25G x 1.5-38mm length [for someone with a larger arm].
- Due to a temporary issue with the fit of syringes to needles, we recommend non-LDS needles with vermicare syringes OR LDS needles with non-vermacare syringes (BD or other brand).
- Ensure the syringe and needles fit firmly together. If the connection is not tight, discard the syringe and needle before starting to draw up vaccine.

Drawing up vaccine

- Slowly withdraw slightly more vaccine than the 0.3 mL dose, then slowly return the plunger to the 0.3 mL dose.
- We recommend you always have syringes ready with both lengths of needles to accommodate all sizes of clients.
- Visually inspect each dose in each syringe just prior to administration:
- Check volume is 0.3 mL.
- If vaccine has leaked out of the needle or hub, then the dose should be discarded.
- Do not use if there is discoloration or particulate matter.
- Administer vaccine intramuscularly into the deltoid.


8. ADMINISTRATION

If vaccine has leaked out of the needle or hub, then the dose should be discarded.

Do not use if there is discoloration or particulate matter.

Administer vaccine intramuscularly into the deltoid.

If you are using non-LDS needles you should have 5 or 6 doses, with LDS needles you will have 6 or 7 doses. If you have more or less than this, a dilution error is likely to have occurred. Discard all the doses, and report as an incident including the vaccine batch number. If the amount of vaccine remaining in the vial cannot provide a full 0.3 mL dose, discard vial and remaining diluted vaccine. Do not pool excess vaccine from multiple vials.

Discard any unused vaccine six hours after dilution.

Larger patients will need 23-25G x 1.5-38mm length. Each vaccinator should have at least one longer needle available. Please see the vaccine administration handout for more information.



CHAPTER 19

THE HAEMATOLOGICAL SYSTEM



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Chapter 19

The Haematological System

General Overview of Haematology

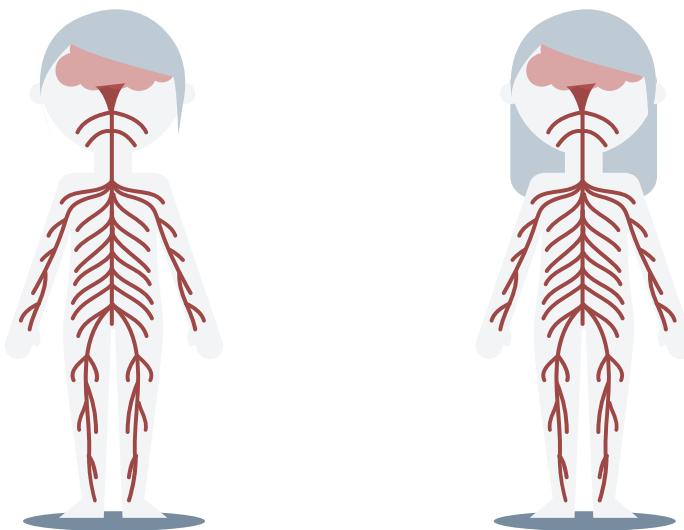
Chapter Resources

Excellent resources for this chapter are:

1. [Anaemia NZF Link](#)
2. [BPAC Complete Blood Count in Primary Care.](#)
3. [BPAC Anaemia on FBC: investigating beyond the pale](#)
4. [Canterbury Red Book for Anaemia](#)

Introduction

In this chapter, we will look into anaemias and its various subtypes. Simply put, anaemia is a deficiency in the **number** and/or **quality** of RBCs in your body. It is defined as Hb < 120g/L in females and Hb < 140 g/L in males.



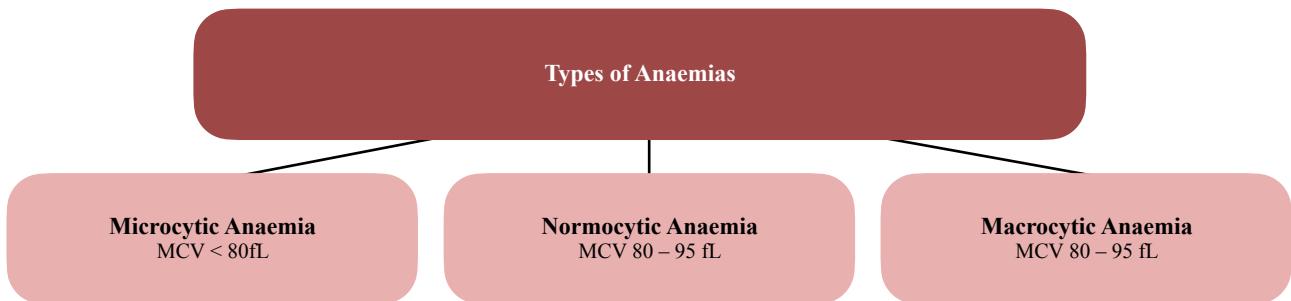
Before we look into it more, we must first understand the components of blood.

Blood Test Parameters		
Test	Description	Range
Haemoglobin	Hemoglobin is a protein in your red blood cells that carries oxygen to your body's organs and tissues and transports carbon dioxide from your organs and tissues back to your lungs. If a hemoglobin test reveals that your hemoglobin level is lower than normal, it means you have a low red blood cell count (anemia).	<ul style="list-style-type: none"> Male: < 130g/L Female: < 115g/L
Ferritin	Ferritin is a blood protein that stores most of our body's iron reserve. It keeps iron in a soluble and non-toxic form. A ferritin test will show the level of iron storage on the body.	<ul style="list-style-type: none"> Male: 12 to 300 ng/mL Female: 12 to 150 ng/mL
Transferrin or Total Iron Binding Capacity (TIBC)	Transferrin is the main protein in the blood involved in the transport of iron throughout the body. When the body's iron stores run low, more transferrin is made by the liver. TIBC is a measure of the maximum amount of iron the blood can carry.	10.74 to 30.43 micromol/L
Haematocrit	Hematocrit is the percentage of RBCs in your blood	<ul style="list-style-type: none"> Males: 40.7–50.3% Females: 36.1–44.3%
Mean Cell/Corpuscular Volume (MCV)	Size of RBCs	<ul style="list-style-type: none"> 80–95 fL
Reticulocyte Count	Level of reticulocytes (RBC precursor cells) in the blood	<ul style="list-style-type: none"> Adults: between 0.5 % to 2.5% Infants: between 2% to 6%

Overview & Summary of Anaemias

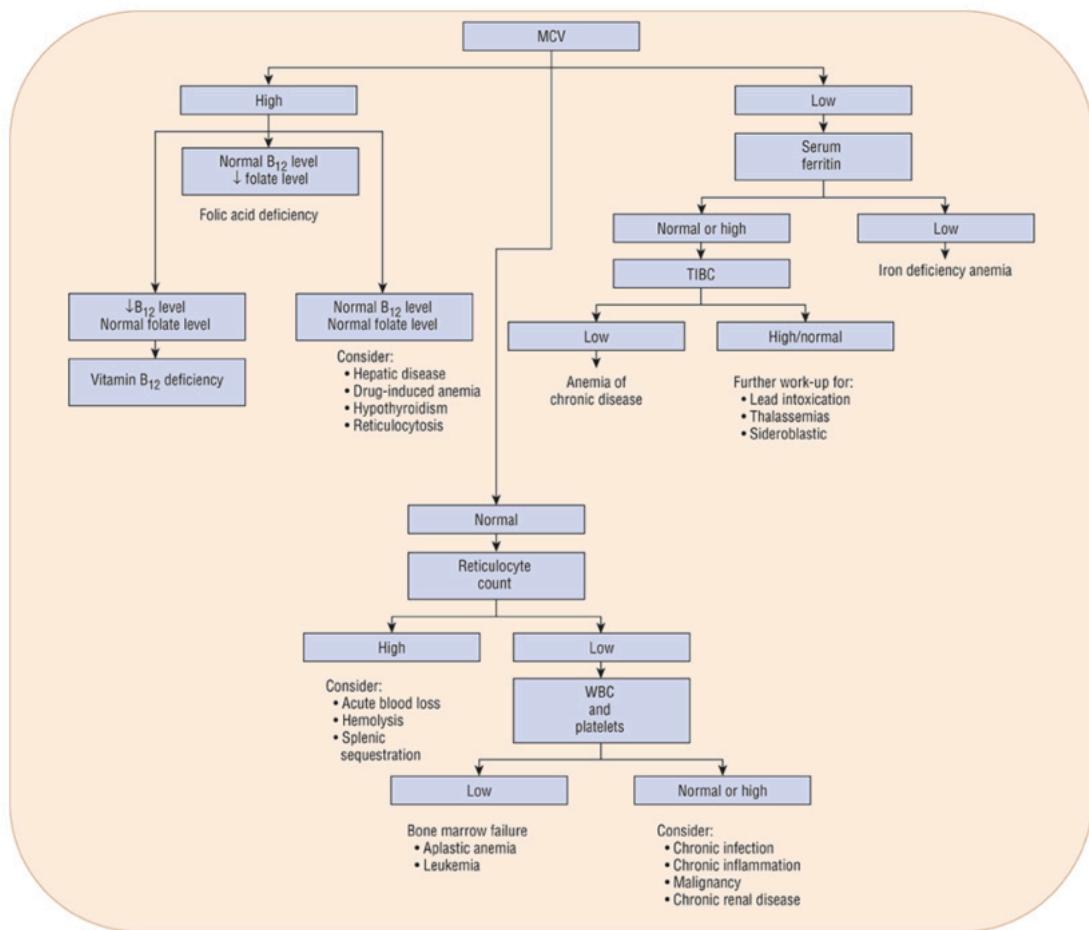
Classification

Many kinds of anaemias exist, each with their own pathophysiology. One way to organise them is according to their size, also known as **Mean Corpuscular Volume (MCV)**.



We will cover each of these anaemias in depth - please find a summary here below.

SUMMARY — Types of Anaemia			
	Microcytic Anaemia MCV < 80fL	Normocytic Anaemic MCV 80 – 95 fL	Macrocytic Anaemia MCV > 95 – 100 fL
Characteristics	<ul style="list-style-type: none"> Small RBCs Not enough of them 	<ul style="list-style-type: none"> Normal sized RBCs <i>but</i> Not enough of them 	<ul style="list-style-type: none"> Large sized RBCs Not enough of them
Pathophysiology	<ul style="list-style-type: none"> RBCs are smaller in size because of reduced haemoglobin. 	<ul style="list-style-type: none"> Lack of RBCs because of poor production or loss. 	RBCs are bigger than normal because: <ul style="list-style-type: none"> Lack of folate and B₁₂ which are required substrates in making RBCs Metabolic conditions such as alcoholism or liver disease causing the accumulation of fats inside RBCs, therefore enlarging them.
Causes	<i>This could be due to:</i> <ol style="list-style-type: none"> Iron deficiency (most common - either due to decreased intake/absorption) Chronic Disease (causing chronic blood loss) Thalassaemia (inherited blood disorder that causes underproduction of Hb) 	<i>Anaemia here could be caused by:</i> <ol style="list-style-type: none"> Haemolytic Anaemia (RBC destruction > production) Ongoing/Acute Blood Loss Aplastic Anaemia (bone marrow disorder) 	Megaloblastic <ol style="list-style-type: none"> Folate Deficiency Vitamin B12 Deficiency Drug induced e.g. MTX and other cytotoxics Non-Megaloblastic <ol style="list-style-type: none"> Hepatic disease Hypothyroidism, alcohol abuse
Diagnostic Tests	<ul style="list-style-type: none"> Serum ferritin TIBC 	<ul style="list-style-type: none"> Reticulocyte count WBC/platelets 	<ul style="list-style-type: none"> B₁₂ Folate
Treatment	<ol style="list-style-type: none"> Iron Rich Diet Iron Salts Parenteral Iron Blood Transfusions (only if Hb < 80g/L) 	<ol style="list-style-type: none"> Blood Transfusions (only if Hb < 80g/L) EPO Stimulating Agents 	<ol style="list-style-type: none"> Sample Dosing B₁₂ Sample Dosing Folic Acid



Risk Factors

Many things can cause anaemia — although cancer and cancer treatment itself are notorious for this.

1. Cancer & Cancer Treatment — *See Chapter 15 | Oncology*
2. Blood loss: GI bleed, heavy menstruation
3. Missing vitamins (e.g. B12, folic acid) or minerals (e.g. iron)
4. Major organ problems: heart, lung, kidney, liver
5. CKD: reduced erythropoietin (EPO) — stimulates RBC production
6. RBCs destroyed faster than they are made (haemolytic anaemia)

Signs & Symptoms

While as we've seen, many kinds of anaemias exist, the symptoms remain the **same for all**.

SYMPTOMS OF ANAEMIA	
System	Description
Eyes	Yellowing
Skin	Pale, cold, yellow, hand/feet swelling, pale brittle nail beds, mouth, gums
Respiratory	SOB
Musculoskeletal	Fatigue (constant weakness/tiredness), dizziness
Gastrointestinal	Changed stool colour, unusual cravings for non-food items of no nutritional value (pica) such as paper
Vascular	Low BP, tachycardia
Central	Fatigue, dizziness, fainting, impaired concentration

Heart	Palpitations, rapid HR, tachycardia, chest pain, angina, heart attack
Spleen	Spleen enlargement
Immunity	Increased susceptibility to infections
Other	Lymphadenopathy, restless leg syndrome
Severe Anaemia	Fainting, chest pain, heart attack

Diagnosis

- Low haemoglobin: male (<130 g/L), female (<115 g/L)
- Mean Corpuscular/Cell Volume (MCV): high, normal, low
- Other labs: Reticulocyte count, WBC/Platelets, Serum Ferritin, TIBC,
- Blood chemistry to check organ function and vitamin/mineral levels (iron, B₁₂, folate)
- Bone marrow exam
- Fecal occult blood test (FOBT)

Complications

- Shortens survival
- CVD and respiratory complications

Goal of Treatment

- Raise haemoglobin levels
- Treat cause
- Prevent complications

ANAEMIAS

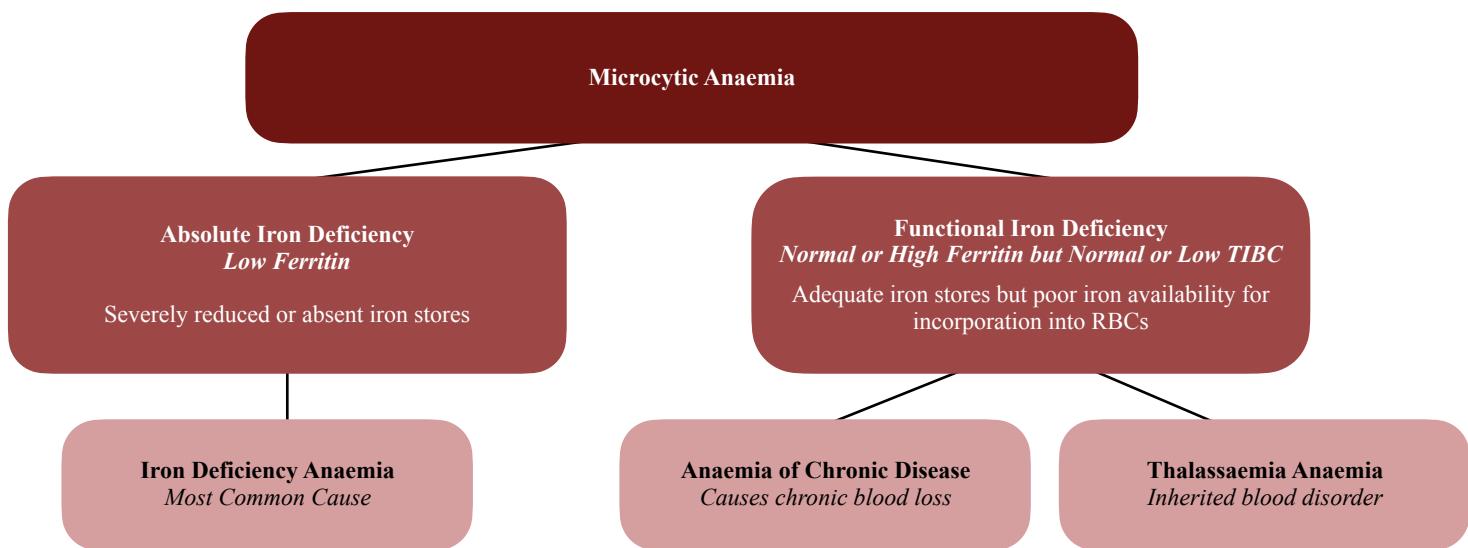
Introduction

We will look into three subtypes: microcytic, normocytic, macrocytic and aplastic anaemia.

Microcytic Anaemia

Description

Microcytic anaemia is a form of anaemia that is used to describe red blood cells that are smaller than usual as well as in low numbers. More specifically, cell size is decreased due to a reduction in haemoglobin. Please note that as Iron Deficiency is the most common cause of anaemia, we will focus on this.



Pathophysiology

Understanding Iron Metabolism

Haemoglobin is an important iron-containing component of RBCs transports O₂ and therefore maintains the pH of the blood. Iron is thus a crucial component in O₂ transport, with the body using ~20mg of it per day to form RBCs. Iron itself is transported throughout the body by **transferrin** and stored as **ferritin** in tissues. Please note that ferric iron must undergo enzymatic reduction to the ferrous.

Understanding Microcytic Anaemia

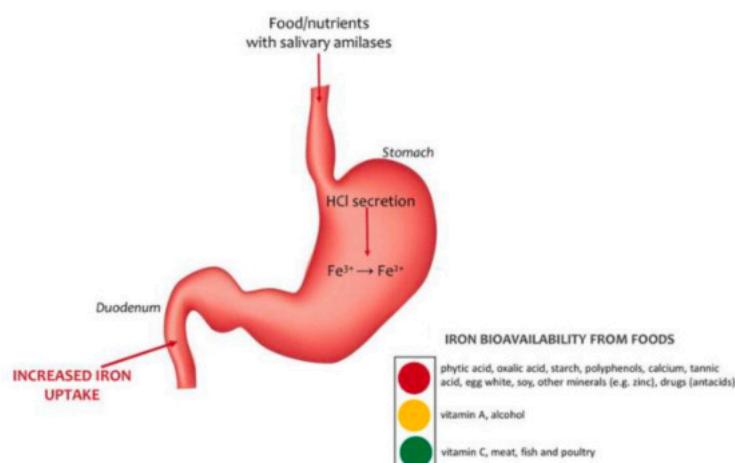
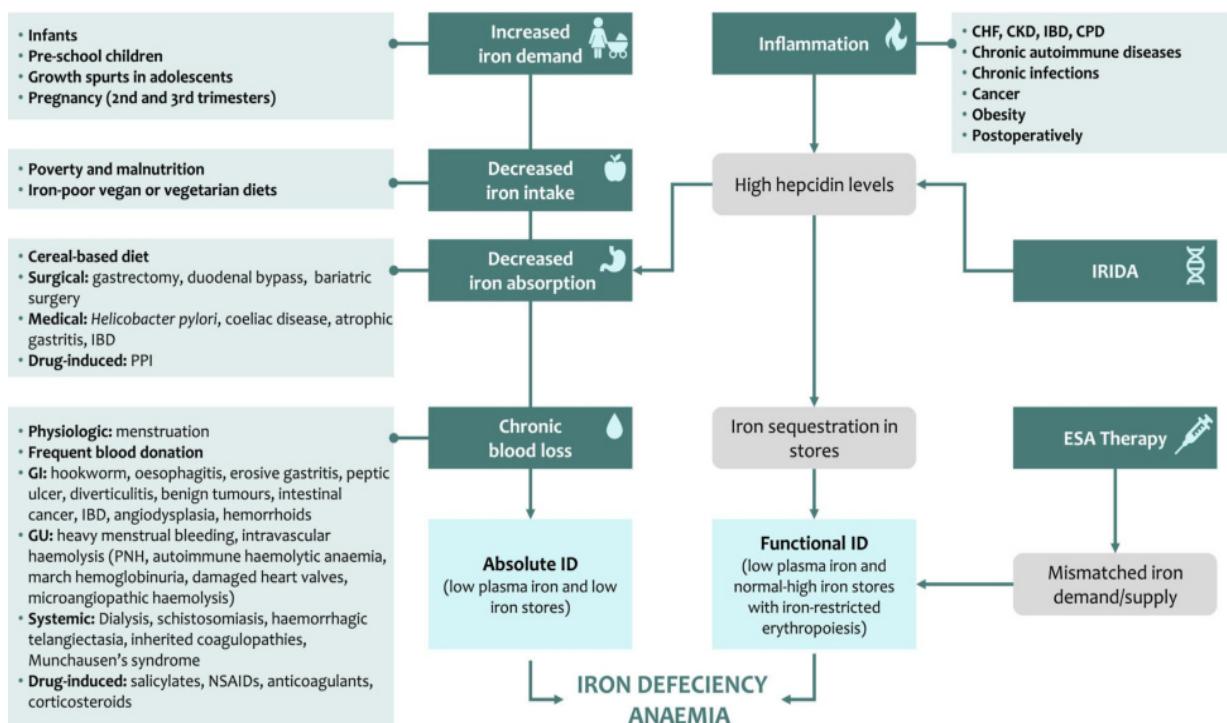
In Microcytic Anaemia, cell size is decreased due to low levels of Hb — this is generally the result of factors that cause poor iron availability e.g. abnormal levels of ferritin and/or transferrin (TIBC).

Causes (Poor Iron Availability)

Thus, poor iron availability can be divided into 2 types:

1. Absolute Iron Deficiency
2. Functional Iron Deficiency

MICROCYTIC (IRON DEFICIENCY) ANAEMIAS	
Anaemia	Cause/Risk Factors
Absolute Iron Deficiency <i>Low Ferritin</i> Severely reduced or absent iron stores	Iron Deficiency <ul style="list-style-type: none"> Nutritional deficiencies: chemo-induced N&V, dietary deficiency, blood loss such as menstruation, malabsorption Increased demand: growth needs in infants, children, adolescents, pregnancy, postpartum, endurance athletes. Decreased intake: poverty, malnutrition, diet - vegetarians, vegans and blood donors at risk. Decreased absorption: cereal-based diets, surgery (bariatric), medical (H.pylori, celiac, IBD), drug-induced (PPIs)
Function Iron Deficiency <i>Normal or High Ferritin</i> <i>Low or Normal TIBC</i> Adequate iron stores but insufficient iron availability for incorporation into erythroid precursors.	Chronic Disease <ul style="list-style-type: none"> Chronic blood loss: menstruation, blood donation, drug-induced (anticoagulants, NSAID, CCS, salicylates), peptic ulcers Inflammation from Chronic Disease: IBD, CKD, CHF, chronic pulmonary disease, chronic autoimmune disease, chronic infections, cancer, obesity, post-operative
	Thalassaemia Inherited blood disorder



Diagnosis

MCV < 80fL

BLOOD TESTS FOR CAUSES OF MICROCYTIC ANAEMIA			
	Iron Deficiency	Chronic Disease Anaemia	Haemoglobinopathies (e.g. thalassaemia)
Serum Ferritin (Storage)	Decreased	Increased	Increased
Serum Iron	Decreased	Normal or Decreased	Normal or Increased
TIBC	Normal or Increased	Normal or Decreased	Normal
Transferrin Saturation	Decreased	Normal or Decreased	Normal or Increased
Serum Soluble Transferrin Receptor	Increased	Normal or Decreased	Increased

Iron Testing

Iron Testing			
Test	Description	Increased in	Decreased in
Serum iron	Measures circulation iron (not diagnostic — fluctuates with diet and diurnal variation)	-	<ul style="list-style-type: none"> • Iron deficiency • Anaemia of chronic disease • Inflammation
Serum transferrin OR Total iron-binding capacity (TIBC)	Transferrin = iron binding sites	<ul style="list-style-type: none"> • Iron deficiency • Pregnancy • OC use 	<ul style="list-style-type: none"> • Chronic disease • Inflammation • Cancers • Iron overload • Protein malnutrition
Transferrin saturation	% of binding sites occupied by iron i.e. a measure of max amount of iron the blood can carry	-	-
Serum ferritin	Acute phase reactant that protects against oxidative stress and inflammation	<ul style="list-style-type: none"> • Inflammation/infection • Liver disease • Heart failure • Cancer 	-

Non-Pharmacological Treatment

While iron deficiency can be helped with dietary changes, it is important to note that dietary interventions alone may not be sufficient.

Iron Rich Diet

- Meat (red), poultry and fish
- Dark green, leafy vegetables such as spinach
- Sweet potatoes
- Dried fruits (prunes, raisins, apricots, peaches), prune juice
- Iron-fortified breads, pasta & cereals
- Beans, (peas, lentils, beans, chickpeas)

Increase foods/drinks rich in **vitamin C** to help absorb iron

- Fruits (citrus such as mandarins/oranges, strawberries, kiwifruit, rockmelon)
- Veges (broccoli, capsicums, tomatoes, brussel sprouts, cabbage, potatoes)

Minimise food/drinks/medications that decrease iron absorption

- Tea, coffee, calcium (in dairy products)
- Alcohol e.g. wine
- **High fibre foods**
- Medicines: calcium, PPIs, Antacids

Pharmacological Treatment (Iron Deficiency)

[BPAC Iron Deficiency Treatment Guidelines](#)

There are 4 treatment options for the treatment of Iron Deficiency Anaemia:

1. Treat Underlying Cause

- Medicines/foods that compete with iron absorption e.g. those that lower stomach acid (antacids, PPIs), calcium
- Iron intake

2. Oral Iron Salts

- Dose should be 100 - 200mg elemental iron daily (e.g. ferrous fumarate 200mg three times daily) - note that lower doses are better absorbed and have less GI ADRs
- Uptake aided by acid (e.g. stomach secretions or dietary acids e.g. ascorbic acid)
- **Oral route NOT effective in heart failure**

3. Parenteral (IV) Iron

- IV iron may be used in those intolerant or unresponsive
- *Indications for IV administration:* decreased iron absorption capacity, severe anaemia, need to recover rapidly, renal disease and taking EPO stimulating agents, IBD

*4. Blood Transfusions (**only if Hb < 80g/L**)*

PHARMACY ONLY MEDICATIONS - ORAL IRONS (NZE)					
Iron Type	Product	Amount (elemental iron)	Funding	Notes	Counselling
Ferric iron in a polymaltose complex	Maltofer tablets	370 mg (100mg)	No	-	<ul style="list-style-type: none"> Lower GI effects Food helps absorption
	Maltofer syrup	37mg/mL (10 mg/mL)	No	<ul style="list-style-type: none"> Contains ethanol 0.325% For ages ≥ 12 years 	<ul style="list-style-type: none"> Swallow whole. Take with a large glass of water Not affected by antacids (not dependent on stomach pH)
Ferrous sulfate	Ferrograd	325mg (105mg)	Yes	<ul style="list-style-type: none"> Modified release* No therapeutic advantage 	<ul style="list-style-type: none"> More effective if taken on an empty stomach. May take with food if stomach upset (but less effective) Take with a large glass of water Do not take with antacids, iron, or calcium
	Ferrograd C	325mg (105mg)	No	<ul style="list-style-type: none"> With ascorbate sodium 562.4mg Minimal therapeutic advantage 	
	Ferrodan solution	150mg/5 mL (30mg/5 mL)	Yes	<ul style="list-style-type: none"> May contain sulphites; risk of hypersensitivity reaction especially in asthmatics Medical advice required for age <2 years 	
Ferrous fumarate	Ferro-tab	200mg (65mg)	Yes	-	<ul style="list-style-type: none"> With folic acid 0.35mg
	Ferro-F-tab	310mg (100mg)	Yes		

ADRs & Iron - Management Options

Managing GI ADRs of Iron



Gastrointestinal ADRs (N/V/D, GI irritation, epigastric pain, constipation) & Iron

Gastrointestinal ADRs (particularly constipation) caused by iron supplements may be an issue for patients - especially in the elderly (risk of faecal impaction). Therefore, management options can be put in place. However, these tend to **decrease iron absorption** i.e. poorer absorption leads to fewer GI effects.

5. Lower doses
6. Less frequent dosing
7. Alternate day dosing
8. Ferric formulations (haem iron (Fe^{2+} | ferrous) are better absorbed than non-haem iron (Fe^{3+} | ferric) thus Fe^{3+} formulations do not cause as much constipation (but are less effective)
9. Modified release preparations (as formulated to release iron gradually but in turn are less effective)
 - MR formulations will exacerbate this in those with inflammatory bowel diseases.
10. Take with food (but this will impact absorption)
11. Avoid foods that decrease absorption e.g. high fibre
12. May conjugate with vitamin C, amino acids, or sugars for better absorption & to protect the GIT
13. Lifestyle: exercise

Darkened / Discoloured Stools (Due to unabsorbed iron)

- Harmless — can ignore

Teeth Staining with Liquid Formulations (temporary discolouration)

- Brush and place drops on back of tongue with dropper/straw)

Overdose: Accidental overdoses common in children and are one of the most common causes of death.

- Parents need to lock them away from reach of children. Call Poisons Centre if needed.

Iron as Prophylaxis

May be appropriate in some conditions e.g. malabsorption, menorrhagia, pregnancy, after subtotal or total gastrectomy, haemodialysis patients, management of low birth-weight infants (i.e. preterm neonates)

Monitoring

Iron Overload/Toxicity

Symptoms are often limited and only become present when organ damage occurs. Causes include transfusions, supplements, increased absorption due to **hereditary haemochromatosis**, liver disease

IRON REQUIREMENTS		
Population	Recommended Daily Intake (mcg/day)	Upper Level of Intake (mcg/day)
<i>Infants</i> 0 - 6 months	0.2 (for breastfeeding)	
<i>Infants</i> 7 - 12 months	11	20
<i>Children</i> 1 - 3 years	9	
<i>Children</i> 4 - 8 years	10	40
<i>Children</i> 9 - 13 years	8	
<i>Adolescents Males</i> 14 - 18 years	11	
<i>Adolescents Females</i> 14 - 18 years	15	
<i>Adult Males & Post Menopausal Females</i>	8	45
<i>Adults Females 19 - Post Menopausal</i>	18	
<i>Pregnancy</i>	27	
<i>Lactation</i>	10 (14 - 18 years) 9 (ages > 18 years)	

Normocytic Anaemia

Description

Normocytic anaemia describes a deficiency in RBCs — which are however, normal sized.

Pathophysiology

Anaemia here is associated with two possible causes:

1. High Reticulocyte Count (Immature RBC)

- Suggests ongoing blood loss in the background of normal bone marrow processes e.g. haemolysis

2. Low Reticulocyte Count

- Suggests there is a problem at the bone marrow level, in which the body is unable to produce RBCs at a healthy rate
- Low WBCs/platelets: Leukaemia/aplastic anaemia
- Normal/High WBCs/platelets: malignancy, chronic conditions (can progress to microcytic as disease progresses)

Diagnosis

MCV 80 – 95 fL

Pharmacological Treatment

1. Blood Transfusion

- Will raise haemoglobin levels quickly to ensure adequate oxygen delivery - ensure to match blood type
- Administered **if Hb < 80g/L**
- Risks: transfusion reaction, transfusion-related lung injury, viral contamination, iron overload.

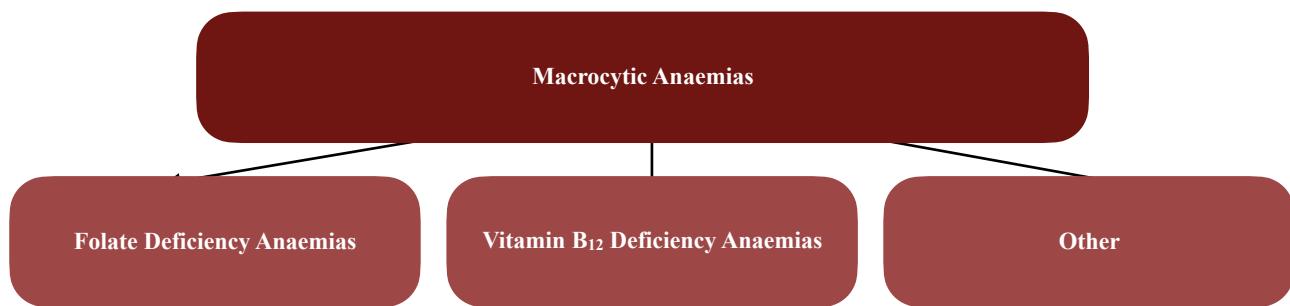
2. EPO Stimulating Agents (bone marrow stimulant): IV or SC

- Epoetin alfa (Binocrit), also known as recombinant human erythropoietin aims to replenish levels by stimulating erythropoiesis.
- Side Effects: Hypertension, GI intolerance, headache, influenza symptoms, very rarely cause red cell aplasia, skin reactions, risk of CV events, thromboembolism (due to increased haematocrit count)

Macrocytic (Megaloblastic) Anaemia

Description

Macrocytic anaemia is a condition in which your body has overly large red blood cells and not enough normal red blood cells.



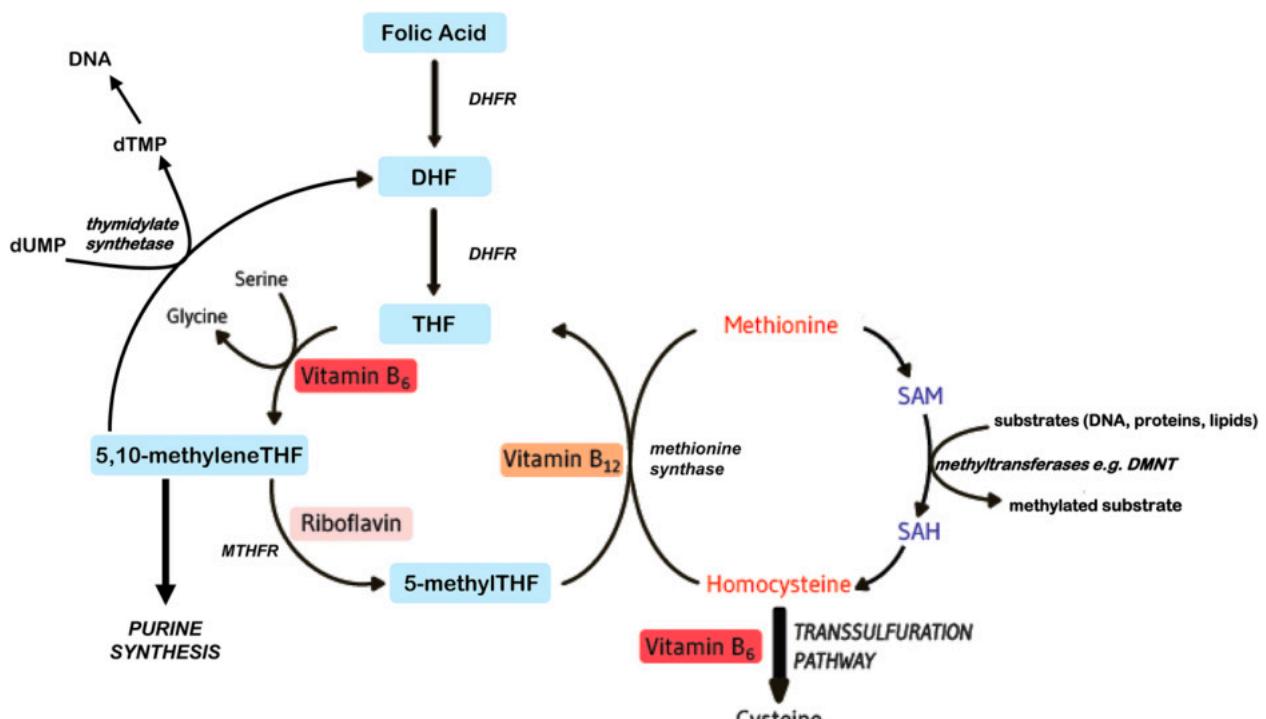
Pathophysiology

Overly large RBCs are most commonly caused by folate and vitamin B12 deficiencies instead of iron, leading to symptoms in rapidly dividing tissues (bone marrow, GI) as they have a higher O₂ requirement.



Note

As there is an interplay between the activation of folate and vitamin B12, if we suspect a deficiency in one, we should always look into the other.



VITAMIN DEFICIENCIES		
	B12 DEFICIENCY Vitamin B ₁₂ (Cobalamin)	FOLATE DEFICIENCY Vitamin B ₉
Function	<ul style="list-style-type: none"> This is also a vitamin involved in the making of RBCs. It is important to note that due to the above pathway, folate and B₁₂ deficiencies are not mutually exclusive - deficiency in one likely indicates a deficiency in the other. 	<ul style="list-style-type: none"> B₉ is an essential nutrient that naturally occurs as folate to produce RBCs. It plays an essential role in DNA biosynthesis in conjunction with vitamin B₁₂ (folate transforms dietary B₁₂ to its active form). Folic acid is the synthetic form of folate available in supplements. It is readily absorbed in the jejunum by passive processes. Folate deficiencies can not only lead to anaemia but also birth defects (e.g. NTD) and cancer.
Causes	Poor Intake	<ol style="list-style-type: none"> High risk groups e.g. vegetarians/vegans and their children, poverty, malnutrition, anorexia, alcoholism, old age Diet Alcohol Bowel diseases e.g. coeliac
	High Demand	<ol style="list-style-type: none"> Pregnancy & Lactation Haemolytic anaemias Pregnancy Dialysis
	Medications	<ol style="list-style-type: none"> H₂ Antagonists, PPIs (Change GI pH) Metformin (inhibit B₁₂ absorption) OCs (reduce haptocorrin levels) Some anticonvulsants e.g. phenytoin
	Autoimmune Conditions	<ol style="list-style-type: none"> Pernicious Anaemia (Lack of IF) Age related atrophic gastritis or H pylori infection (Change GI pH) -
	Malabsorptive Conditions	<ol style="list-style-type: none"> Altered GI absorption Terminal ileal diseases Pancreatic insufficiency, ileal or gastric resection, Celiac disease, Crohn's disease -
	Small Bowel Bacterial Overgrowth	<ol style="list-style-type: none"> Bacteria compete for and break down IF-B12 complex -

Diagnosis

- Generally: MCV, Hb, FBC, RBC count
- Check serum folate AND B₁₂ levels

Folic Acid Deficiency

- MCV, Hb
- Low serum folate & red cell folate
- PLUS** check serum B₁₂ levels

B₁₂ Deficiency

- Serum B₁₂ level
- Intrinsic factor antibodies (Present in 50% of those with pernicious anaemia)

Non-Pharmacological Treatment

Food sources of the following:

B12 DEFICIENCY <u>Vitamin B12 - B12 (Cobalamin) Deficiency</u>	FOLATE DEFICIENCY <u>Vitamin B9 - Folate Deficiency</u>
Mainly meat - there is no natural non-animal source of B ₁₂	Mainly fruit & veggies
Meat Sources Fish & Shellfish	Fruit Sources • Raw, esp citrus • Fruit juice
Dairy Sources Milk & Milk products	Vegetable Sources • Fresh, raw or lightly cooked such as leafy greens e.g. spinach, asparagus • Corn • Cooked dried beans, peas and lentils
For Vegans - obtain through: 1. Diet e.g. B ₁₂ fortified cereals, non-dairy milk, nutritional yeast, marmite 2. Supplements Please note that B ₁₂ is very efficiently recycled by the body & stored in the liver. Often takes a long time (~3 yrs) for deficiencies to develop in vegans.	Folic acid fortified foods • Breakfast cereals • Bread (wholegrain)
For Vegetarians - obtain through: 1. Diet e.g. dairy products 2. Supplements	Yeast extracts • Marmite, vegemite
	Meat sources Freshly cooked liver & kidney (no more than 1 serving a week)

Pharmacological Treatment

Supplementation (oral *or* injection if poor absorption)

Folate & B ₁₂ Treatments		
Drug	Indications	Side Effects
Folic Acid Products (NZF) Also in many multi-vitamin tablets	Folic Acid Tablets 0.8mg, 5mg - Funded 0.5mg - Not funded Oral Liquid 0.05mg/ml - Funded (Section 29) Ferro-F-Tabs 0.35mg Folic Acid with ferrous fumarate - Funded	Indications: <ol style="list-style-type: none"> Folate-deficiency anaemia: 5mg OD for 4 months Prophylaxis in chronic haemolytic states, malabsorption, renal dialysis Prevention of MTX ADRs Prevention of NTDs before and during pregnancy Obesity surgery (bariatric, gastric bypass) causes absorption issues <p>Folic Acid can:</p> <ul style="list-style-type: none"> Mask B₁₂ deficiency thus measure levels before initiating treatment Tablets contain gluten - caution in coeliac disease (e.g. folic acid 0.8mg) Toxicity is not a common concern
Vitamin B12 Products (NZF)	[GENERAL SALE] Hydroxocobalamin 1mg/ml IM amps - Funded Methylcobalamin, Cyanocobalamin - not Funded	<p>A synthetic form of cobalamin (retained in body longer than cyanocobalamin)</p> <p>Indications:</p> <ol style="list-style-type: none"> B₁₂ deficiency: <ul style="list-style-type: none"> <i>Oral:</i> 50-150 mcg/day between meals in diet deficiencies (better absorbed on an empty stomach) Pernicious anaemia without neurological involvement: <ul style="list-style-type: none"> <i>Oral:</i> 1-2mg OD for 1-2 weeks, followed by 1mg OD <i>IM (can be administered by Pharmacist Vaccinator):</i> Initially replenish depleted body stores using 1 mg three times a wk x 2 weeks, then q3months usually for life Also used for cyanide poisoning <p>Mechanism of Action</p> <ul style="list-style-type: none"> Oral/SL forms suitable for vegan supplementation. Sublingual forms may be better absorbed than other oral forms due to bypass of GIT <p>Cyanocobalamin - Synthetic form of cobalamin Methylcobalamin - Active form of cobalamin</p> <p>Usually well tolerated - mild injection site reactions such as pain, redness</p> <ul style="list-style-type: none"> Rare: hypersensitivity reactions Monitoring: in severe anaemia, ↑ in reticulocytes (precursors of RBCs) in 1- 2 wk

Monitoring

Both diabetes and B₁₂ deficiency can cause **peripheral neuropathy**. Check B₁₂ levels if:

- Any concerns (e.g. elderly, long-term use)
- Symptoms of anaemia
- Peripheral neuropathy

FOLATE REQUIREMENTS			B12 FOLATE REQUIREMENTS	
Population	Recommended Daily Intake (mcg/day)	Upper Level of Intake (mcg/day)	Population	Recommended Daily Intake (mcg/day)
<i>Infants</i> 0 - 6 months	65	-	<i>Infants</i> 0 - 6 months	0.4
<i>Infants</i> 7 - 12 months	80	-	<i>Infants</i> 7 - 12 months	0.5
<i>Children</i> 1 - 3 years	150	300	<i>Children</i> 1 - 3 years	0.9
<i>Children</i> 4 - 8 years	200	400	<i>Children</i> 4 - 8 years	1.2
<i>Children</i> 9 - 13 years	300	600	<i>Children</i> 9 - 13 years	1.8
<i>Adolescents</i> 14 - 18 years	400	800	<i>Adolescents</i> 14 - 18 years	2.4
<i>Adults</i>	400	1000	<i>Adults</i>	2.4
<i>Pregnancy</i>	600	800 (14 - 18 years) 1000 (> 18 years)	<i>Pregnancy</i>	2.6
<i>Lactation</i>	500		<i>Lactation</i>	2.8

Aplastic Anaemia

Description

This is a non-malignant condition where the bone marrow fails to produce enough blood cells (RBCs, WBCs and platelets). While this condition can occur anytime, it is usually associated with bone marrow damage. This exposes patients to anaemia (RBC), infections (WBC), and bleeding (platelets).



Did You Know?

Aplastic anaemia is a very well known cause of **normocytic** anaemia.

Causes

- Chemotherapy, antibiotics, propylthiouracil, phenytoin, quinine
- Exposure to certain chemicals such as benzene
- Radiation exposure
- Viruses

Treatment

- Blood transfusions
- Stem cell transplant
- Bone marrow stimulants e.g. EPO stimulating agents
- Immunosuppressants (cyclosporine, anti-thymocyte globulin) — may be given with *corticosteroids*
 - MoA: Suppresses activity of immune cells that are damaging the bone marrow



CHAPTER 20

FEVER, PAIN & INFECTION



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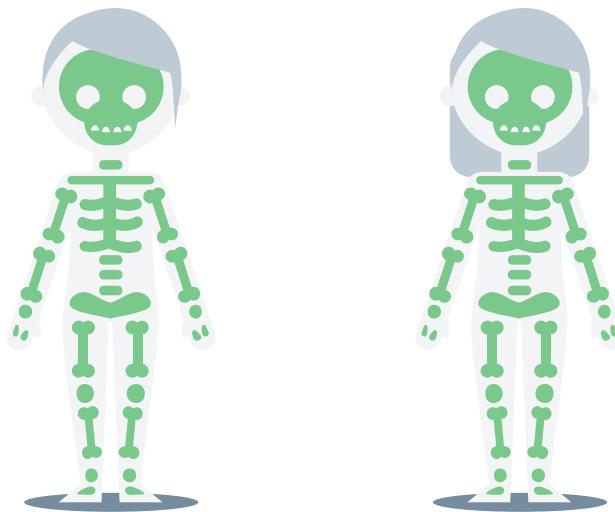


Chapter 20

Fever, Pain & Infection

Introduction

This chapter aims to cover things that can virtually be applicable to all the topics we have seen so far:



Revisit

Certain topics below are relevant to conditions we have already covered, revisit the mentioned chapters if you need a refresher.

GENERAL SYMPTOMS

Introduction

We will begin this chapter with fever and pain!

Fever

[Fever in Adults Health Govt](#)

Description

Fevers are a normal immune system response to a virus or bacterial infection. They are defined as a rise in body temperature above normal ($38^{\circ}\text{C} +/- 1$; rectal = 0.5°C higher, underarm = 0.5°C lower than oral temperature). The production of pyrogens raises the core body temperature to the new set point. Normal body temperature is 37°C

Risk Factors

Bacterial/Viral infection, vaccination, allergic reactions (hayfever), bronchitis, sinusitis, rheumatoid arthritis.

Diagnosis

A digital thermometer (in the ear) is the best type to use to get an accurate temperature reading.

In children aged 4 weeks to 5 years:

- use electronic thermometer in axilla OR
- chemical dot thermometer in axilla OR
- infrared tympanic (eardrum) thermometer

Differential Diagnosis

Rheumatic Fever (*sore throat*), Meningitis (*skin rash, stiff neck*)

Signs & Symptoms

They are usually well tolerated by most healthy adults. Generally signs and symptoms are a high body temperature, irritable, facial flushing, chills, vomiting, aching.

38–38.9°C – mild fever

Flushed cheeks, lethargy, warm to touch. Generally able to carry out normal daily activities.

39–39.9°C – high fever

Muscle aches and pains, hot to touch. Generally unwell enough to not be able to go to work. Children may be fussy, not want to eat and be less active. Pregnant women with temperatures $> 38.5^{\circ}\text{C}$ should consult their lead maternity care.

40°C or higher – very high fever

Inactive/bedridden. Loss of appetite, hot to touch. Generally unable to carry out normal activities. Children may additionally seem very listless. Recommend to see doctor if in this temperature range.

Note: Be careful of the risk of dehydration in children (a dry mouth, sunken eyes, no tears, their skin does not relax after being pinched, in babies, their fontanelle may be sunken.)

Red Flags (ED): Skin discolouration, respiratory changes such as trouble breathing, drowsiness, reduced activity levels, behavioural changes such as confusion, faster heart rate, reduced slow turgor, elevated temperatures **>38.5°C in children**, uncontrollable shaking, headaches that don't seem to go away, skin rash, stiff neck, hallucinations, seizures, an infection that goes away but returns the next day.

Automatic Referral: Infants under 3 months

Non-Pharmacological Treatment

Most fevers last only three to four days – and a mild fever may not need any treatment at all.

1. Ensure adequate hydration and food intake
2. Cool compress on face and neck — do not use any rapid cooling methods as shivering can worsen fever.
3. Get plenty of rest.
4. Wear light weight clothes and use lighter bedding. Keep the room temperature normal.

Pharmacological Treatment



Medications in Fever

Only consider pharmacological interventions if the child is extremely unwell or distressed. Do not use for anti-pyretic purposes. **Warning:** do not use aspirin in children < 16 due to the risk of Reye's syndrome

1. *Paracetamol q4 - 6h*
 - Children: Pamol, Paracare
2. *NSAIDs (Ibuprofen q6 - 8h)*
 - Children: Ibuprofen Liquid

OSCE Points

- Eating, drinking (hydration level), sleeping, responding, number of wet nappies?
- Any inconsolable crying?
- Any other symptoms? Duration?
- Medical conditions e.g. asthma
- Recommendation: paracetamol, ibuprofen (shake well)
- Check for **age and weight**

Traffic Light System of Identifying risk of serious illness in children with fever (NICE Guidelines)

CLINICAL CONDITION	Low risk	Intermediate risk	High risk
Skin appearance	Normal colour of skin, lips and tongue	Pallor reported by parent/carer	Pale, mottled, ashen, blue
Responsiveness	<ul style="list-style-type: none"> ▪ Responds normally to social cues ▪ Content/smiles ▪ Stays awake or awakens quickly ▪ Strong normal cry or not crying 	<ul style="list-style-type: none"> ▪ Not responding normally to social cues ▪ Wakes only with prolonged stimulation ▪ Decreased activity ▪ No smile 	<ul style="list-style-type: none"> ▪ No response to social cues ▪ Appears ill to a healthcare professional ▪ Does not wake or if roused does not stay awake ▪ Weak, high pitched or continuous cry
Respiratory	Normal	<ul style="list-style-type: none"> ▪ Nasal flaring ▪ Tachypnoea: <ul style="list-style-type: none"> 6–12 months RR > 50 breaths/minute >12 months RR > 40 breaths/minute ▪ Oxygen saturation ≤ 95% in air ▪ Crackles/chest signs 	<ul style="list-style-type: none"> ▪ Grunting ▪ Tachypnoea: <ul style="list-style-type: none"> RR > 60 breaths/minute ▪ Moderate or severe chest indrawing
Hydration	<ul style="list-style-type: none"> ▪ Normal skin and eyes ▪ Moist mucous membranes 	<ul style="list-style-type: none"> ▪ Dry mucous membranes ▪ Poor feeding in infants ▪ Capillary refill time (CRT) ≥ 3 seconds ▪ Reduced urine output 	<ul style="list-style-type: none"> ▪ Reduced skin turgor
Other	<ul style="list-style-type: none"> ▪ None of the amber or red symptoms or signs 	<ul style="list-style-type: none"> ▪ Fever for ≥ 5 days ▪ Swelling of a limb or joint ▪ Non-weight bearing, not using an extremity ▪ A new lump > 2 cm ▪ None of the red symptoms or signs 	<ul style="list-style-type: none"> ▪ Age 0 – 3 months, temperature ≥ 38°C ▪ Age 3 – 6 months, temperature ≥ 39°C ▪ Non-blanching rash ▪ Bulging fontanelle ▪ Neck stiffness ▪ Status epilepticus ▪ Focal neurological signs ▪ Focal seizures ▪ Bile-stained vomiting
ACTION	Reassure	Review	Refer

Pain

Description

Pain is a highly unpleasant sensation that occurs in response to injury or illness. 4 categories exist:

Acute Pain

Lasts < 3 months

Goes away when underlying cause does

Chronic Pain

Lasts > 3 months

Does not go away when expected

Cancer Pain

Pain occurs due to pressure of tumour on surrounding tissues (nerves, bones, spinal cord, organs)

Phantom Pain

Pain feeling like it is coming from a body part that is no longer there, caused by mixed signals from brain or spinal cord

Likewise, 4 types exist:

Nociceptive Pain

e.g. burn, sprains, bone fractures, bruises

A type of pain caused by damage to body tissue (can be of somatic or visceral origin)

Neuropathic Pain

e.g. neuralgia, phantom pain, CTS, peripheral neuropathy

Pain caused by CNS dysfunction in which there is **no** physical injury

Mixed Category Pain

e.g. migraines (neuralgia, parasthesia, tight feeling)

Complex mixture of nociceptive and neuropathic pain

Central Pain

e.g. fibromyalgia

CNS dysfunction causing widespread pain of the whole body

Pathophysiology

The pathophysiology of pain occurs in the steps as follows:

1. Transduction of Pain

- Noxious stimuli are detected by nociceptors from the affected part of the body. The signal travels to the spinal cord via afferent nociceptive fibres which then form synapses in its dorsal horn.

2. Transmission of Pain

- First order neurons release neurotransmitters into the synaptic cleft, depolarising the second neurons, which then send information to the thalamus via the anterolateral pathway.

3. Perception of Pain

- Once the signal has reached the thalamus and is processed, it initiates the conscious realisation of pain. The hypothalamus then responds e.g. emotional response to pain signals, the memory of pain intensity.

4. Modulation of Pain

- The hypothalamus can then request the release of specific hormones (serotonin, adrenaline) or chemicals (substance P, Enkephalins, activation of endogenous opioid receptors) that have analgesic effects that reduce/inhibit the pain sensation by interrupting the impulses to the thalamus.

Effects of Pain

- Sympathetic Response
- Parasympathetic Response

Factors Influencing Pain

- Development Factors* (age, dementia)
- Physiological Factors* (fatigue)
- Social Factors* (attention, previous experience)
- Psychological* (anxiety, coping style)

Non-Pharmacological Treatment

TENS (Transcutaneous electrical nerve stimulation), physiotherapy, acupuncture, massage, relaxation

Pharmacological Treatment

WHO Pain Ladder

- Non-Opioids*: Paracetamol, aspirin, NSAIDs +/- adjuvant
- Mild Opioids*: Codeine, tramadol +/- adjuvant
- Strong Opioids*: Morphine, oxycodone, fentanyl, pethidine +/- adjuvant

Category	Ingredients	Mechanism of Action	Side Effects
<i>1st Line Non-Opioids</i>	[GENERAL SALE] Paracetamol Pharmacare	Anti-pyretic, analgesic properties	Liver Toxicity
	[GENERAL SALE] NSAIDs + PPI Ibuprofen	Reduces prostaglandin production by inhibiting COX enzymes	GIMIRI If taking long term should be taken with a PPI such as omeprazole to prevent gastric ulcers
<i>2nd Line Mild Opioids</i>	[PRESCRIPTION] Class C + Laxative Codeine, Tramadol	<p>Metabolised in liver to morphine, binds to opiate receptors which inhibits ascending pain pathway. Reduces intestinal motility as well as causes cough suppression.</p> <p>Controlled drug class C. Weak binding to receptor prevents euphoria and hence associated with less abuse</p>	Opioid side effects (Respiratory depression, sedation, cough suppression, constipation , N/V)
<i>3rd Line Strong Opioids</i>	[PRESCRIPTION] Class A & B + Laxative Morphine, Oxycodone, Fentanyl (patches), Pethidine	<p>Morphine is a full opioid agonist. Opioid agonists bind to opiate receptors (mainly mu GPCR but also kappa and sigma) in the brain and spinal cord resulting in inhibition of the ascending pain pathways</p>	<p>Opioid side effects (Respiratory depression, sedation, cough suppression, constipation, N/V)</p> <p>May cause opioid dependence and addiction due to euphoric feeling produced by the strong binding to the opiate receptor.</p> <p>Mainly used as a strong pain reliever in cancer patients and palliative care.</p>

Analgesics & Types of Pain - [BPAC Opioids](#)

Type of Pain	Treatment Examples
Neuropathic Pain	<ul style="list-style-type: none"> Tricyclic antidepressants: amitriptyline, nortriptyline Antiepileptics: gabapentin, sodium valproate Capsaicin
Bone Pain	<ul style="list-style-type: none"> NSAIDs: ibuprofen, diclofenac, naproxen Bisphosphonates: zoledronic acid
Palliative Care Pain	Waitemata DHB Guidelines Morphine
Breakthrough Pain	Immediate release (short-acting) opioid: 1/6th or 10% of total daily dose for 'as required' use — can be repeated every 2 - 4 hours <i>or</i> every 1 hour if pain is severe
Pain from skeletal muscle spasm	<ul style="list-style-type: none"> Muscle relaxant: diazepam, clonazepam, baclofen
Pain from smooth muscle pain	<ul style="list-style-type: none"> Anticholinergic/antimuscarinics: hyoscine butylbromide (Discontinue prokinetics and stimulant laxatives)
Bladder pain	<ul style="list-style-type: none"> Urethral or suprapubic catheterisation for lower urinary tract obstructions
Increased intracranial pressure	
Liver capsule stretch (visceral pain)	<ul style="list-style-type: none"> Steroids: dexamethasone
Tenesmus due to tumour	

ANALGESICS

Introduction

Analgesics, sometimes called painkillers or pain relievers, are medications used to relieve pain (shocking we know). Unlike medications used for anesthesia during surgery, analgesics don't turn off nerves, change the ability to sense your surroundings or alter consciousness.

We will look into 3 classes: Paracetamol, NSAIDs and Opioids - which are the three main classes indicated for pain. A fourth class exists however (as you would've seen earlier), called the Co-Analgesics - these medications are drugs that have a primary use other than pain relief, but also help improve analgesia for some painful conditions. Many of these medication provide an "opioid sparing" effect and have become a mainstay in the treatment of neuropathic pain e.g. TCAs

Paracetamol

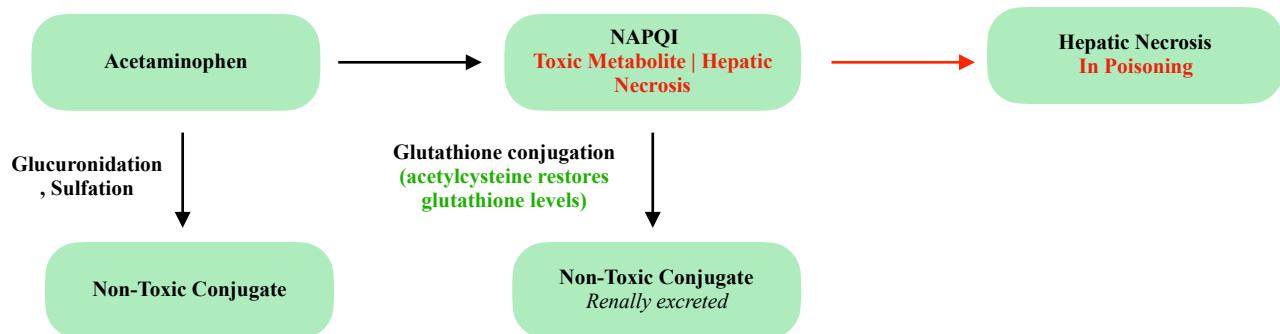
Please revisit *Chapter 5 - The Hepatic System* for more information on Paracetamol Poisoning

Description

Paracetamol is an analgesic and antipyretic drug that is used to temporarily relieve mild-to-moderate pain and fever with very few interactions with other agents.

Mechanism of Action

It works similarly to NSAIDs by working on COX enzymes - see next page. However as we've seen earlier in this Handbook, it can cause Liver Toxicity in overdose.



Pharmacological Treatment

Formulations Available

1. Capsule
2. Injection
3. Oral Liquid
4. Powder
5. Suppository
6. Tablet (gelatin coated, modified release, soluble)
7. In combination with other products e.g. ibuprofen, opioids and so forth.

NSAIDs

Description

Non Steroidal Anti-Inflammatory Drugs (NSAIDs) are mild-moderate analgesics indicated for their:

1. Anti-Inflammatory
2. Anti-Pyretic
3. Anti-Platelet and
4. Analgesic Properties.

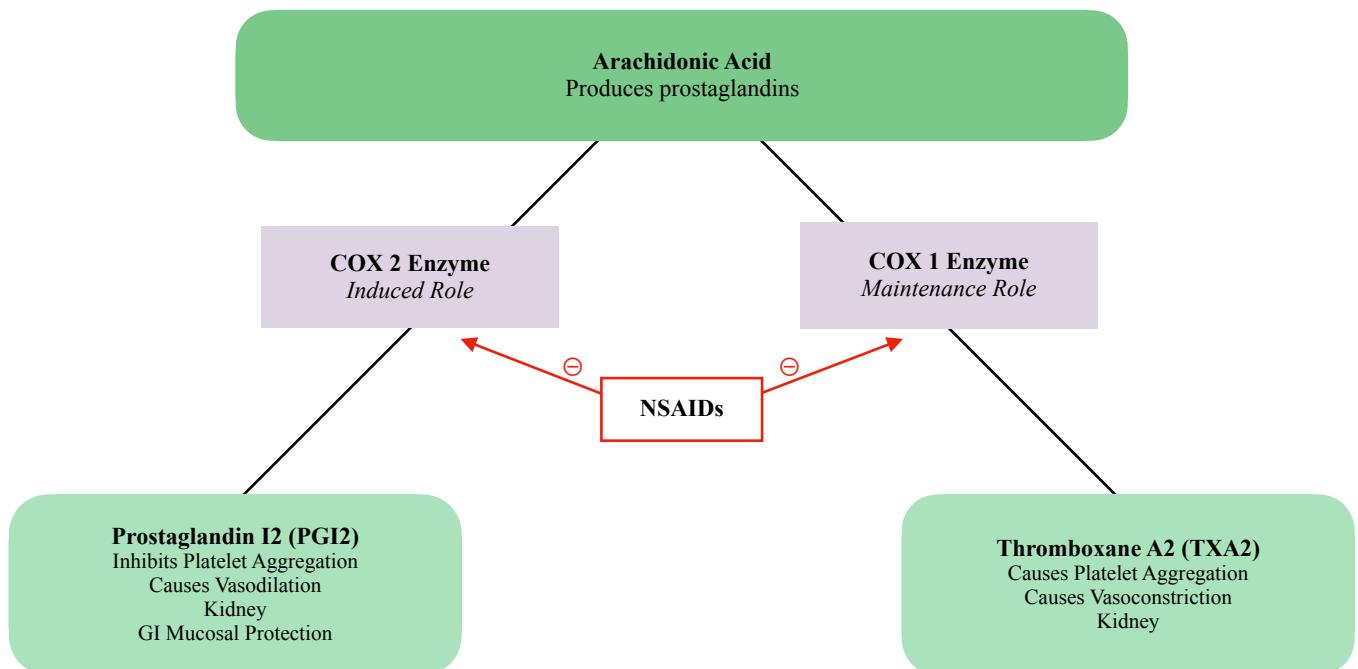


Paracetamol Is Not A True NSAID & That's A Good Thing

Please note that Paracetamol is not an NSAID - while it holds anti-pyretic and analgesic properties, it lacks anti-inflammatory ones. This however does mean that it lacks many of the side effects and contraindications associated with NSAIDs e.g. bleeding events and it can be dosed in combination with NSAIDs e.g. Maxigesic is a combination of Ibuprofen + Paracetamol.

Mechanisms of Action

Majority of NSAIDs (and paracetamol) exhibit the above effects by inhibiting an enzyme called cyclooxygenase (COX). COX enzymes are responsible for catalysing Arachidonic Acid to Prostaglandins - which are mediators of inflammation. While many prostaglandins are produced in this reaction (e.g. such as PGE2, PGF, PGD), the two particularly of note are PGI2 and TXA2. Pay close attention to their respective actions.



Selecting NSAIDs

As you would've seen in *Chapter 6 - The MSK System*, there is no clear evidence to suggest one NSAID is more efficient than another when it comes to controlling pain **IF** dosed appropriately. This section will guide you on how to select the most appropriate NSAID for a patient based on individual factors. In order to do we must first understand how COX Isoforms differ and the selectivity of NSAIDs.

COX ISOFORMS				
	COX 1	COX 2		
Function	COX 1 enzymes have a 'housekeeping/homeostatic' role. They are responsible for the production of prostaglandins associated with normal physiologic function e.g. maintaining the mucosal integrity of the gastric mucosa.	COX 2 Enzymes have more of a 'pathological role.' They are quickly upregulated in tissue damage to generate large amounts of prostanooids for pain, inflammation and fever.		
Effect	NSAIDs that Inhibit COX-1 or Non Selective are: CV Protective but have Increased GI events (loss of mucosal integrity)	NSAIDs that Inhibit COX-2 or Semi Selective are: GI Protective but have Increased CV events (unopposed platelet aggregation)		
	Selectivity of choice if patients have a history or risk factors for heart events.	Selectivity of choice if patients have a history or risk factors for gastric events.		
Examples	COX-1 Selective NSAIDs Keterolac	Non Selective NSAIDs Aspirin, Ibuprofen, Naproxen	Semi Selective NSAIDs Meloxicam, Diclofenac, Etodolax, Indomethacin, Piroxicam, Nabumetone, Sulindac	COX-2 Selective NSAIDs Celecoxib
Note	<p><i>Note:</i> Aspirin (non-selective salicylate) irreversibly acetylates COX1 (anti-platelet activity) & COX2.</p> <p><i>Note:</i> Co-prescription of ibuprofen, indomethacin, naproxen can block aspirin's anti-platelet effect</p>			

Risks (GIMIRI)

All NSAIDs are generally associated with 3 types of ADRs:

1. GI (GI ulcers, GI bleeds)
2. MI (Myocardial infarction, heart attack, stroke and other CV events)
3. RI (Renal impairment, renal failure)
4. *Additional:* Hypersensitivity, teratogenicity if taken after 28 weeks of gestation

As we've seen, the frequency of the above varies depending on which COX Isoform they are selective for. While classical NSAIDs are generally non-selective, some vary in selectivity depending on the dose.



NSAIDs, Hypersensitivity & Asthmatics

Arachidonic acid is not only catalysed to prostaglandins but also to leukotrienes, which causes mast cell degranulation in the lungs. For this reason, NSAIDs can cause hypersensitivity reactions in some people and are therefore **contraindicated in asthmatics**.

Opioids

Description

Opioids are a broad group of pain-relieving drugs that work by interacting with opioid receptors in your cells. Opioids can be made from the poppy plant — for example, morphine or synthesised in a laboratory — for example, fentanyl.



The Opioid Overdose Crisis

While extremely effective for pain, opioids are a dangerous class of medications. The opioid epidemic is **one of the worst public health disasters affecting the USA and Canada**. It is crucial to monitor patients on these medications.

Mechanism of Action

Opioids act by binding to G protein-coupled opioid receptors (μ , κ , δ) to inhibit adenylate cyclase and cause either \uparrow K⁺ efflux or \downarrow Ca⁺ influx, which decreases transmission of nociceptive impulses (\downarrow pain perception)

1. μ -receptor (Endorphins) → Analgesia, Euphoria (**preferred pathway for synthetic opioids**)
2. κ -receptor (Dynorphines) → Analgesia, Sedation
3. δ -receptor (Enkephalins) → Analgesia, Dysphoria

For all patients on opioids, also prescribe:

1. **Regular** combination laxative: Laxsol
2. **PRN** antiemetic: metoclopramide 10mg TDS

Management of ADRs associated with opioids

1. N/V: tolerance develops within 1-2 weeks
2. Constipation: regular laxatives
3. Dry mouth: sugar-free gum, saliva substitute or pilocarpine, lozenge/ice cube
4. Drowsiness: resolves in a few days
5. Confusion: dose reduction, switch opioids, or add haloperidol
6. Hallucinations: switch opioids or add haloperidol
7. Pruritus: switch opioids or trial antihistamine
8. Opioid-induced hyperalgesia: reduce dose or switch opioids

Stopping Opioids

Please revisit *Chapter 14 - Geriatrics* for more information. Always taper opioids and do not stop taking opioids suddenly as this may result in:

- Flu-like illness, excessive sweating, diarrhoea, other abnormal reactions

Switching Opioids - [Switching Opioids NZF](#)

Please revisit *Chapter 15 - Palliative Care* for more information.

While morphine is generally preferred, there are a few reasons why switching to a different opioid may be needed, for example:

- Uncontrollable adverse effects that limit up-titration of the opioid
- Deterioration in renal function, associated with increasing adverse effects
- Poor response despite adequate up-titration of the opioid (it is important to consider adherence to medication prior to switching the opioid).

Thus we generally observe patients who change opioids begin on morphine and then switch to oxycodone, fentanyl or methadone - the convention is to convert to “OME’s” or “oral morphine equivalents”

Oral to Oral				
Conversion from	Conversion to	Ratio	Calculation	Example
Oral codeine	Oral morphine	10:1	Divide 24 hour codeine dose by 10	Oral codeine 240 mg/24 hours ≈ oral morphine 24mg/24 hours
Oral dihydrocodeine	Oral morphine	10:1	Divide 24 hour dihydrocodeine dose by 10	Oral dihydrocodeine 240 mg/24 hours ≈ oral morphine 24 mg/24 hours
Oral tramadol	Oral morphine	10:1	Divide 24 hour tramadol dose by 10	Oral tramadol 400 mg/24 hours ≈ oral morphine 40 mg/24 hours
Oral morphine	Oral oxycodone	1.5:1	Divide 24 hour morphine dose by 1.5	Oral morphine 60 mg/24 hours ≈ oral oxycodone 40 mg/24 hours
		2:1	Divide 24 hour morphine dose by 2	Oral morphine 60 mg/24 hours ≈ oral oxycodone 30 mg/24 hours
Oral morphine	Oral methadone	Variable—see methadone (conversion is dose-dependant and non linear)		

Oral to Subcutaneous/Intravenous (see note)				
Conversion from	Conversion to	Ratio	Calculation	Example
Oral morphine	SC/IV morphine	2:1	Divide 24 hour oral morphine dose by 2	Oral morphine 60 mg/24 hours ≈ SC/IV morphine 30 mg/24 hours
		3:1	Divide 24 hour oral morphine dose by 3	Oral morphine 60 mg/24 hours ≈ SC/IV morphine 20 mg/24 hours
Oral morphine	SC/IV oxycodone	2:1	Divide 24 hour oral morphine dose by 2	Oral morphine 60 mg/24 hours ≈ SC/IV oxycodone 30 mg/24 hours
Oral oxycodone	SC/IV oxycodone	1.5:1	Divide 24 hour oxycodone dose by 1.5	Oral oxycodone 30 mg/24 hours ≈ SC/IV oxycodone 20 mg/24 hours
		2:1	Divide 24 hour oxycodone dose by 2	Oral oxycodone 30 mg/24 hours ≈ SC/IV oxycodone 15 mg/24 hours
Oral morphine	SC/IV fentanyl	100:1	Divide 24 hour oral morphine dose by 100	Oral morphine 60 mg/24 hours ≈ SC/IV fentanyl 0.6 mg/24 hours(600 micrograms/24 hours)
		150:1	Divide 24 hour oral morphine dose by 150	Oral morphine 60 mg/24 hours ≈ SC/IV fentanyl 0.4 mg/24 hours(400 micrograms/24 hours)
Oral methadone	SC/IV methadone	1:1	Use the same dose as the 24 hour oral methadone dose	Oral methadone 30 mg/24 hours ≈ SC/IV methadone 30 mg/24 hours
		2:1	Divide 24 hour oral methadone dose by 2	Oral methadone 30 mg/24 hours ≈ SC/IV methadone 15 mg/24 hours
Oral morphine	SC/IV methadone	Variable—see methadone (conversion is dose-dependant and non linear)		

Oral to Transdermal			
Conversion from	Conversion to	Ratio	
Oral morphine	Transdermal fentanyl	Conversion can range from 100:1 to 150:1 depending on previous opioid exposure, refer to Medicine Data Sheet	
Oral oxycodone	Transdermal fentanyl	Conversion can range from 66:1 to 75:1	

Subcutaneous/Intravenous to Subcutaneous/Intravenous (see note)				
Conversion from	Conversion to	Ratio	Calculation	Example
SC/IV morphine	SC/IV oxycodone	1:1	Use the same dose as 24 hour morphine dose	SC/IV Morphine 30 mg/24 hours ≈ SC/IV oxycodone 30 mg/24 hours
SC/IV morphine	SC/IV methadone	Variable—see methadone (conversion is dose-dependant and non linear)		

Opioid switch from morphine to fentanyl depending on previous opioid exposure

Opioid Naïve		Opioid-Tolerant	
Oral 24h morphine (mg/day)	Fentanyl Dose (mcg/hour)	Oral 24h morphine (mg/day)	Fentanyl Dose (mcg/hour)
<60	12.5	<44	12
60 - 134	25	45 - 89	25
135 - 224	50	90 - 149	50
225 - 314	75	150 - 209	100
315 - 404	100	210 - 269	125
405 - 494	125	270 - 329	150
495 - 584	150	330 - 389	175
585 - 674	175	390 - 449	200
675 - 764	200	450 - 509	225
765 - 854	225	510 - 569	250
855 - 944	250	570 - 629	275
945 - 1034	275	630 - 689	300
1035 - 1124	300	690 - 749	

ANTIMICROBIALS

Introduction

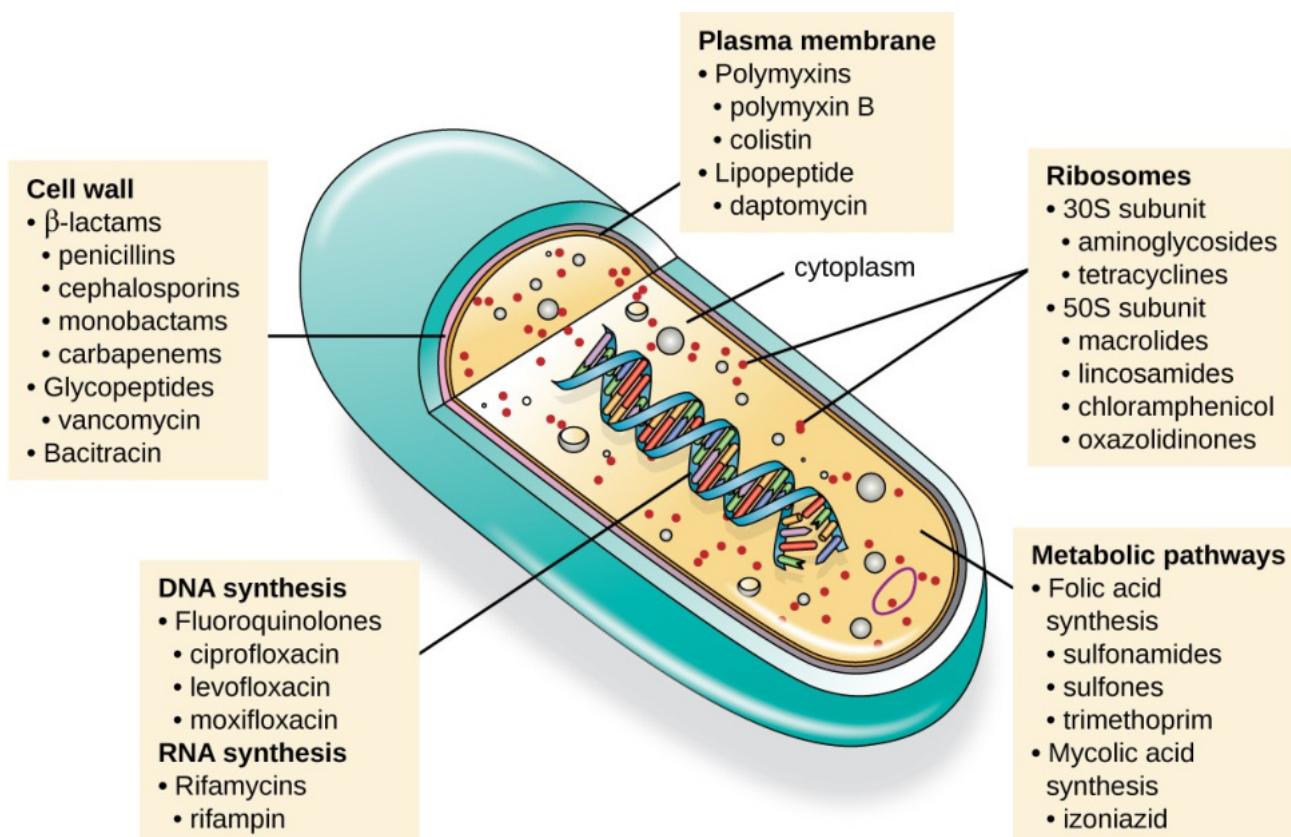
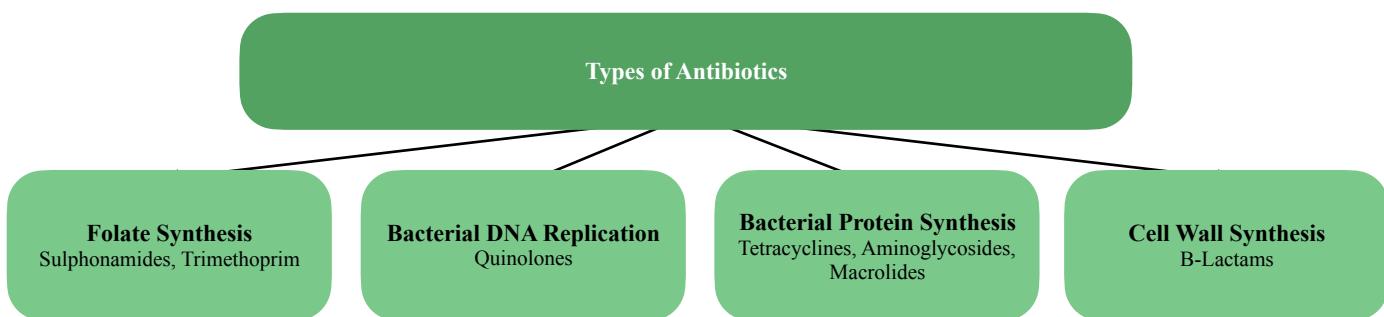
We will cover three classes of anti-microbials: antibiotics, antifungals and antivirals.

Antibiotics

[Starship Paediatric Guidelines](#), [Pink Book Adult Guidelines](#), [BPAC Guidelines](#)

Introduction

Antibiotics are a class of medications that selectively target a variety of bacterial characteristics, including: folic acid synthesis, the cell wall, cytoplasmic membrane, protein synthesis and replication.



CLASSES OF ANTIBIOTICS										
Drug Target	Drug Class	MoA	PAE	Route	Metabolised	Excreted	Interactions of Note	Toxicity	Indication	Accumulation Site
Folate Synthesis	Sulfonamides <i>Sulfadiazine, sulfasalazine</i>	Static (Gram +/-) Time Dependent Folic acid is required for DNA/RNA synthesis and the metabolic pathway leading to its synthesis is due to bacteria (humans must get it from their food).		Oral	Liver	Kidneys $t_{1/2} = 12\text{h}$	N/A	<ul style="list-style-type: none"> Hypersensitivity Hepatitis Bone marrow suppression Stevens Johnson Syndrome 	Use is limited by resistance <ul style="list-style-type: none"> IBD Infected burns 	
	Trimethoprim	Both sulfonamides and trimethoprim compete with a key enzyme in folate synthesis by imitating its substrates in order to halt the pathway. • SYNERGISM trimethoprim + sulfamethazole		Oral		Kidneys $t_{1/2} = 24\text{h}$		<ul style="list-style-type: none"> Folate deficiency with long term use (\rightarrow megaloblastic anaemia) Blood disorders Hypersensitivity 	Alone <ul style="list-style-type: none"> UTIs <i>Cotrimoxazole:</i> <ul style="list-style-type: none"> Toxoplasmosis, Nocardiosis 	lungs, kidney, CSF
DNA Replication	Quinolones <i>Ciprofloxacin, Moxifloxacin</i>	Cidal (Gram +/-) Time and Conc Dependent <ul style="list-style-type: none"> Inhibits Topoisomerase II in Gram (-) Inhibits Topoisomerase IV in Gram (+) Note: quinolones do NOT cross BBB (except ofloxacin)	Strong	Oral	Liver CYP 450	Kidneys	CYP1A2 Inhibition with Ciprofloxacin <ul style="list-style-type: none"> Increased conc of caffeine, theophylline, clozapine, olanzapine, tizanidine Antacids (Al, Mg) <ul style="list-style-type: none"> Inhibit absorption 	<ul style="list-style-type: none"> GI (c.difficile colitis with <i>ciprofloxacin</i>) Skin rashes Tendon rupture Arthropathy (joints) CNS symptoms (headache, dizziness) 	Reserved for Serious Infections - R&B First Line Most Severe Traveller's Diarrhoea Gonorrhoea Prostatitis Bone & Joint infections	lung, kidney, prostate
Protein Synthesis	Tetracycline <i>Doxycycline, Minocycline</i>	Static (Gram +/-) Time Dependent <ul style="list-style-type: none"> Binds to 30S ribosomal subunit - which inhibits binding of aa-tRNA 		Oral or Parenteral	Liver	Liver & Kidneys	<ul style="list-style-type: none"> Give on empty stomach Avoid in children and pregnancy Avoid dairy (Ca^{2+}), antacids (Al, Mg), iron supplements (Fe) 	<ul style="list-style-type: none"> GI disturbances Ca^{2+} chelation, deposited in bones, teeth Photosensitivity Hepatotoxicity Renal failure 	<ul style="list-style-type: none"> Respiratory infections (chronic bronchitis, CAP) Acne 	
	Aminoglycosides <i>Gentamicin, Tobramycin</i>	Cidal (Gram +/-) Cone Dependent <ul style="list-style-type: none"> Irreversible inhibition of 30S ribosomal subunit - causing misreading of codons on mRNA and thus improper protein expression Cross placenta but not BBB Use IDEAL body weight (IBW) SYNERGISM with penicillins 		Strong	IV or IM	N/A	Kidneys	N/A	<ul style="list-style-type: none"> Ototoxicity Nephrotoxicity Paralysis 	Hospital Only <ul style="list-style-type: none"> Pneumonia Meningitis
	Macrolides <i>Azithromycin, Clarithromycin, Erythromycin, Roxithromycin</i>	Static (Gram +) Time Dependent <ul style="list-style-type: none"> Reversible inhibition of 50S ribosomal subunit, causing dissociation of tRNA 		Oral or Parenteral	Liver	Liver	CYP3A4/1A2 Inhibition with Erythromycin/ Clarithromycin. <ul style="list-style-type: none"> Increased conc of benzodiazepines, antipsychotics, simvastatin, warfarin 	<ul style="list-style-type: none"> GI (<i>erythromycin</i>) Cardiac toxicity (arrhythmias, QT prolongation) Hepatotoxicity (<i>clarithromycin</i>) 	<ul style="list-style-type: none"> Respiratory infections (Pertussis, Legionella) Chlamydia Mycoplasma infections Skin infections 	
β -Lactams Inhibit Cell Wall Synthesis	Penicillins <i>Ampicillin, Amoxicillin, Flucloxacillin</i>	Cidal (Gram +/-) Time Dependent <ul style="list-style-type: none"> Frequently administered with β-lactamase inhibitors such as clavulanic acid (e.g. Augmentin) or sulbactam (e.g. Unasyn) SYNERGISM with aminoglycosides 		Oral	Liver	Kidneys $t_{1/2} = 30-90\text{ min}$		<ul style="list-style-type: none"> Hypersensitivity GI change in gut flora (diarrhoea, c.difficile colitis) 	<ul style="list-style-type: none"> URTI UTI Meningitis Salmonella infections 	joint, pleural, pericardial fluid, bile
	Cephalosporin <i>1st Gen Cefalexin, 2nd Gen Cefaclor, 3rd Gen Ceftriaxone, 4th Gen Cefepime</i>	Cidal (Gram +/-) Time Dependent <ul style="list-style-type: none"> Cephalosporins are more resistant to β-lactamase Successive generations of Cephalosporins have better Gram-activity and ↑BBB penetration. 		Weak/Absent	Oral (except ceftriaxone IV or IM)	Liver	Kidneys	<ul style="list-style-type: none"> Hypersensitivity Hepatotoxicity Antibiotic-associated colitis (with broad spectrum agents) Neurotoxicity CROSS-REACTIVITY with penicillins 	<ul style="list-style-type: none"> 1st gen: skin, soft tissue infections 2nd gen: pneumonia, resistant/ pregnancy UTIs 3rd gen: Gonorrhoea, meningitis, CAP 4th gen: hospital acquired (nosocomial) infections 	synovial and pericardial fluid
	Carbapenems <i>Imipenem, Meropenem, Ertapenem</i>	Cidal (Gram +/-) Time Dependent <ul style="list-style-type: none"> Carbapenems are the broadest spectrum β-lactams and are very resistant to β-lactamase 	Mod	Parenteral (imipenem)	Unchanged	Kidneys		<ul style="list-style-type: none"> Neurotoxicity Seizures Renal failure CNS injury/ disease 	<ul style="list-style-type: none"> Severe hospital acquired infections Septicaemia Hospital-acquired pneumonia Intra-abdominal infections Complicated UTIs 	
	Monobactams <i>Aztreonam</i>	Cidal (Gram -) Time Dependent <ul style="list-style-type: none"> Interacts with PBP, causing formation of long filamentous bacteria (susceptibility) Resistant to many β-lactamases Similar to aminoglycosides Little cross-reactivity with penicillins, except <i>ceftazidime</i> 	Weak/Absent	IV or IM	Unchanged	Kidney		Generally well tolerated	Gram-infections: <ul style="list-style-type: none"> <i>Pseudomonas aeruginosa</i> <i>Haemophilus influenzae</i> <i>Neisseria Meningitidis</i> 	
	Glycopeptides <i>Vancomycin, Teicoplanin, Daptomycin</i>	Cidal (Gram +) Time Dependent <ul style="list-style-type: none"> Prevent addition of muramic monomers to peptide chain Note: Vancomycin = MRSA 	Mod	IV or IM $t_{1/2} = 8\text{h}$	Unchanged	Kidney		<ul style="list-style-type: none"> Nephrotoxicity (worse with aminoglycoside) Hypersensitivity SJS/TEN Red man syndrome 	Serious gram+ infections <ul style="list-style-type: none"> MRSA Bacterial endocarditis C difficile colitis (oral metronidazole preferred due to resistance) 	

Types of Bacteria

GRAM POSITIVE (+)				
Thick Peptidoglycan Cell Wall (Purple/Blue Stain)				
Genus	Bacteria	Commonly Found In	Complication	Antibiotics
Staphylococcus	Aureus (MSSA)	Skin	Cellulitis, pneumonia, infected lines, sepsis, endocarditis, wound & blood infections	Flucloxacillin Cefazolin, Cefalexin Clindamycin
	MRSA	Skin, URT, Gut	Abscesses, bacteria, lung, bone and joint, surgical	Vancomycin Linezolid Co-trimoxazole Ceftaroline
	Epidermis	Skin	Boils, Biofilm in prosthesis and lines/catheters	Methicillin susceptible: Cefazolin Methicillin resistant: Vancomycin, Linezolid
Streptococcus	Group A Strep (GAS) i.e. strep pyogenes	URT, Skin	Strep Throat (RF, RHD), Cellulitis	Penicillin, Amoxicillin Cefalexin
	Group B Strep	Reproductive tract, GIT	Passes from mother to baby (sepsis)	Benzylpenicillin, Amoxicillin Cefazolin Vancomycin
	Viridians	Oral Cavity	Endocarditis	Benzylpenicillin Ceftriazone Vancomycin
	Pneumoniae	URT	Pneumonia, Meningitis, Sinusitis, Otitis media	Benzylpenicillin, Amoxicillin Ceftriaxone (Depends where infection is)
Enterococcus	Faecium	GI	UTI, sepsis, wound infections, catheter infections	Benzylpenicillin Vancomycin Ceftriaxone, Ceftaroline (high dose) If cystitis: Nitrofurantoin, fosfomycin
	Faecalis	GI	Dental infections, endocarditis, sepsis, UTIs	Benzylpenicillin, Amoxicillin

GRAM NEGATIVE (-)				
Thin Peptidoglycan Cell Wall (Pink Stain)				
Genus	Bacteria	Commonly Found	Complication	Antibiotics
Neisseria	Neisseria meningitis	Nasopharynx	Meningococcal meningitis, septicaemia	Ceftriaxone Benzylpenicillin (high dose)
Haemophilus	Haemophilus influenza (Hib)	Nasopharynx	CAP, Otitis media, Meningitis, Cellulitis	Augmentin Co-trimoxazole Azithromycin
Escherichia	E.coli	GI	UTI, GI-gastro	Nitrofurantoin (cystitis only) Ceftriaxone Augmentin Gentamicin ESBL: Meropenem, ertapenem
Klebsiella	-	Nasopharynx, GI	Pneumonia, UTI, Sepsis, Meningitis	Gentamicin Ceftriaxone Meropenem, Imipenem, Ertapenem
Pseudomonas aeruginosa	Pseudomonas aeruginosa	Opportunistic, environmental (water, soil)	Sepsis, Pneumonia, Skin/Wounds	Ceftazidime, Piperacillin+Tazobactam Meropenem, Imipenem Ciprofloxacin
Helicobacter pylori	-	Gut	Stomach ulcers	Amoxicillin+Clavulanic Acid Metronidazole

ATYPICAL BACTERIA				
Usually No Peptidoglycan Cell Wall (No Stain)				
Bacteria	Gram Stain	Commonly Found	Complication	Antibiotics
Legionella	Gram -	Not endogenous, soil and water	Pneumonia (Legionnaires disease)	Macrolides (Azithromycin, Clarithromycin) Doxycycline Fluoroquinolones (Levofloxacin, Moxifloxacin)
Chlamydia pneumoniae	Gram -	Crowded living, long term care, hospitals	Pneumonia	Macrolides (Azithromycin, Clarithromycin) Doxycycline Fluoroquinolones (Levofloxacin, Moxifloxacin)
Mycoplasma pneumoniae	Gram -	Back of nose or throat of humans, can spread to other people	Pneumonia	Macrolides (Azithromycin, Clarithromycin) Doxycycline Fluoroquinolones (Levofloxacin, Moxifloxacin)

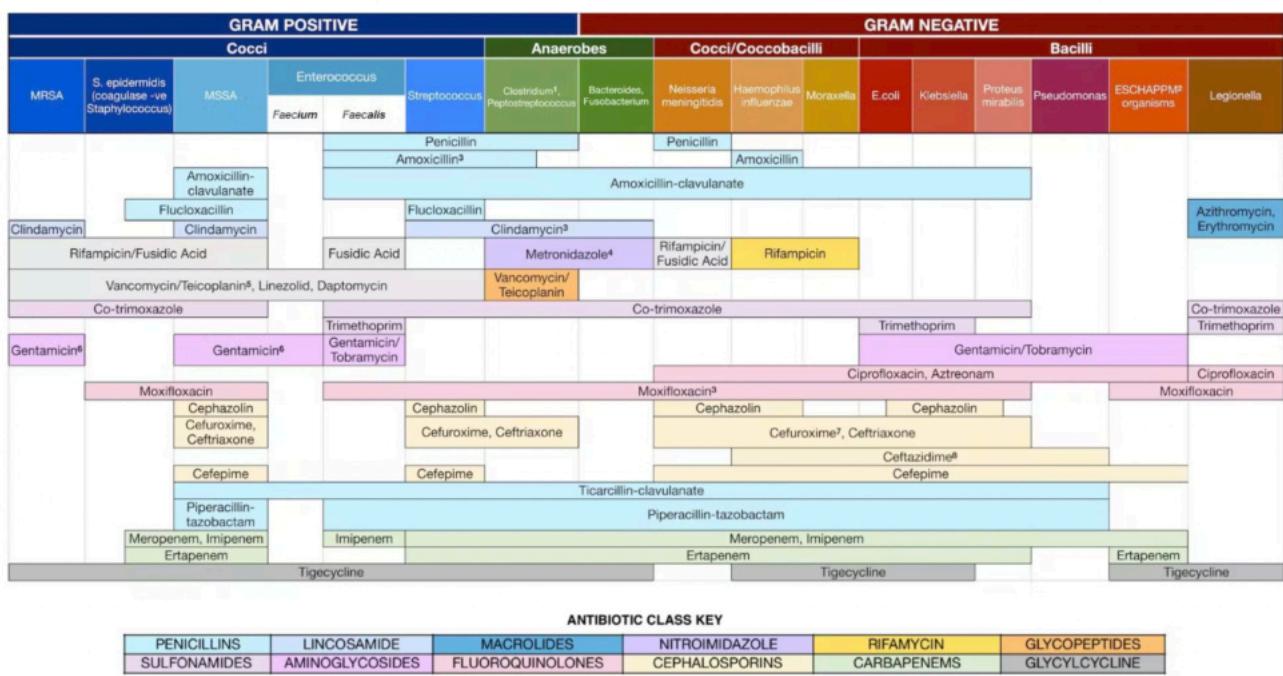
ANAEROBIC BACTERIA				
Grows in absence of oxygen				
Bacteria	Gram Stain	Commonly Found	Complication	Antibiotics
Bacteroides	Gram -	GI	Peritoneal, sepsis, appendix, wound/ulcer	Metronidazole Piperillin+Tazobactam Augmentin
Actinomyces	Gram +	Skin, GI, Oral cavity, Vagina	Dental, abscesses/ complications, sinus	Amoxicillin, Augmentin Ceftriaxone Doxycycline Azithromycin Metronidazole NOT effective
Clostridium difficile	Gram +	GI, 4C's Antibiotic associated [Clindamycin, Cephalosporins, Co-amoxiclav, Ciprofloxacin]	Diarrhoea, colitis	Oral Metronidazole Oral Vancomycin

Antibiotic Classes

Antibiotic Class	Activity	Examples
Macrolides	Static	Erythromycin, Roxithromycin, Azithromycin, Clarithromycin
Tetracyclines	Static	Doxycycline, Minocycline
Aminoglycosides	Cidal	Gentamicin, Tobramycin
Carbapenems	Cidal	Imipenem, Meropenem, Ertapenem
Glycopeptides	Cidal	Vancomycin, Teicoplanin, Daptomycin
Penicillin	Cidal	Amoxicillin, Flucloxacillin
Quinolones	Cidal	Ciprofloxacin, Norfloxacin, Moxifloxacin
Cephalosporins	Cidal	1. CeFAZolin, CeFAlexin, CeFAzroxil, CePHAlothin
1. ce-FA (except cefaclor)		2. CeFUroxime CefalCLOR, CeFOXitin,
2. FURRY CoLORed FOX		3. CeftriaxONE, CefotaxIME, CeftazidIME
3. 1ONE + 2tIME		4. CefePIme
4. PIe		5. CeftaroLINE
5. End of LINE		

Bacterial Spectrum

Mainly Gram +	Mainly Gram -	Broad Spectrum
Penicillin, Amoxicillin, Flucloxacillin	Fluoroquinolones (ciprofloxacin)	Amoxicillin + Clavulanic Acid (Augmentin)
Benzylpenicillin (IV)	Aminoglycosides (gentamicin)	Tetracyclines (doxycycline covers MRSA)
Phenoxy-methylpenicillin (oral)	Trimethoprim (H.influenza, E.Coli)	Carbapenems (ESBL, anti-pseudomonal except ertapenem)
Macrolides (atypical , H.influenzae)	Nitrofurantoin (E.Coli)	Piperacillin + Tazobactam (anti-pseudomonal)
Vancomycin (MRSA)	2nd Gen cephalosporins	3rd gen cephalosporins
1st gen cephalosporins		4th gen cephalosporins
		5th gen cephalosporins (MRSA)



Bacterial Flora in a Normal Person in the Community

Upper Respiratory Tract

- Staphylococcus* spp.
- Streptococcus* spp.
 - *Streptococcus pneumoniae*
 - Alpha-haemolytic
 - Streptococcus* spp.
- Haemophilus* spp.
- Anaerobes

Skin

- Staphylococcus* spp.
- Coryneform bacteria or "Diphtheroids"
- Cutibacterium* spp.

Gastrointestinal Tract

- Anaerobes
- Enterococcus* spp.
- Enterobacteriaceae
 - *Escherichia coli*
 - *Klebsiella* spp.
- Streptococcus* spp.
 - *Streptococcus anginosus* group
- Lactobacillus* spp.
- Candida* spp.

Genital Tract

- Lactobacillus* spp.
- Streptococcus* spp.
 - *Streptococcus agalactiae*

Bacterial Flora in a Normal Person in a Hospital or Long-term Care Facility

Upper Respiratory Tract

- Staphylococcus* spp.
- Anaerobes
- Enterobacteriaceae
 - *Escherichia coli*
 - *Klebsiella* spp.
- Candida* spp.
- Pseudomonas* spp.

Skin

- Staphylococcus* spp.
- Enterobacteriaceae
 - *Escherichia coli*
 - *Klebsiella* spp.

Gastrointestinal Tract

- Anaerobes
- Enterococcus* spp.
- Enterobacteriaceae
 - *Escherichia coli*
 - *Klebsiella* spp.
- Candida* spp.
- Pseudomonas* spp.

Genital Tract

- Candida* spp.

Antibiotic Side Effects

Side effects of Antibiotics can be divided into 2 types:

Type A

Type B

1. Type A Reactions

Type A reactions are dose dependent, predictable on pharmacology.

- i. Gastrointestinal Toxicity (N/V/D) - result of changes to microbiota
- ii. Nephrotoxicity - result of antibiotic renal excretion

2. Type B Reactions

Type B reactions are idiosyncratic reactions, these are rare, cannot be predicted and can affect any organ.

- i. Skin - rashes, eruptions, itching
- ii. Liver - hepatotoxicity
- iii. Blood Cells - haematological toxicity e.g. anaemia

A Note on Antibiotics

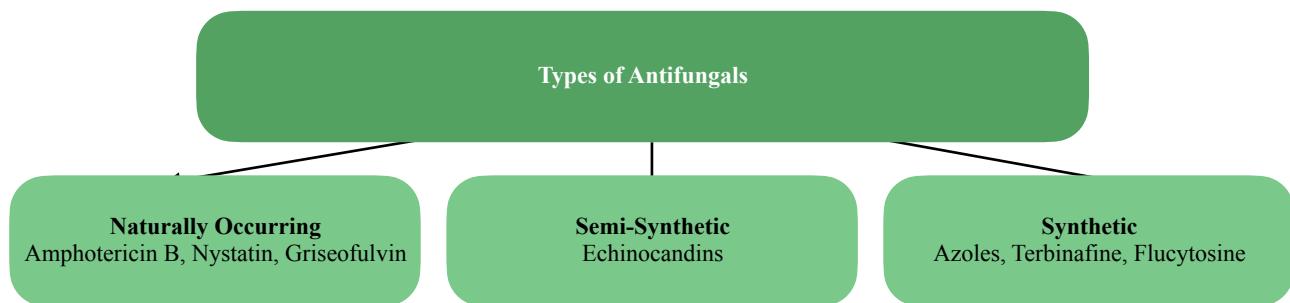
- Check patients allergy status of antibiotics
- Always finish course of antibiotics
- If upset stomach, take antibiotics with food. Can also take probiotics after antibiotics
- May cause diarrhoea (antibiotic-associated diarrhoea). Drink plenty of fluids
- Flucloxacillin: Best to take on an empty stomach
- Doxycycline/Minocycline: Take with food and water. Stay upright for 30 minutes after taking. Do not take iron, calcium (Gaviscon, Mylanta) within two hours of taking.
- Roxithromycin: Take 15 minutes before food
- Metronidazole is the only antibiotic you cannot take alcohol with it

Antifungals

Introduction

In healthy people, fungal infections tend to be minor and easily resolved. However they become serious when they affect patients that are immunocompromised or become systemic in nature. Please note that resistance is not as much of a concern with fungal infections as fungi mutate much more slowly than bacteria.

Note: Use Wood's light (UV) to distinguish between fungal vs non-fungal infections



Classes of Antifungals								
Type	Drug Class	MoA	Administered	Metabolised	Excreted	Interaction	Toxicity	Indication
Natural	Amphotericin B	Static & Cidal Broad Spectrum <i>Target Cell Membrane</i> Polyene antibiotic that binds to ergosterol in fungal membranes and forms pores/channels, increasing permeability & leakage.	Topical or IV	Unchanged	Kidneys		<ul style="list-style-type: none"> Renal Toxicity Hypokalaemia Infusion-related toxicity Nephrotoxicity 	<ul style="list-style-type: none"> HIV/AIDS Candida Mucormycosis Cryptococcus Meningitis
	Nystatin	Static & Cidal Broad Spectrum <i>Target Cell Membrane</i> Tetraene macrolide similar MoA to Amphotericin B	Topical	Unchanged	Faeces		None of note	<ul style="list-style-type: none"> NOT for systemic infections Candidiasis ONLY Preparations for skin, vaginal, oromucosal and oral administration
	Griseofulvin	Static Narrow Spectrum <i>Target Mitosis</i> Interacts with fungal microtubules, therefore interfering with mitosis. Taken up selectively by newly formed skin, concentrating in keratin	Oral	Liver	Kidneys	CYP1A2 inducer - Warfarin metabolism	<ul style="list-style-type: none"> Teratogenic GI upset Headache Photosensitivity 	Tinea infections of skin, hair, nails
Semi-Synthetic	Echinocandins <i>Caspofungin, Micafungin, Anidulafungin</i>	Static & Cidal Broad Spectrum Inhibits synthesis of key polymers of the fungal wall, decreasing structural integrity, leading to death Echinocandins do NOT penetrate CSF thus NOT for CNS fungal infections	IV	Liver	-	<ul style="list-style-type: none"> Mild CYP3A4 inhibitors ↑ tacrolimus CYP3A4 Inducers e.g. Rifampicin: ↓ Caspofungin 	<ul style="list-style-type: none"> Well tolerated Phlebitis at injection site (caspofungin) Histamine-like effects (rapid infusion) 	<ul style="list-style-type: none"> Deeply invasive candidiasis Invasive aspergillosis
Synthetic	Azoles <i>Fluconazole, Itraconazole, Miconazole, Voriconazole, Posaconazole</i>	Static Broad Spectrum <i>Target Cell Membrane</i> Some impair ergosterol synthesis and some increase plasma membrane permeability in topical use.	Topical, Oral or IV	-	-	• CYP substrates AND inhibitors	<ul style="list-style-type: none"> Teratogenic SJS 	<ul style="list-style-type: none"> Candidiasis Seborrhic dermatitis Cryptococcal meningitis Invasive Aspergillosis <p>Note: Emergence of fluconazole resistant strains of Candida</p>
	Terbinafine Lamisil	Cidal Broad Spectrum <i>Target Cell Membrane</i> Allylamine antibiotic that inhibits ergosterol synthesis by inhibiting the fungal squalene monooxygenase/ epoxidase Accumulates in skin, hair, nails	Topical or Oral	Liver	Kidney	<ul style="list-style-type: none"> Rifampicin ↓ [terbinafine] Cimetidine ↑ [terbinafine] 	Teratogenic	<ul style="list-style-type: none"> Nail Onychomycosis Tinea Pedis
	Flucytosine [unapproved medicine]	Static Broad Spectrum <i>Targets DNA & Protein Synthesis</i> Converted to anti-metabolite 5-fluorouracil in fungi, which inhibits thymidylate synthase & substitutes for uracil in DNA synthesis SYNERGISM with amphotericin and/or azole	Oral or IV	-	Kidney t _{1/2} ~3-5h		<ul style="list-style-type: none"> Anaemia Neutropenia Alopecia 	Serious fungal infections <ul style="list-style-type: none"> Cryptococcal meningitis Candidiasis Chromomycosis

Antivirals

NZF Antivirals

Introduction

Antivirals target one of the nine following viral infections:

- HIV infections
- hepatitis B virus (HBV) infections
- hepatitis C virus (HCV) infections
- herpesvirus infections
- influenza virus infections
- human cytomegalovirus infections
- varicella-zoster virus infections
- respiratory syncytial virus infections
- external anogenital warts caused by human papillomavirus (HPV) infections

Class	Description
Attachment Inhibitors	Attachment inhibitors are direct virus-targeting antivirals. Viral infections begin with the virus binding to the host cell via proteins on the cell's surface. This class of antivirals prevents this binding from happening.
Entry Inhibitors	Another type of direct virus-targeting antivirals is entry inhibitors. These prevent the virus from entering the host cells. Viruses can either enter the cell via fusion or phagocytosis. One class of entry inhibitors, fusion inhibitors, prevent the conformational changes required for membrane fusion.
Uncoating Inhibitors	The next type of antiviral targets the uncoating phase of the viral life cycle. Uncoating inhibitors prevent capsid disintegration, preventing the virus' genetic material from being released into the host cell.
Protease Inhibitors <i>Atazanavir, Darunavir, Ritonavir</i>	Protease inhibitors prevent viral replication by blocking proteolytic cleavage of protein precursors necessary for producing infectious particles.
Polymerase Inhibitors	Polymerase inhibitors help prevent further gene expression by blocking enzymatic function, thus preventing the virus from multiplying. Nucleoside and non-nucleoside inhibitors are both types of polymerase inhibitors. Nucleoside inhibitors bind directly to the polymerase's active site, while non-nucleoside inhibitors bind to the allosteric site. Both of which change the structure of the polymerase, preventing their action.
Nucleoside and Nucleotide Reverse Transcriptase Inhibitor (NRTIs) <i>Abacavir, Emtricitabine, Lamivudine, Tenofovir, Zidovudine</i>	These types of antivirals are predominantly used for the treatment of HIV. Once incorporated, they serve as chain-terminators of viral reverse transcripts, thus, acting on the viral replication cycle by inhibiting a critical step of proviral DNA synthesis prior to integration into the host cell genome.
Non-Nucleoside Reverse-Transcriptase Inhibitors (NNRTIs) <i>Efavirenz, Etravirine, Nevirapine, Rilpivirine</i>	These types of antivirals are used to treat HIV and AIDS. These reverse transcriptase inhibitors do not compete with nucleoside reverse transcriptase inhibitors as they work at a different site.
Integrase Inhibitors <i>Dolutegravir, Elvitegravir, Raltegravir</i>	These drugs prevent the virus's DNA from being incorporated into the host cell's DNA by inhibiting integrase enzymes
Indirect Virus-Targeting Antivirals	There has been some research done on indirect virus-targeting antivirals. Rather than target the actual viral factors, these approaches target cellular factors or pathways that allow for viral replication. While some indirect antivirals prevent intracellular signaling cascades, others block replication and transcription.



CHAPTER 21

LAW & ETHICS



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Chapter 21

Pharmacy Law & Ethics

Introduction & Resources

Description

The philosophy of pharmacy practice acknowledges pharmacists as health professionals with the knowledge, skills and attributes to take responsibility for the management and utilisation of medicines, in order to optimise medicines related health outcomes. Pharmacy Law & Ethics govern the **specific** legal restrictions pharmacists, along other health care practitioners, need to abide by in order to ensure the safety of their patients.

Important Links

1. [Medicines Act 1981](#)
2. [Medicines Regulations 1984](#)
3. [Pharmacy Procedures Manual](#)
4. [Medicines \(Standing Order\) Regulations 2002](#)
5. [PCNZ Code of Ethics 2018](#)
6. [Pharmac Schedule](#)
7. [New Zealand Formulary](#)
8. [Medicines \(Designated Pharmacist Prescribers\) Regulations 2013 \(MDPPR\)](#)
9. [HDC Code of Health and Disability Services Consumers' Rights \(Code of Rights or COR\)](#)
10. [Health Information Privacy Code 2020 \(HIPC\)](#)
11. [PCNZ PSNZ Advertising Guidelines \(updated Nov 2020\)](#)

Citing Legislation

When citing the law, you need to specify which piece of legislation you are referring to

Examples:

For the Medicines Act 1981 Section 18

You can use the shorthand **MA s.18**

If referring to a particular part or subpart this should also be specified (for example) **MA s.18(2A)(a)**

Other examples:

Medicines Regulations 1984 Regulation 41. Shorthand = **MR r.41**

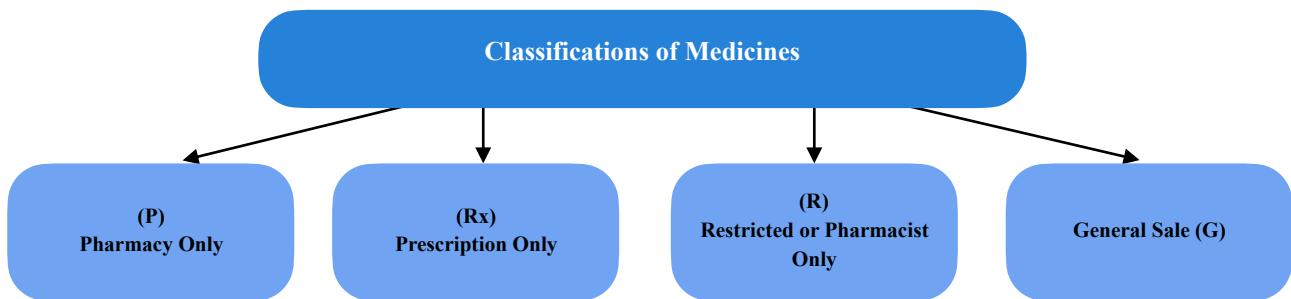
Pharmacy Council of New Zealand Code of Ethics 2018 Principle 3A. Shorthand = **COE 3A**

Classifications of Medicines

In New Zealand medicines are classified into four different categories (excluding controlled drugs). The [Medsafe Website](#) contains a section that allows you to check the classification of the medicine. Please see this for information on controlled drugs.

Four Main Classifications of Medicines — [MA s.3](#)

1. Pharmacy Only — [MA s.18](#)
2. Prescription Only
3. Restricted/Pharmacist Only — [MA s.18](#)
4. General Sale



Function of Classifications

"Prescription except when..."

You might also see some medicines are "Prescription only, except when" with a series of conditions stated. When the medicine is sold according to those conditions, it is legally a general sale medicine. One important difference is that they do not need to be sold in a pharmacy — this enables pharmacists to provide these medicines off-site.



Example

An example is the influenza vaccine, in which the classification aims to increase access and convenience of obtaining a vaccination. Therefore, this is a prescription item *except when...*

- a) Administered to a person >13 years old by a registered pharmacist who has successfully completed a vaccinator training course approved by the MoH.

A Note on Classification Status and Availability

Classification status does not mean the product is available to provide (e.g vaginal econazole is classified as a restricted medicine but no vaginal product is registered in NZ).

PHARMACIST & PHARMACY ONLY MEDICINES

Sale Records of Medicines

Recording Sale of OTC / Pharmacist Only Medicines — [MR R.54A & 55](#)

1. Recording the sale of OTC medicines

Wherever a consultation has occurred between a pharmacist and a patient, it is valuable to record a summary of that consultation on the patient's file e.g. SOAP notes

2. Recording the sale and supply of Pharmacist Only Medicines

The Pharmacy Council outline the requirements for the sale of Pharmacist Only medicines and also additional requirements regarding information to be recorded and to be provided to the patient when treating a chronic condition — [\(Pharmacy Council Protocol\)](#)

In addition, there are some legal requirements for keeping record of the sale of restricted/pharmacist only medicines — [MR R.54A & 55](#)

- The date of the sale
- The **buyer's** name and address
- The name of the medicine sold
- The quantity of the medicine sold
- The name of the person making the sale

PREScription ONLY MEDICINES

Prescribing

Categories of Prescribers | Authorised & Designated — [MAS.2](#)

Prescribers may only prescribe medicines for patients under their care and within their scope of practice, which is defined by notice published in the *Gazette* as required by the Health Practitioners Competence Assurance Act 2003.



Prescribers

Prescription medicines can be prescribed by the following NZ-Registered Health Care Professionals.
Note: Overseas practitioners may **not** prescribe in New Zealand unless registered here.

Authorised Prescribers

- Medical practitioner
- Dentist
- Midwife
- Nurse practitioner
- Optometrist
- Veterinarian

Designated prescribers

- Designated nurse prescriber
- Designated pharmacist prescribers
- Dieticians

Authorised Prescribers

This may be a medical doctor, a dentist, a nurse practitioner, an optometrist, a midwife or a *designated prescriber*. Other than a designated prescriber, an authorised prescriber may prescribe any **registered** pharmaceuticals for patients under their care and within their scope of practice.

1. *Medical Practitioners*

Medical Practitioners are exempt from the rule ‘may prescribe any **registered** pharmaceutical products.’
Unregistered pharmaceuticals (i.e. unapproved medicines) may be prescribed for the treatment of a patient under their care.

2. *Nurse Practitioner*

A registered nurse with advanced nursing qualifications and experience allows them to prescribe any medicines (including controlled drugs) relevant to their scope of practice, knowledge and competence.

3. *Veterinarian*

Veterinary prescriptions must be under the **owner’s** name and address (and not the animal’s) i.e. [animal’s name (type of animal) owner’s surname]

4. Optometrist Prescriber

A registered optometrist who is authorised to prescribe certain prescription medicines for optometric use after completing the required qualification and training by the Optometrists and Dispensing Opticians Board. Note: not all optometrists can prescribe.



Ophthalmologists are NOT optometrists.

- *Optometrists* are qualified to provide all aspects of **primary** eye health care including prescribing glasses or contact lenses. They may also prescribe or sell a range of medicines for treating eye infections and allergies. They must be registered and you can ask to see their annual practising certificate and scope of practice documents.
- *Ophthalmologists* are medical specialists who treat serious diseases of the eye by surgical or therapeutic means. Their specialisation and skill level means they are providers of **secondary** and **tertiary** eye health care who work in hospitals and private clinics. Ophthalmologists have completed a medical degree with further specialist training in the field of ophthalmology. These specialists are fully qualified doctors and so can prescribe a much wider range of medicines including a wider range of medicines for eye treatment than optometrists or GPs. Like all prescribers they are still only to prescribe for ‘a patient under their care’.

5. Midwife

A registered midwife is an authorised prescriber and may prescribe a medicine for the mother and the newborn during pregnancy, labour, and for up to 6 weeks of postpartum of the **expected** DOB* (6 weeks from 38-40 weeks gestational age). Please see the statement from the Midwifery Council on this.



The 6 Week Postpartum Period

The *6-week postpartum period* is defined as starting from the expected date of birth (not the actual date of birth). i.e. for preterm babies, the postpartum midwifery role may extend beyond 6 calendar weeks.

- Controlled drug prescriptions include **morphine, fentanyl, and pethidine** during intralpartum period **only**
- They cannot prescribe for an underlying medical condition (e.g. salbutamol for asthma)
- They cannot prescribe section 29 medicines.

Designated Prescribers

A designated prescriber (such as a pharmacist prescriber, registered nurse or dietitian) are prescribers that have undergone suitable training in order to be given prescribing rights, thus not all nurses, pharmacists,

optometrists or dieticians can prescribe. Those that can, may only prescribe from a Schedule of Medicines within their scope of practice.

1. *Registered Nurse*

- a) Registered nurse prescribing in primary health (PHO) and specialty teams (DHB)
 - Prescribe from a schedule of [common medicines for common and long-term conditions](#)
- b) Registered nurse prescribing in community health
 - Prescribe from a [limited schedule of medicines](#).

For nurses to able to prescribe controlled drugs, additional training is required.

2. *Pharmacist Prescriber*

A registered pharmacist prescriber with accredited qualification, training and competence set by the Pharmacy Council, who can prescribe specified prescription medicines within their scope of practice.

Pharmacist prescribers: 6 months OC, 3 months from [Gazette](#)

3. *Dietitian*

A dietitian with *additional training*, who is able to make a nutrition diagnosis and prescribe to treat patient independently. A dietitian prescriber can only prescribe medicines, vitamins and minerals and related products from a specific list. May only prescribe: **Cholecalciferol (Vitamin D), Zinc, Pancreatic enzymes**

- [Medicines \(Designated Prescriber - Dietitians\) Regulations 2015](#)
- [Specified Prescription Medicines for Designated Dietitian Prescribers, Gazette NZ](#)



Dietitians

Dietitians who are **not** designated prescribers may write prescription forms for funded [Special Foods listed in Schedule D of the Pharmaceutical Schedule](#) or any Pharmaceutical identified in Section D as being able to be prescribed by a dietitian.

Prescription Form

Form of Prescription — [MR R.41](#)

Prescriber

- Prescribing Date (valid for 6 months, subsidised if picked up within 3 months)
- Prescriber's name, address, phone number, signature



Note

NZePS prescription may be signature-less if it they don't include CDs (unless it is exempt/partially exempt Class C CDs) and the barcode can be scanned — [Prescription Medicines](#)

The temporary waiver for non-NZePS signature exempt prescription — expires 17 June 2022

1. [Controlled Drugs](#)
2. [Prescription Medicines](#)
3. [Frequently Asked Questions](#)

Patient

- Patient's each given name, surname, address
- DOB if under 13 (under 12 for controlled drugs)

Medicine

- Medicine name, strength, quantity or total period of supply
- Dose and frequency (internal medicine) or method and frequency (external medicine)

Pharmacy to Add

- Stamp (name, address, date)
- Third part label
- Annotation (quantity given, in what lots, pharmacist initials)

Note:

- Information must be legible and indelible i.e. cannot be written in pencil
- Prescriptions may be generated using an approved electronic system (e.g. NZePS) given the barcode must be scanned. Amendments cannot be handwritten on barcoded prescriptions (must match NZePS record)
- An envelope symbol on e-script indicates either: a) an attached written component by the prescriber OR b) a request to notify the prescriber within a select number of days if the pharmaceutical has not been dispensed.

Medicine Dispensing

Who Can Dispense Prescription Medicines — [MDR R.42](#)

- Authorised prescribers (including vets) + pharmacists
- Under the supervision of a pharmacist: dispensary technicians, pharmacy graduates, pharmacy technicians, pharmacy students
- Retail staff **cannot** dispense medicines.

Generic Substitution — [MR R42\(4\)](#)

Many situations can result in pharmacists needing to substitute a generic for a specified brand of medicine without the need of a signature, for example:

- The manufacturer's price is greater than the subsidy (not funded or only partially funded)
- The drug is not available in NZ and has a fully subsidised alternative available

They can supply an alternative brand of medicine provided that:

1. The prescriber referred to the medicine by its **trade mark/name/manufacturer name**
2. The prescriber did not indicate ‘no brand substitution permitted’
3. The substituted brand contains the same active ingredient(s) (and no other), is in the same dose form, strength and frequency as the prescribed brand and there is no clinical reason why the substitution shouldn't occur e.g. thyroid medications, anti-epileptics and so forth.
4. The pharmacist records the brand substitution on the prescription
5. Signs and dates the prescription
6. Informs the patient of the brand substitution



Note

Laws regulating generic substitution for controlled drugs differ. Changes required to a Controlled Drug prescription should be **re-written/regenerated** and signed by the Prescriber for both NZePS Controlled Drug prescriptions and triplicate paper prescriptions.

Alteration to Quantity Dispensed

Often times, pharmacists may run out of certain strengths of certain medicines (e.g. Celecoxib 100mg vs 200mg). In those events (and similar others), an alteration can be made to the **unit quantity** dispensed if it does not affect the end amount of pharmaceutical prescribed e.g. if the prescription reads “500 mg, one tablet per day, 30” the provider may dispense “250 mg tablets, two tablets per day, 60.”

Alteration to Presentation Dispensed

Alternatively, a change in *presentation* of pharmaceutical (such as from tablets to mixtures) can also be made as long as both the individual dose and total daily dose is not altered.

Rereading Medicines

Pharmacists may repackage dispensary medicines into pharmacy only/ general sale in certain scenarios.

If Pharmacy Only Naproxen is out of stock. Pharmacist may repack a dispensary stock of naproxen 250mg provided it is no more than 30 tabs/caps. This is possible if the Medsafe Classification does not specify that the Pharmacy Only product must be in the original manufacturer's pack.

Ingredient	Conditions (if any)	Classification
Naproxen	except when specified elsewhere in this schedule	Prescription
Naproxen	in solid dose form containing 250 milligrams or less per dose form in packs of not more than 30 tablets or capsules	Pharmacy Only

Period of Supply of Medicines

Before supplying pharmaceuticals to a patient - you must check their name and address. This prevents medicines from going to the wrong person!

Limit on Period of Supply — [MR R39A](#)

1. *Subsidised supply*: within 3 months (6 months for oral contraceptives)
2. *Non-subsidised supply*: between 3 - 6 months (9 months for oral contraceptives)
3. *Expired, cannot supply*: after 6 months (9 months for oral contraceptives)

Note that dentists can only supply from a period of 5 days for prescription items, or a total of 10 days in aggregate if there are repeats i.e. 5 + 5

Note:

- Not all registered pharmaceuticals are subsidised.
- A 3 month supply of unregistered pharmaceuticals is still applicable to ensure regular review by practitioner.

STAT dispensing of community pharmaceuticals can be signed if the patient:

- a) Has limited physical mobility
- b) Lives and works more than 30 minutes from the nearest pharmacy by their normal form of transport
- c) Is relocating to another area
- d) Is travelling and will be away when the repeat prescriptions are due

Urgently Required Prescriptions

Fax/Telephone/Pharmacy-Generated Prescriptions — [MR R.40A](#)

Urgently required prescriptions of prescription medicines may be communicated orally if:

- a) The prescription is urgently required
- b) The original written prescription must be forwarded to the pharmacist within **7 days confirming** the oral communication (within **2** days for controlled drugs).
- c) The prescriber is known personally to the pharmacist.

Emergency Supply of Medicines

Prescriptions for prescription medicines not required in certain cases — [MR R.44\(m\)](#)

Pharmacists in practice are sometimes faced with a request for supply of a prescription medicine without a prescription. The Medicines Regulations allow for this supply to occur in certain circumstances provided the following 5 conditions are met:

Conditions	Description
Condition 1	The medicine is not a CD MDR R.20, MDR R.34 OR a section 29 (MA s.29) <ul style="list-style-type: none">• This is because controlled drugs are not included in this legislation (regulation 44(m) schedule), so cannot be supplied without <i>either</i> a prescription <i>or</i> personal telephone call from the prescriber known to the pharmacist. This means that even Class C controlled drugs that don't require a controlled drug prescription form — such as codeine or benzodiazepines may not be sold as an emergency supply.• For an emergency supply, the pharmacist is the 'Prescriber' — cannot 'prescribe' section 29 medicines - but approved medicine with unapproved uses are fine.
Condition 2	The patient has been prescribed this medicine by an authorised prescriber for a particular condition <ul style="list-style-type: none">• Good practice for the medicine to have been prescribed within the last 3 to 6 months
Condition 3	Pharmacist is satisfied that the person requires the emergency supply <ul style="list-style-type: none">• No definition of emergency supply, must use professional judgment.
Condition 4	Gives no more than a 72 hour supply <ul style="list-style-type: none">• or minimum practicable e.g. 1 inhaler or 1 month supply of OC or 1 cartridge of insulin• The emergency supply is unfunded• Ensure patient is not using emergency supply as regular supply and that the dose is appropriate
Condition 5	Documents the supply <ul style="list-style-type: none">• The pharmacist should record the emergency supply on the patient's notes and• Inform the prescriber of this supply

Travelling with Prescription Medicines

A person is allowed to have prescription medicines:

1. They have been lawfully supplied that medicine to use themselves or for someone under their care
2. They do not have the same medicine supplied by another prescriber for the same purpose
3. Quantity of drug is no more than a 3 months supply (6 months if OC), 1 month if CD.

If someone is entering NZ with a prescription medicine/controlled drug, they need:

1. Demonstrate to NZ customs that the drug is required for a medical condition for them or someone under their care that is travelling with them
2. Evidence that they have been lawfully supplied that medicine e.g. original/copy letter from NZ authorised prescriber OR the original/copy prescription
3. If they are importing the medicine, they need to show evidence that the prescriber is aware they are authorising that import
4. Declare the drug on the arrival card
5. Carry the drug in their original labelled containers

If someone is leaving NZ with a prescription medicine/controlled drug, they need:

1. Rules differ per country - advise patients to contact their embassy

Security of Pharmacies

Storage Requirements for Prescription & Restricted Medicines — [MA s.42B](#)

To ensure the security of pharmaceuticals - prescription and restricted medicines must be stored in a way that prevents the public gaining ready access to them.

Standing Orders

Legislation

[Medicines \(Standing Order\) Regulations 2002](#)

What is a Standing Order? — [MA s.2](#)

A standing order is an issued document which *authorises* another person involved in the delivery of health-care services to supply or administer specified medicines to a specified class of people under certain circumstances **without** a prescription.

A standing order:

- Does not give someone the authority to write a prescription, only to supply or administer specified medicines to a specified class of people in particular circumstances.
- It does **not** enable a non-authorised prescriber to prescribe medicines
- It **permits** certain people to supply/administer, however it **cannot require** them to do so

Purpose

Standing orders were originally developed for use within a hospital environment:

- During an emergency
- Where the prescriber was not available

However their use has evolved with time:

- Ambulance services
- Non-emergency services to various populations e.g. patient with diabetes, sexual health services
- Rural areas with limited doctor services
- Rest homes

Who Can Issue A Standing Order — [MSOR R3](#)

- Medical practitioner, dentist, nurse practitioner, optometrist
- Note: Veterinarians **cannot** issue standing orders

Who can ACT under a Standing Order? — [MSOR R.4](#)

- Limited to a person engaged in delivery of a health service (i.e. someone who has the ability to make a clinical judgement)
- The class of person permitted to supply/administered the medicine must be specified under the SO

Legal Requirements of a Standing Order — [MSOR R.5](#)

- Written by an issuer
- State why the SO is necessary
- The class of persons permitted to supply/administer the medicine
- The level of competency & training of the class of person supplying/administering the medicine
- The class of persons to whom the medicine may be supplied
- The period for which the SO applies
- The circumstances in which the SO applies
- The treatment to which it applies
- The medicines, indications, dose/dose range, method of administration
- Whether **countersigning** is required or not — [MSOR R.6A](#)
 - If yes, the period of time within which the issuer must countersign the charted treatment
 - If no, then issuer must audit a sample of charted treatments at least **once each month**



Note

Countersigning means the **issuer** of the standing order (or the delegated authority) signs the charted treatment of a patient to whom medicine has been administered or supplied under a standing order

What Medicines can be Supplied/Administered? — [MSOR R3\(1\)](#)

- Pharmacy Only Medicines
- Restricted (Pharmacist Only) medicines
- Prescription Medicines
- Some Controlled drugs:
 - Parts 1 + 3 of Schedule 2 of MDA (i.e. B1 + B3)
 - Parts 2 - 7 of Schedule 3 of MDA (i.e. C2 - C7)

How is the Standing Order Used

Person supplying/administering the medicine under a SO must:

- Only supply/admin medicine in accordance with the SO
- Record or chart: the assessment, treatment, monitoring and follow up of the patient

Annual Review — [MSOR R7](#)

- Standing orders must be reviewed at least **once** each year

Data Retention of Prescription Medicines

Legislation

[Pharmacy Procedures Manual](#)

Data Type	Retention Period
Prescriptions <ul style="list-style-type: none">• Original physical copy<ul style="list-style-type: none">- Subsidised- Non-subsidised• Certified Repeat Copies (or daily dispensing /recording sheets)• Controlled Drug Prescriptions (top white copy)	<ul style="list-style-type: none">• 5 months (then sent to Sector Operations)• 3 years⁷³• 3 years⁷¹• 4 years⁷⁴• Note: Physical prescriptions containing patient information must be kept in a secure, retrievable format (e.g. electronic dispensing system) for a further 7 years (total 10 years) after completion of the Medicines legislation and NZ Pharmacy Services Standards retention requirements.⁷¹
Other Records <ul style="list-style-type: none">• Computer Records (for example PhMS)• Controlled Drugs Register• Incident Reports on Errors/Near Misses• Compliance Unit Dose Packaging Records (with identifiable patient information)• Compounding Job Sheets for Individual Service User (with identifiable patient information)• Batch Compounding Sheets• Extemporaneous Compounding Sheets	<ul style="list-style-type: none">• 10 years⁶⁸• 4 years⁷⁵ (Details of any dispensing which contain patient information should subsequently be retained in a retrievable format for another 7 years)⁷¹• 10 years⁶⁸• 10 years⁷¹• 10 years⁷¹• 3 years⁷⁶• 3 years⁷⁴

Controlled Drugs

Introduction & Relevant Legislations

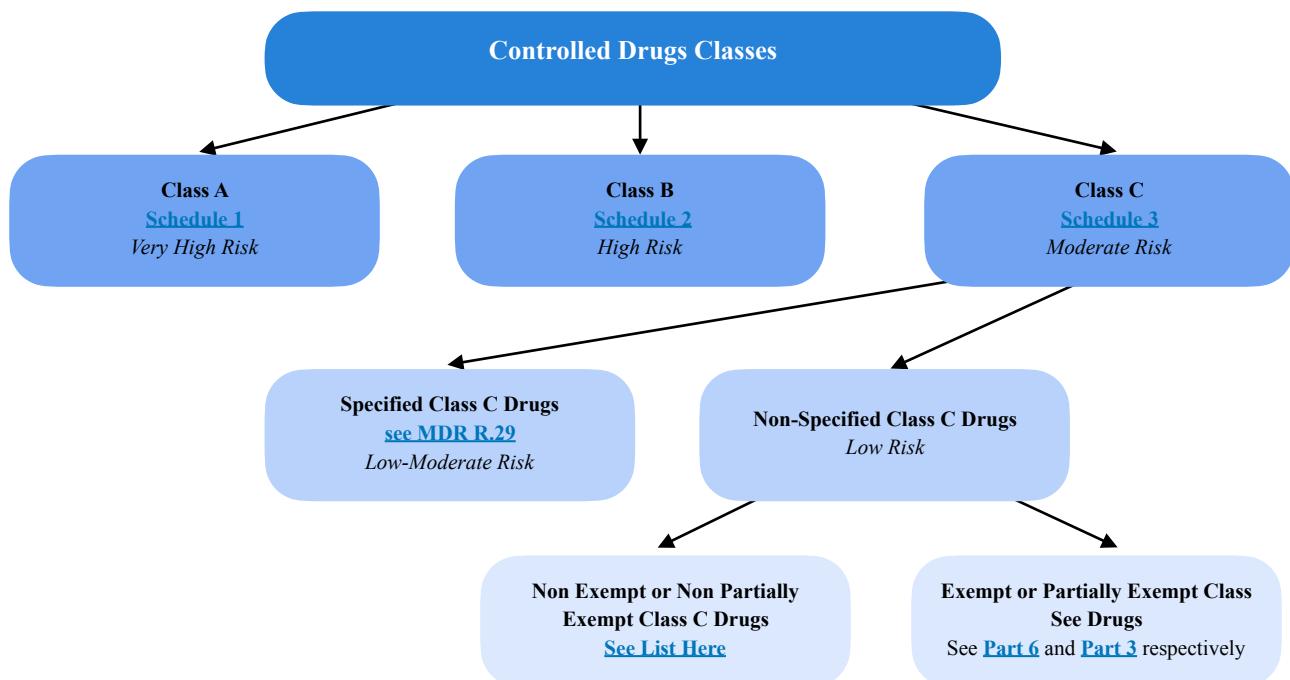
Relevant Legislations

1. [Misuse of Drugs Act 1975](#) — “No one can do anything with Controlled Drugs”
2. [Misuse of Drugs Regulations 1977](#)
3. [Schedules](#) of the Misuse of Drugs Act — lists drugs in the different classes (A, B, C)
4. [Medsafe's Classification Database](#) and [NZF](#) can also help indicate the Drug Class.

Introduction

Strict legal controls are needed for certain medicines and illegal drugs as they may cause serious problems like dependence ('addiction') and harm if they are not used properly.

Drugs are classified based on their risk of harm to individuals or society by their misuse, with safety measures respective to each class being in place to ensure they are prescribed, supplied, used, and stored safely and legally. Generally the level of 'control' dictated by the legislation is greatest for Class A drugs, followed by Class B, with relatively fewer restrictions and requirements for Class C drugs.



Note

Not all controlled drugs listed in the Schedules are used therapeutically. The Misuse of Drugs Act & Regulations was primarily put in place to regulate the use of **illegal** psychoactive substances, and provides **exceptions** where certain drugs can be used therapeutically.

Specified Class C controlled drugs (either in combination or not): amobarbital, amobarbital sodium, buprenorphine, butobarbitone, glutethimide, ketamine, secobarbital, secobarbital sodium.

These products do not fall under this category if they are combined with another substance **not** in Schedule 3, Part 4 (1) of the Misuse of Drugs Act 1975. *For example: A Prescription for buprenorphine on its own must meet all the requirements specified on the list, whereas a Prescription for buprenorphine plus naloxone does not need to meet the requirements on the list.*

Appendix 2

Class C Controlled Drugs (NOT exempt or partially exempt)

Prescriptions for the following list of medicines require the prescriber signature and the original prescription sent to the pharmacy (Misuse of Drugs Regulations 1977).

Class C Controlled Drugs (except Class C5)		
Generic name	Brand and form	Strength available
Buprenorphine	Buprenorphine Naloxone BNM sublingual tablet	2 mg with naloxone 0.5 mg 8 mg with naloxone 2 mg
Codeine	Tablet	15 mg, 30 mg, 60 mg
Dihydrocodeine	DHC Continus long-acting tablet	60 mg
Phenobarbitone	Tablet Max Health injection Aspen injection	15 mg, 30mg 200 mg/mL 200 mg/mL
Benzodiazepines (Class C5 Controlled Drug)		
Generic name	Brand and form	Strength available
Alprazolam	Xanax tablet Arrow-Alprazolam tablet	250 microgram, 500 microgram, 1 mg 250 microgram, 500 microgram, 1 mg, 2 mg
Clobazam	Frisium tablet	10 mg
Clonazepam	Paxam tablet Rivotril oral drops Rivotril injection	500 microgram, 2 mg 2.5 mg/mL 1 mg/mL
Diazepam	Arrow-Diazepam tablet Stesolid rectal tube Hospira injection	2 mg, 5 mg 5 mg, 10 mg 5 mg/mL
Lorazepam	Ativan tablet	1 mg, 2.5 mg
Midazolam	Midazolam-Claris injection Pfizer injection	1 mg/mL, 5 mg/mL 1 mg/mL, 5 mg/mL
Nitrazepam	Nitrados tablet	5 mg
Oxazepam	Ox-Pam tablet	10 mg, 15 mg
Phentermine	Duromine capsule Metermine capsule	15 mg, 30 mg 15 mg, 30 mg
Temazepam	Normison tablet	10 mg
Triazolam	Hypam tablet	125 microgram,

Updated 16 March 2022

		250 microgram
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Class C Controlled Drugs (that ARE exempt or partially exempt)

Prescriptions for the following list of medicines DO NOT require the prescriber signature and original prescription sent to the pharmacy (Misuse of Drugs Regulations 1977).

Class C (exempt and partially exempt) C Controlled Drugs
Gee's Linctus
Paracetamol and codeine combination preparations
Pholcodine

Controlled Drugs Prescribing

Introduction

The types/amounts of CDs that can be prescribed is different for different healthcare practitioners - [MDA s.8](#)



Change to the Duration of Supply of Class B Controlled Drugs

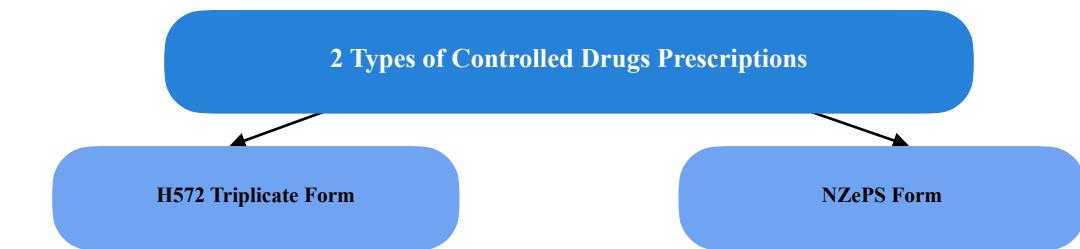
As of 25/11/2022, Class B CDs can now be supplied for up to 3 months [Regulation 7\(5D\)](#) in monthly intervals (or shorter) [Regulation 12\(5\)](#) if prescribed through an approved electronic system (the NZePS) - if prescribed outside of this system, then they can only be supplied for a maximum of 1 month in 10 day lots - [Regulation 31\(1\)\(d\)](#)

Professional Group	Misuse of Drugs Act and Regulations (Period of Supply)	Repeats	Restrictions on Dispensing
Medical Practitioners & Nurse Practitioners	<p><i>Class A and B:</i> 1 month supply <i>Class C:</i> 3 month supply</p> <p>Within their scope of practice + for a patient in their care</p> <p>MDR Regulation 12A(1)(d)</p>	May authorise repeats	<p><i>Class A & B:</i></p> <ul style="list-style-type: none"> Not more than 7 days after date of prescription Repeats must be dispensed no more than 7 days after the previous supply is exhausted <p><i>Class C:</i></p> <ul style="list-style-type: none"> Subsidised: within 3 months Non-subsidised: 3-6 months
Dentists	<p><i>Any within scope:</i> 7 days</p> <p>‘For dental treatment only’</p> <p>Note: NOT authorised to telephone prescriptions for controlled drugs</p> <p>MDR Regulation 21(3)(b)</p>	May NOT authorise repeats	<p><i>Class B:</i></p> <ul style="list-style-type: none"> Not more than 7 days after date of prescription Only subsidised for 5 days treatment <p><i>Class C:</i></p> <ul style="list-style-type: none"> Only subsidised for 7 days treatment
Veterinarians	<p><i>Class A and B:</i> 1 month <i>Class C:</i> 3 months</p> <p>“For animal treatment only”</p> <p>Note: NOT authorised to telephone prescriptions for controlled drugs</p>	May NOT authorise repeats	<p>Veterinarians are <u>not</u> required to prescribe controlled drugs on a Triplicate Prescription Form</p> <p>Veterinary prescriptions are UNFUNDDED</p>
Midwives	<p>Schedule 1C: 1 month max (morphine, pethidine, fentanyl ONLY) during the intrapartum (labour, delivery and immediate postnatal period only)</p> <p>‘For midwifery use only’</p> <p>MDR Regulation 12A(1)(c)</p> <p><i>Midwifery Council Statement</i></p>	May only authorise 1 repeat at a specified interval	<ul style="list-style-type: none"> Not more than 4 days after date of prescription Repeat must be dispensed no more than 4 days after the previous supply is exhausted
Designated Pharmacist Prescribers	<p>Schedule 1B: 3 days supply</p> <p>MDR Regulation 12A(1)(b)</p>	May NOT authorise repeats	<ul style="list-style-type: none"> Not more than 7 days after date of prescription
Designated Nurse Prescribers	<p>Schedule 1A: 7 days supply</p> <p>MDR Regulation 12A(1)(a)</p> <p><i>Nursing Council</i></p>	May NOT authorise repeats	<ul style="list-style-type: none"> Not more than 7 days after date of prescription
Optometrists	Optometrists have NO prescribing rights for controlled drugs		

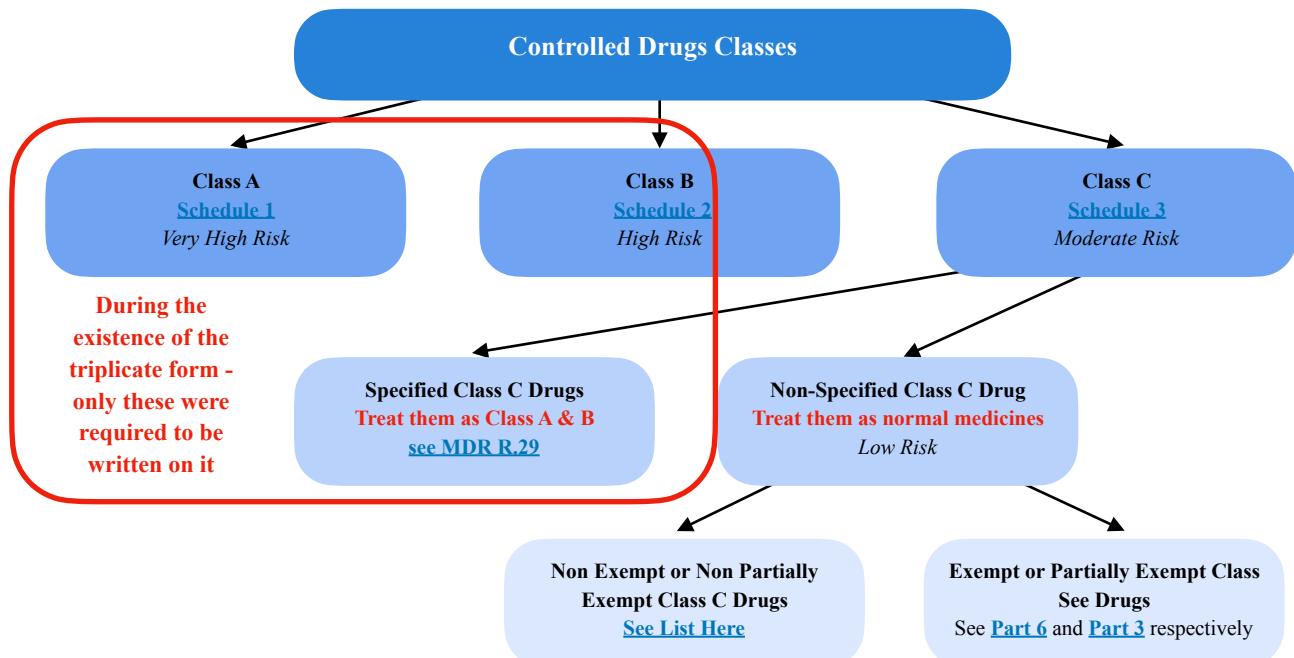
Controlled Drug Prescription Form

Controlled Drug Prescription Forms

There are 2 types that exist:



Form	Description
H572 Triplicate Form	<p>In the past, Class A and B CDs were required to be handwritten on a triplicate prescription form (H572). This type of prescription is becoming less common as controlled drugs can now be written via the New Zealand Electronic Prescription System (NZePS). However it is still important to know how it works as you may encounter it in practice:</p> <ol style="list-style-type: none">1. Class A, B and Specified Class C Controlled Drugs were required to be written on it2. Prescriber's address had to be stamped on all three copies3. Non-controlled medicines did not have to be written separately
NZePS Form - NZePS	<p>This form has become popular due to the pandemic. Pharmacists can dispense controlled drugs (Classes A, B, C) from an ePrescription provided it is:</p> <ol style="list-style-type: none">1. Generated via NZePS and contains a barcode that can be scanned or manually entered2. Controlled drugs listed on it are written separately to other classes of medicines e.g. non specified Class drug, non-controlled medicines<ul style="list-style-type: none">• This means codeine (class C) and morphine (class B) will need to be on separate scripts but codeine and paracetamol can be on the same script3. Prescription contains a wet ink signature by the prescriber - this is because the signature waiver does not apply to CD prescriptions <p>Please note:</p> <ul style="list-style-type: none">• Amendments cannot be handwritten on barcoded prescriptions as it must match the NZePS record.• The original of a faxed NZePS controlled drug prescription must be obtained within 2 business days.





Non Specified Class C Drugs still cannot be given in emergency supply and still require a wet signature, but required to be prescribed separately to a Class A & B on barcoded scripts and can be placed on the same script as other non-controlled medications.

Form of Prescription — [MDR R.29](#)

The legal requirements for a CD prescription are similar to those required for a non-controlled drug.

For Class A, Class B, and specified Class C controlled drugs:

- a) Surname, initials of the first names, and address of the: patient OR person who has custody of the animal
 - b) DOB of the person if under 12 for controlled drugs; set out in years and months
 - c) Signed physically by the controlled drug prescribed in his or her own handwriting
 - d) Be legible and indelible
 - e) Dated with the date on which it was signed
 - f) Set out the name of the controlled drug to be supplied — not be in cipher, or abbreviated, otherwise than by recognised abbreviation
 - g) Indicate the total amount of the controlled drug that may be sold or dispensed on the 1 occasion, or on each of the several occasions, authorised by that prescription
 - h) Set out the dose and frequency of the dose, or directions for use if for external use
 - i) Where unusual or regarded dangerous dose, the dose should be underlined and initialled by prescriber
-
- Any amendments must be signed. If electronically generated, a new amended prescription must be issued.
 - Controlled drugs (except for exempt/partially exempt Class C CDs) need to be written on a separate prescription to non-controlled items

Verification of Controlled Drugs Prescriptions — [MDR R.32](#)

The pharmacist must be confident that the signature on the controlled drug prescription is genuine particularly if they are not familiar with the prescriber.

- Any alterations on a controlled drug prescription must be signed by the prescriber.
- Any forged or altered controlled drug prescriptions must be retained and the Police notified.

Prescription Annotations — [MDR R.29](#)

These legal requirements must be added by the pharmacy to all 3 copies of the triplicate form, or the **original** NZePS CD prescription form:

- Name and address of the pharmacy (i.e. the stamp)
- Each item annotated with the date of dispensing on **each** occasion
- Each item annotated with its unique identifying number on **each** occasion for the CDs — the third part label is **NOT** sufficient. You need to write out the number.

- Each item annotated with the quantity of the controlled drug dispensed on **each** occasion — circling the prescribed quantity is **NOT** sufficient. You need to write out the number.
- Each item annotated with the strength of the controlled drug dispensed on **each** occasion.

Period of Supply for Controlled Drug

Supply Quantity — [MDR R.31\(1\), 31A](#)

Prescriber determines the frequency (e.g. weekly dispensing) and this cannot be over-ruled.

Class A & B: Maximum supply quantity is 1 month (in 10 day lots) **EXCEPT** for methylphenidate hydrochloride and dexamfetamine sulfate which are dispensed STAT — [PHARMAC Schedule 4.4.2](#) lists drugs that can be dispensed 1 month stat.

Class C: Maximum supply quantity is 3 months (in monthly lots)



Remember

Methylphenidate and Dexamfetamine are used in the treatment of ADHD.

Directed Dispensing Intervals — [MDR 31A\(7\)](#)

For special reasons relating to the protection of the patient, or for the purpose of limiting the quantity of any controlled drug in the possession of any person, the controlled drug prescriber (**not being a dentist or veterinarian**) who signs a prescription directs on the prescription that the controlled drug is to be dispensed daily or at such other regular intervals as the controlled drug prescriber considers necessary for a specified period not exceeding 1 month, the controlled drug may be supplied on not more than the number of occasions indicated, and not more frequently than the intervals directed.

STAT Dispensing of Class B CDs — [PHARMAC Schedule 4.4.2](#)

- Similar to STAT dispensing of community pharmaceuticals, a patient or a representative can sign for the prescription to be dispensed STAT if the patient:
 - a) Has limited physical mobility
 - b) Live and work more than 30 minutes from the nearest pharmacy by their normal form of transport
 - c) Is relocating to another area
 - d) Is travelling and will be away when the repeat prescriptions are due

Prescription & Repeat Expiry — [MDR R.31\(1\), 31A](#)

- Class A & B: Prescription expires **after** 7 days after the date of the prescription (**4 days for midwife Rx's**)
- Class C: Prescription expires **after** 6 months after the date of the prescription
- *Note:* The earliest pickup for a controlled drug repeat is when the patient reaches **2/3 of the period of supply** — this is when the previous supply is *substantially* exhausted.

Dispensing scenario example for 'earliest pickup':

- An initial dispensing given on the 1 August with a period of supply of 10 days.

- Maximum compliance indicates next supply pickup date of 11 August, but supply can be given between 8 August and 18 August (2/3 of 10 days is 3 days).

Collection of Repeat Controlled Drugs

If the patient does not collect the first repeat within the 7 day timeframe, they are not eligible for any remaining repeats. This does not apply to Midwives as they may only prescribe 1 repeat.

Controlled Drugs with Prescribing Restrictions

Ministerial Approval is required before these (Class B2 controlled drugs) are prescribed or supplied: pseudoephedrine, ephedrine, methylphenidate, and dexamfetamine.

<https://www.health.govt.nz/our-work/regulation-health-and-disability-system/medicines-control/controlled-drugs/restrictions-supply-certain-controlled-drugs>

Note on Methylphenidate (CD — B2)

Methylphenidate is a class B2 controlled drug that requires specialist approval before it can be prescribed
BUT **special authority** is not a legal requirement.

- It can be given by medical practitioners:
 1. Specialising in Paediatrics or Psychiatry for the treatment of Attention Deficit Hyperactivity Disorder.
 2. Specialising in Internal Medicine for the treatment of Narcolepsy
 3. Specialising in Palliative Medicine for use in palliative care

Note on Ephedrine & Pseudoephedrine (CD — B2)

- Can only be given to by medical practitioners

Urgently Required Controlled Drug Prescriptions

Emergency Supply — MR R.44(m). [MDR R.20](#), [MDR R.34](#)

Controlled drugs **CANNOT** be provided as an emergency supply at the request of a patient. If a supply is urgently required, you need an oral prescription.

Oral (Telephone) Prescriptions for Controlled Drugs — [MDR R.34](#)

Controlled drugs can be prescribed via phone or a fax if:

1. Authorised or Designated prescribers **EXCEPT** for Dentists and Veterinarians (but can for normal Rx's)
2. In the case of **emergency**
3. Prescriber is personally known to the pharmacist
4. An original script must be sent within 2 business days **AND** should indicate that it is confirmation of a phoned prescription
5. **No repeat** of the telephone or faxed controlled drug Prescription Form is permitted until the **original** controlled drug prescription forms is received by the pharmacy.

Travelling with Controlled Drugs

A person is allowed to have controlled medicines on them when entering/leaving NZ if — [Health Govt](#)

1. They required it for the treatment of a medical condition that is their own or someone's under their care/control
2. Drug was lawfully supplied/prescribed by a NZ prescriber OR lawfully supplied to the person overseas for the purpose of treating a medical condition
3. Quantity of drug is no more than 1 month's supply (all classes)

If someone is entering NZ with a prescription medicine/controlled drug, they need:

1. Demonstrate to NZ customs that the drug is required for a medical condition for them or someone under their care that is travelling with them
2. Evidence that they have been lawfully supplied that medicine e.g. original/copy letter from NZ authorised prescriber OR the original/copy prescription
3. If they are importing the medicine, they need to show evidence that the prescriber is aware they are authorising that import
4. Declare the drug on the arrival card
5. Carry the drug in their original labelled containers

If someone is leaving NZ with medicines

The rules *vary* in different countries and so do the classifications. Check with the embassy and apply above rules.

Supply & Possession of Prescribed Controlled Drugs

Collection of Controlled Drugs — [MDR R.24](#)

Only to the person being prescribed the CD, unless:

- Written authority from the patient
- Satisfied that person collecting prescription is a caregiver (e.g. phone call or written confirmation from the person)

Possession of Controlled Drugs — [MDA s.8](#)

A person can have a controlled drug in their possession if lawfully prescribed for them or for someone in their care

Storage of Controlled Drugs

Safe Requirements — [MDR R.28](#)

This does not apply to: [partially exempted Class C drugs](#), codeine syrup/linctus, pholcodine linctus

CDs (**including Class C**) must be locked in:

- Safe/cupboard/compartment that is made of metal/concrete — approved by Medsafe
- Safe must be securely fixed to the premises (e.g. bolted to the ground) and
- Has a lock & key (key must not be within the building when not occupied), or combination lock

Disposal (Destruction) of Returned Controlled Drugs

- Enter in the register immediately on a **designated page** specifically for drugs to be disposed. This can be at the rear of the register or in a separate destruction register.
- The type, quantity, and (where possible) the source of the returned CDs should be entered in the register.
- Two pharmacists, or a pharmacist and a responsible person (such as a doctor or police officer), may subsequently destroy them.
 - Technicians and interns are NOT considered appropriate for countersigning CD destruction.
- Both parties must witness the destruction, and both must sign the destroyed drugs out of the register.

Documentation & Stocktaking of Controlled Drugs

Controlled Drug Register — [MDR R.37 - R.48](#)

Pharmacists are required to maintain accurate records of controlled drugs received and dispensed by the pharmacy.

What Drugs are Registered — [MDR R.37](#)

- Class A & B drugs to be recorded in the CD Register.
- Class C drugs do not have to be recorded, but still need to be stored in the safe — [MDR R.48](#)
 - *Class C5 do not need to be kept in the safe but its a good idea*

What Should The Register Contain — [MDR R.37](#)

- The CD register must be a bound volume of consecutively numbered pages in [form 1](#) of Schedule 1, in which each page shall have entries relating only to 1 form of 1 controlled drug
- Must contain a separate record of EVERY prescription dispensed (including any REPEATED prescriptions) that contains any portion of a controlled drug showing:
 - Patient first name initials, surname and address
 - Prescriber first name initials, surname and address
 - Proportion and total amount of CD dispensed
 - Date on which this was delivered to the person or their authorised person

Entry of Controlled Drugs — [MDR R.40](#)

- Record must be entered **by the end of the next business day** (but best to do it at the time of dispensing)
- Do **NOT** obliterate, alter, or cancel any entry
- Must not be in pencil (black or blue pen preferred as they are photocopied the clearest)

Stocktaking Guidelines — [MDR R.43](#)

- Stocktake twice a year (30th June & 31st December)
- Don't wait until these are due to discover a problem, best practice to check stock after every CD dispensing.
- Do an arithmetic check of all transactions in and out at the end of EACH page.
- Do a physical stock take on receipt of all new stock of controlled drugs. Compare this to the running balance in the book.
- Check the computer stock on hand compared with the book at regular intervals.

What to do if you discover a discrepancy

- Look for entries with similar quantities as the variance.
- Look for double the quantity (has an out been put into the in column?)
- Look at dispensing record for that drug since the last recorded physical stock take.
- Check all repeats are entered.
- Check entries on the pages for the same drug, but different strengths.

Once you find the cause of the error:

1. NO crossing out in the register.
2. A new entry must be made on the next available line and a note written outlining the reason for the new entry (e.g. error 30/6/15). See picture above.
3. Place the number in the 'IN' or the 'OUT' column to account for the error and ensure the running total is now back to being correct.
4. Alert the Medicines Control Officer when no obvious conclusion can be reached.

Data Retention of Controlled Drugs Prescriptions

Completed Controlled Drug Prescription Forms

- Top copy (white) is retained in the pharmacy for 4 years
- Second copy (yellow) and third copy (red) are filed in the bundle of prescriptions on the date of initial dispensing or the bundle of prescriptions on the date of the final dispensing.

Issued Orders to Prevent Misuse of Controlled Drugs

Restricted Persons — [MDA s.20 & MDA s.25](#)

- Medical Officer of Health may prevent supply of a CD to a person
- May restrict who can prescribe and/or supply CDs to particular people 'restricted people'

Opioid Substitution Programme

Introduction

Methadone (liquid) and Suboxone (sublingual tablet) are two products in NZ available to be prescribed for the treatment of opioid dependence.

Pharmacists' responsibilities

- Confidential service reducing stigma
- Comply with all legislative requirements for OST dispensing, recording, storage of meds
- SOP and auditable systems to minimise risk and errors
- Ensure adequate supervision of the consumption of OST doses
- Liaise with OST providers on a regular basis
- **Once a dose has been dispensed, another one cannot be given no matter the circumstance.**

Takeaway doses

- Dispensed in individually daily doses
- Appropriately labelled
- CRC (child resistance cap)
- Can change so must keep up to date with correspondence
- Dosing in police cells

	Prescription Form	Controlled Drugs Register	Storage
Methadone	H572M/H572 Prescription Form	Yes	Locked in safe at all times
Suboxone	Controlled Drug Form or Prescription form	No	Locked in safe at all times

Step	Methadone	Buprenorphine
1	Ensure script is legal and starts on a consumption day; check for any communications regarding changes to dispensing. Correctly identify client, verifying identification if necessary. Assess for signs of intoxication (client should remove sunglasses). Ensure client does not have anything in their mouth (eg, chewing gum) and is not holding a drink bottle or other container.	
2	Measure dose using syringe, burette or Dispensette® into clear, disposable cup. Dispense takeaways as individual daily doses in appropriately labelled containers with child-resistant closures. Do not dilute takeaways unless specifically instructed by the prescriber. Give dose for observed consumption to client.	Break (crumble) tablets to reduce risk of diversion and reduce dissolution time. Place tablets into a clear medication pottle and instruct client to tip tablets under tongue. Advise client not to chew or suck tablets or swallow saliva. If tablets move away from position, instruct client to tip head forward to move them into place under the tongue.
3	Ensure whole dose is taken by having client drink and/or speak after dose. Ask client to place disposable cup into appropriate waste container before leaving, to reduce risk of diversion.	Observe client until satisfied tablets are not able to be diverted (three minutes). If whole tablets are given, supervise client until tablets have dissolved (4–7 minutes) and check his or her mouth periodically during dissolution
4	Where applicable, hand takeaways to client, checking they are closed properly to avoid subsequent problems with claims of spillage. Ensure client is aware of safe storage requirements, especially if he or she lives with children.	Where applicable, give client dispensed takeaways. Ensure client is aware of safe storage requirements, especially if he or she lives with children.

Methadone (Biodone — Class B3)

Methadone for Opioid Dependent Clients— [MDA s.24](#)

Methadone is a synthetic opioid agonist used for opioid dependence (and also for chronic pain).

Biodone (3 strengths):

- 2mg/ml (pink)
- 5mg/ml (clear) — Forte
- 10mg/ml (orange) — Extra Forte

Who can Prescribe Methadone — [MDA s.24](#)

- Prescribers in authorised methadone maintenance treatment clinic (e.g. Specialist Addiction Services SAS)
- Individual GPs authorised in writing by a specific prescriber in a gazetted treatment service e.g SAS
- Exemption permitting emergency treatment for dependence in hospital and not exceeding 3 days
- Other specified Prescribers working in approved addiction clinics or hospital care institutions

Note: Specified authorised prescriber nurse practitioners, designated prescriber nurses, and pharmacists can prescribe these pharmaceuticals.

METHADONE DISPENSING RECORD SHEET															Name of Pharmacy <i>Anytown Phcy Ltd</i>				
Methadone Solution <i>5</i> mg/ml			Record for month <i>January</i> year <i>2003</i>																
all recorded doses expressed in ml of the above solution																			
Days of the month →																			
PATIENT	Script numbers	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15			
LONG D.	243105	11	11	11	11	11	22	X	11	11	11	11	11	11	11	11			
WRIGHT J.	242963	14	42	X	X	42	X	X	14	42	X	X	42						
KERR B.	242660	243527	9	27	X	X	③	24	X	X	8	24	X	X					
MCPHERSON R.	243328		18	36	X	18	18	-18								(in prison)			
BROOK K.	243560						16	32	X	32	X	32	X	32	X	16			
NEW PATIENT STARTS																			
dispensed, but not collected																			
new script, dose reduced to 8ml per day																			
includes 18ml dispensed but not collected, so destroyed.																			
TOTALS (ml)	⇒⇒	52	116	11	29	95	96	0	57	61	67	11	69						

Totals to be transferred daily to controlled drug register

Note:

1. All recorded doses to be expressed in ml of the above solution.
2. Script numbers – two columns to provide for old & new script. The first supply from new script to be circled.

3. Enter X for days covered by takeaways.
4. Enter – for uncollected doses.

Buprenorphine + Naloxone (Suboxone — Class C4)

Suboxone (Buprenorphine + Naloxone) Prescriptions for Opioid Dependent Clients

Suboxone is a combination of Buprenorphine + Naloxone. Buprenorphine is a μ opioid receptor partial agonist and κ opioid receptor antagonist. Naloxone is an antagonist at μ , δ , κ opioid receptors — Naloxone (CD C4) is used as a **deterrent** in this case.

Suboxone is a **sublingual tablet**.

- Need to wait till the tablet is fully dissolved.
- Suboxone may be crushed, but **not** into a powder to prevent swallowing

Needle Exchange Programme (NEP)

Needles & Syringes

Relevant Legislation

[Health \(Needles & Syringes\) Regulations 1998 HNSR R3, 7, 12](#)

Introduction

A needle exchange programme is a service which provides safe needle disposal and to give new clean needles. This is aimed to reduce potential harm from injecting drug use.

Aim

- Minimise spread of HIV, Hep C, and other blood borne viruses
- Focus on health and well-being
- Addictive drug use as a health issue vs criminal or moral issue

Objectives: harm reduction

- Provide services required for supplying sterile syringes/needles
- Promote greater safety in injecting
- Promote safe sex practices
- Collect used syringes for safe disposal

Pharmacists and employees may sell needles and syringes — [HNSR R.5](#)

- From a registered pharmacy
- To anyone for use for a therapeutic purpose (e.g. Intravenous Drug Use)
- To any person >16 y (doesn't necessarily have to be for a therapeutic reason)
- To a person <16 y if they have a prescription

Return of used needles and syringes — [HNSR R9](#)

- Pharmacists must accept for disposal a used needle or syringe (which must be in an approved container)
- Returned needles/syringes must be in an approved container by the Director-General

Unapproved Medicines & Uses (Prescription Medicines)

Dispensing Unapproved Medicines (Section 29 medicines)

Legislation

Unapproved Medicines or Uses (Section 29 Medicines) — [MA s.20](#) and [MA s.2](#)

Medsafe Unapproved Medicines

Medsafe Product Application — tells you what medicines are unapproved and approved

Introduction

Approved Medicines

An approved medicine is a medicine evaluated by the Ministry of Health for safety, efficacy and quality. The consent is notified in the NZ Gazette, where it can then be distributed, sold, and marketed under the conditions set out in the Medicine Data Sheet. Note that this approval only applies to the particular **brand** of medicine.

Unapproved Medicines (Section 29 Medicines)

An unapproved medicine is a medicine for which consent has **not** been given by the Minister of Health for sale, distribution or marketing in **New Zealand**. However, these medicines (both branded and generic) may be approved overseas — thus these medicines may be safe, but are just **not** registered in NZ.

Unapproved medicines may still be prescribed to patients by prescribers — their use is indicated for rare diseases for which there are few or no treatment options approved in the country, or if the approved medicines are unable to be supplied (i.e. supply chain problem). Note that some medicines that are **controlled drugs cannot be used for an unapproved use** without Ministerial approval — [Contact Medicines Control](#)

Procurement (Obtaining) & Supply of Unapproved Medicines — [MA s.25 & MA s.29](#)

Who can obtain Unapproved Medicines? — [MA s.25](#)

- **Any** authorised prescriber can obtain unapproved medicines - but only medical practitioners can prescribe them to a patient.
- Section 25 allows an authorised prescriber to use any medicine for the treatment of a patient in their care (within their scope of practice), regardless of whether it is approved or unapproved in New Zealand
- All authorised prescriber can sell, supply, procure, administer, manufacture and arrange administration of an unapproved medicine for a particular identifiable patients or if another prescriber asks.

Who can supply authorised prescribers with Unapproved Medicines? — [MA s.29](#)

- Pharmacists can dispense an unapproved medicine **only to medical practitioners** for the treatment of a particular patient. This means that only medical practitioners can get unapproved medicines from pharmacists.

- All other authorised prescribers must obtain unapproved medicines either from other authorised prescribers or by directly importing (and going through Medsafe) — e.g. a doctor can order an unapproved medicine from overseas for a particular patient.

Documentation Required Upon Supply

1. *Manufacturer → Prescriber* — [MA s.29](#)

Section 29 of the Medicines Act allows the sale or supply of unapproved medicines. The person or company who supplies the medicine must notify the Director-General of Health of the supply (via Medsafe), and record the name of the prescribing medical practitioner, the patient for whom the medicine was prescribed and the name and place of supply.

2. *Prescriber → Patient*

If supplying an unapproved medicine, the prescriber must always provide a professional and ethical standard of care, which includes having informed consent from the patient for use of that medicine. This includes complying with the following *Code of Rights* principles:

- COR R.4 — services to be provided with reasonable care and skill
- COR R.6 & 7 — patients must be informed and give informed consent.

Approved Medicines for Unapproved Use (Off-Label Prescribing) — [MA s.25](#)

'Off-label' prescribing of an approved medicine for an unapproved condition. Section 25 allows an **authorised prescriber** to use **any** medicine for the treatment of a patient in their care. Off-label prescribing is at the discretion of the practitioner based on their clinical experience and judgement, and in consultation with the patient. There is no reporting requirements associated with such supply.

Summary of Unapproved Medicines & Approved Medicines for Unapproved Use

For Unapproved Use	Unapproved Medicines			Approved Medicines (Off Label)		
	HCP	Procurement (Obtain)	Prescribing	Emergency Supply	Procurement (Obtain)	Prescribing
Pharmacist	Yes, from another pharmacy or manufacturer (if supplying a doctor's prescription)	N/A	No	N/A	N/A	Yes
Medical Practitioners	Yes (from pharmacist, another doctor or through import)	Yes	N/A	Yes	Yes	N/A
Other Authorised Prescribers	Yes (from a doctor or through import)	No	N/A	Yes	Yes	N/A

Authorised prescribers can:

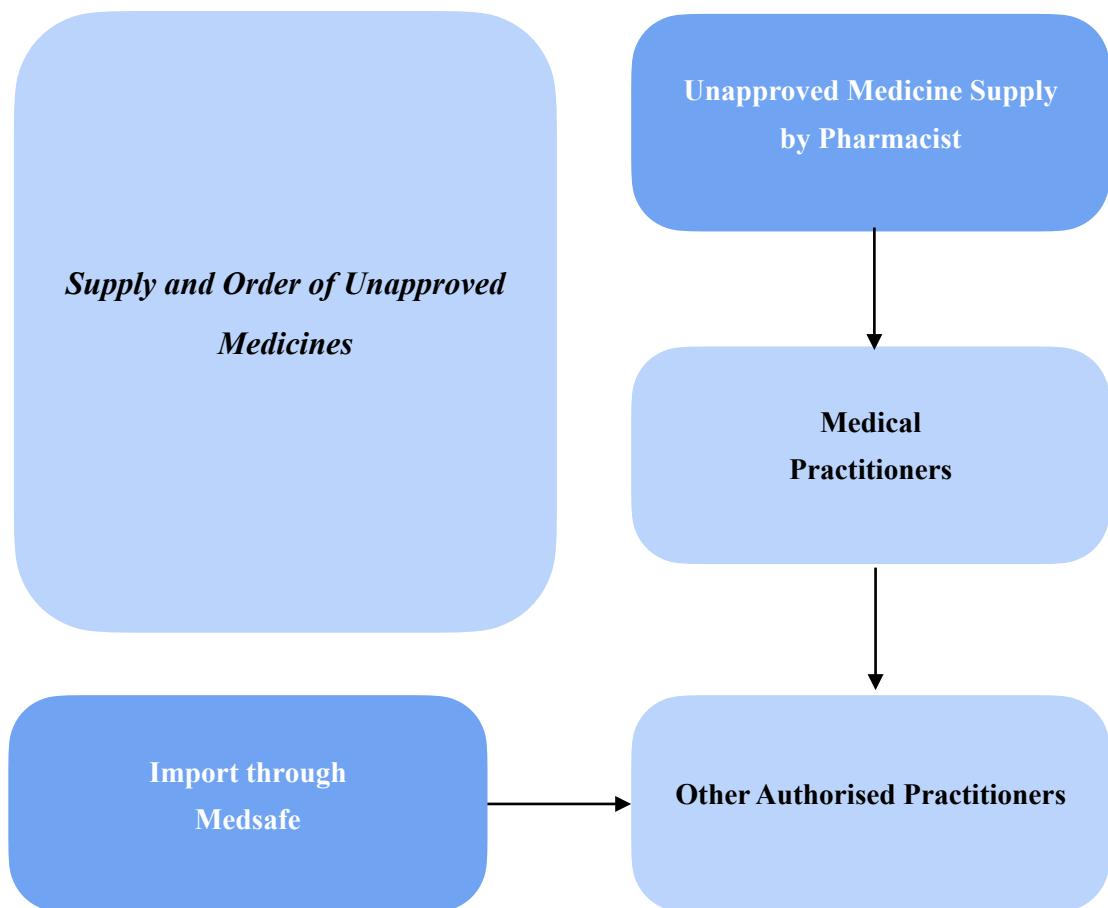
- Prescribe an **approved** medicine for an unapproved use
- **Obtain** an **unapproved** medicine for a known patient under their care (eg, direct importation or by requesting a pharmacy compound a medicine) but **cannot prescribe** unapproved medicines (section 29 of the Medicines Act)

Medical practitioners can:

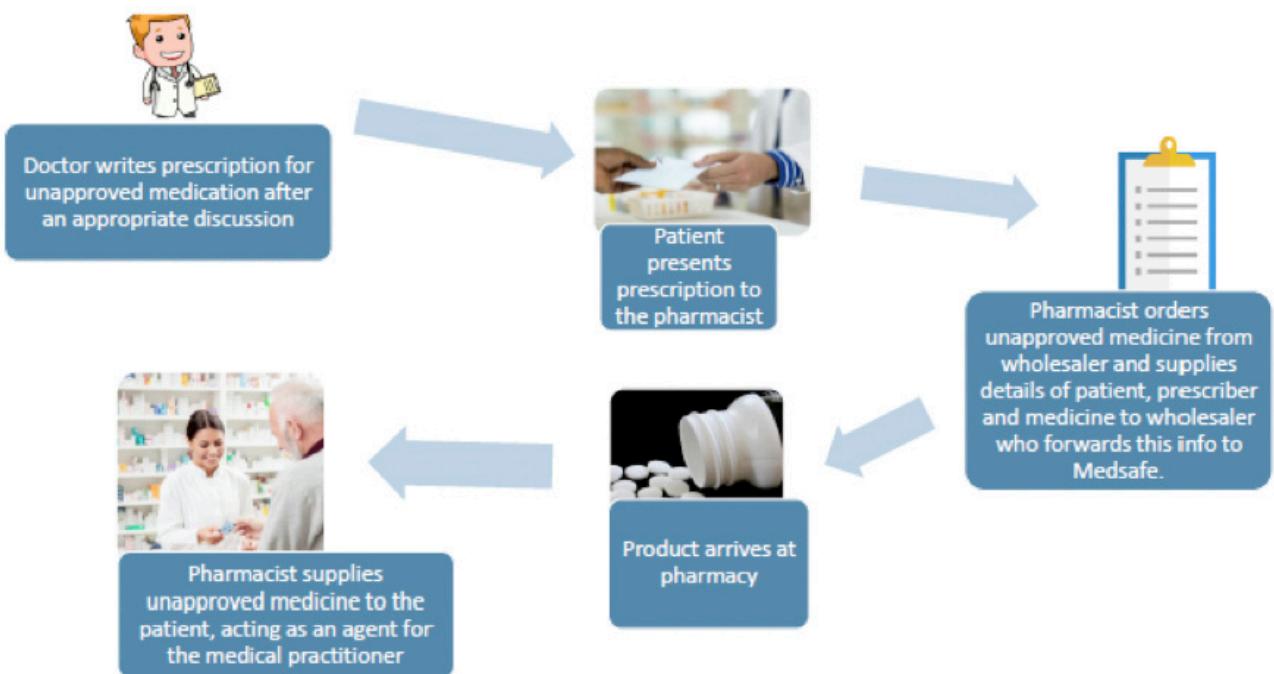
- Prescribe an **approved** medicine for an unapproved use
- **Obtain** an **unapproved** medicine for a known patient under their care (eg, direct importation, by requesting pharmacy compound a medicine)
- **Prescribe unapproved** medicines that have been manufactured in New Zealand or imported into New Zealand under section 29 of the Medicines Act 1981.

Pharmacists can:

- Supply an unapproved medicine to a patient on a doctor's prescription.
- Supply an approved medicine on prescription by any authorised prescriber for an unapproved indication
- CANNOT supply an unapproved medicine to a nurse prescriber for a particular patient.



What happens in pharmacy practice?



Medicinal Cannabis

Introduction

Medicinal Cannabis products refer to all forms of cannabis used to treat medical conditions or symptoms (e.g. severe epilepsy, MS and chronic pain).

Any doctor can prescribe a product listed below (these are unapproved medicines). A specialist recommendation and Ministerial approval are **NOT** required.

In New Zealand, all medicinal cannabis products (except Sati-vex) are **unapproved medicines**.

Three types of cannabis products exist:

1. *Cannabidiol (CBD)* | *Prescription Medicine Section 29* — [MSA s.2A definition](#)
 - Cannabinoid content must comprise > 98% CBD
 - Must not contain any other controlled drug or psychoactive substance
2. *Tetrahydrocannabinol (THC)* | *Class B1 Controlled Drug Section 29* — [MDR R. 22](#)
 - Requires ministry approval
3. *Sativex (CBD + THC)* | *Class B1 Controlled Drug Not Section 29*
 - Pharmaceutical grade cannabis based product
 - Approved medicine in NZ as an add on treatment in mod-severe MS
 - Since April 2020, any NZ medical practitioner can prescribe

Prescription for medicinal cannabis products

- Should specific the brand and prohibit any generic substitutions
- Must not be for a product in a form intended for smoking
- Must not be for a product meeting the definition of ‘food’ under the Food Act 2014
- Must not be for a product in a sterile dosage form (e.g: eye drops)

In addition:

- Prescriptions for CBD products must be for no more than a 3 months supply
- Prescription for any other medicinal cannabis product including Sativex must be handwritten on a controlled drug prescription form or signed barcoded NZePs prescription and be for no more than a 1 month supply.

Describe the medicinal cannabis scheme and how pharmacists may be involved

- The Govt wanted to make medicinal cannabis available for people with terminal illness or chronic pain. After the 1st of April 2020, the scheme came into effect and it aimed to improve access to quality medicinal cannabis products for patients. It is an unapproved medicine available on prescription from a doctor. Manufacturers must provide evidence of quality.

- Before the scheme, unapproved THC products and off label Sativex needed approval by the Ministry of Health for each patient. (On label Sativex didn't).
- After the scheme, doctors can prescribe off and on label Sativex. Other non sativex cannabis must be assessed by the agency as meeting minimum quality standards. But they still need ministry approval for prescribing unapproved THC products for a patient.
- Specialists can continue to prescribe unapproved THC products for existing patients that have approval (suppliers can continue to supply existing products for up to 6 months - this permission expired 1st October 2021 (was extended twice due to unavailability of products, but now as of 1st October, only medicinal cannabis products that have been verified can be supplied)

Date Verified	Product	Classification	Dose Form	Active Ingredient	Pack Sizes	Administration	Licence Holder
4 October 2021	SubDrops™ CBD100	Prescription Medicine	Sublingual Solution	Total THC (THC+THCA) <1 mg/mL Total CBD (CBD+CBDA) 100 mg/mL	30 mL	Sublingual, supplied with a 1 mL dropper with 0.25 mL volume markings	Helius Therapeutics Limited
4 October 2021	SubDrops™ CBD25	Prescription Medicine	Sublingual Solution	Total THC (THC+THCA) <1 mg/mL Total CBD (CBD+CBDA) 25 mg/mL	30 mL	Sublingual, supplied with a 1 mL dropper with 0.25 mL volume markings	Helius Therapeutics Limited
12 April 2021	Tilray FS Oral Solution THC 25	Controlled Drug B1	Solution, Oral	Total THC (THC+THCA) 26.6 mg / g (25 mg / mL) Total CBD (CBD+CBDA) < 0.5 mg/g	40 mL	Oral, 1 mL dropper with volume markings	CDC Pharmaceuticals Ltd
19 March 2021	Tilray FS Oral Solution THC 10: CBD 10	Controlled Drug B1	Solution, Oral	Total THC (THC+THCA) 10.6 mg/g Total CBD (CBD+CBDA) 10.6 mg/g	25 mL 40 mL	Oral, 1 mL dropper with volume markings	CDC Pharmaceuticals Ltd
5 March 2021	Tilray P Oral Solution CBD 100	Prescription Medicine	Solution, Oral	Total CBD (CBD+CBDA) 106.4 mg/g (100 mg/mL) Total THC (THC+THCA) <0.1 mg/g	25 mL 40 mL	Oral, 1 mL dropper with volume markings	CDC Pharmaceuticals Ltd
5 March 2021	Tilray P Oral Solution CBD 25	Prescription Medicine	Solution, Oral	Total CBD (CBD+CBDA) 26.6 mg/g (25 mg/mL) Total THC (THC+THCA) <0.1 mg/g	40 mL	Oral, 1 mL dropper with volume markings	CDC Pharmaceuticals Ltd

ADDITIONAL INFORMATION FOR PRESCRIPTION ITEMS

Introduction

In this section we will look into co-payments, legal prescription paperwork, dispensing prescription items and supply orders. Let's start with co-payments!

Co-Payments

Subsidy Requirements

Introduction

The Pharmaceutical Management Agency, better known as Pharmac, is a New Zealand Crown entity that decides, on behalf of District Health Boards, which medicines and pharmaceutical products are subsidised for use in the community and public hospitals. The subsidy a medication gets depends on the **GMS code** listed on a prescription.

PHARMAC Schedule

✓ = Fully Subsidised (patients only have to pay a co-payment of \$5)

* = Subsidised if dispensed as 3 or 6 months, as applicable (STAT)

Δ = 3 month supply may be dispensed at one time if endorsed “certified exemption” by the prescriber or pharmacist

Y	Youth (0-13 years)
J	Junior (14-17 years)
A	Adult (over 18 years)
Z	HUHC Holder
H	Hokianga resident enrolled with the HHET (see below)
O	Oral Contraceptive
1	CSC Card Holder
3	No CSC, and not Approved Prescriber
4	Approved Prescriber
NS	Not subsidised



A Note on Contraception

- Code ‘O’ if indicated for contraceptive use = 6 month’s supply and co-payment is \$5
- If not indicated for contraceptive use = 3 months and co-payment is respective to patient code

A Note on PHARMAC Funding

1. *Midwives* provide a fully publicly funded service so prescriptions from midwives may be coded A4 (for mother) or Y4 (baby).
2. *Nurse practitioners and prescribers* usually work as part of a publicly funded Primary Health Organisation or other District Board funded service. Prescriptions from these nurses may be coded A4 and are generally fully funded.
3. *Pharmacist prescribers* are generally part of a publicly funded primary health organisation or other District Health Board. The prescription patient code category is A4 (for adults), J4 for children over 13 years and Y4 for children 13 and under.
4. Medicines written by *optometrists* and *dentists* in **private/specialist** practices are coded A3, J3 or Y3 depending on the age of the patient. This generally means the medicine(s) will be funded but will carry a higher patient co-payment than a prescription from a GP.
5. *Veterinary* prescriptions are classified as NS

Pharmaceutical Subsidy Card (PhMS system)

A family unit who have received 20 subsidised pharmaceuticals dispensing that have attracted a co-payment in the year commencing 1 February to 31 January, can be issued with a PSC.

Service User Categories and Co-Payment Requirements

Note: HUHC = High Use Health Card

Youth (ages 0 to 13 years)* – Y Code

	HUHC Holder / Care Plus Service User	Service User Category	Maximum Pharmaceutical Co-payment	
			No PSC	With PSC
Approved Prescriber	Yes	Y4Z	\$0	\$0
	No	Y4	\$0	\$0
CSC Holder	Yes	Y1Z	\$0	\$0
	No	Y1	\$0	\$0
Neither of the above	Yes	Y3Z	\$0	\$0
	No	Y3	\$0	\$0

*The Service User must be an Eligible Person

Adult (ages 18 and above)* – A code

	HUHC Holder / Care Plus Service User	Service User Category	Maximum Pharmaceutical Co-payment	
			No PSC	With PSC
Approved Prescriber	Yes	A4Z	\$5	\$0
	No	A4	\$5	\$0
CSC Holder	Yes	A1Z	\$5	\$0
	No	A1	\$5	\$0
Neither of the above	Yes	A3Z	\$5	\$0
	No	A3	\$15	\$0
Oral Contraceptives	Yes	O	\$5	\$0
	No	O	\$5	\$0

*The Service User must be an Eligible Person

Junior (ages 14 to 17 years*) – J Code

	HUHC Holder / Care Plus Service User	Service User Category	Maximum Pharmaceutical Co-payment	
			No PSC	With PSC
Approved Prescriber	Yes	J4Z	\$5	\$0
	No	J4	\$5	\$0
CSC Holder	Yes	J1Z	\$5	\$0
	No	J1	\$5	\$0
Neither of the above	Yes	J3Z	\$5	\$0
	No	J3	\$10	\$0
Oral Contraceptives	Yes	O	\$5	\$0
	No	O	\$5	\$0

* The Service User must be an Eligible Person

Hokianga Ward of the Far North District* – H Code

	HUHC Holder / Care Plus Service User	Service User Category	Maximum Pharmaceutical Co-payment	
			No PSC	With PSC
Approved Prescriber	Yes	H4Z	\$0	\$0
	No	H4	\$0	\$0
CSC Holder	Yes	H1Z	\$0	\$0
	No	H1	\$0	\$0
Neither of the above	Yes	H3Z	\$0	\$0
	No	H3	\$0	\$0

* The Service User must be an Eligible Person

Legal Prescription Paperwork

Certified Repeat Prescriptions

Repeats

A Certified Repeat Copy (CRC) is a computer-generated record of a repeat Prescription Form. A CRC can be used for Dispensing a repeat item as an alternative to Dispensing from the original Prescription Form.

- Stat = Dispense all at once (▲)
- Non-Stat = Dispense at intervals

Holding Prescription Items

Holding or Splitting a Prescription Form

A **Certified True Copy** (annotated with the words “Certified True Copy”, signed and dated) of the Prescription Form must be made to ensure there is an original Prescription Form filed for each Dispensing.

All dispensing of controlled drugs must be annotated on the **original** triplicate Prescription Form (no Certified True Copies).

Owings of Prescription Items

Owings

Annotate the quantity dispensed and the quantity owed with the timeframe for collection for the owed item where the availability is known.

For owing of controlled drugs, the first dispensing (Class B only) can be claimed as two split dispensing within the *same* day. Subsequent repeats where insufficient stock is available must be claimed as one repeat and an “owe”.



Example

If a patient comes in with a script for morphine for 30 days ($10 + 10 + 10$), and you only have 5 in stock, you will dispense 5, then vary repeats ($5 + 5 + 10 + 10$), with the first repeat to be picked up within 5 days.

Data Retention

Data Type	Retention Period
Prescriptions <ul style="list-style-type: none">• Original physical copy⁶⁸<ul style="list-style-type: none">- Subsidised- Non-subsidised• Certified Repeat Copies (or daily dispensing /recording sheets)• Controlled Drug Prescriptions (top white copy)	<ul style="list-style-type: none">• 5 months (then sent to Sector Operations)• 3 years⁶⁸• 3 years⁶⁵• 4 years⁶⁹
Other Records <ul style="list-style-type: none">• Computer Records (for example PhMS)• Controlled Drugs Register• Incident Reports on Errors/Near Misses• Compliance Unit Dose Packaging Records• Compounding Job Sheets for Individual Service User• Batch Compounding Sheets• Extemporaneous Compounding Sheets	<ul style="list-style-type: none">• 10 years⁷⁰• 4 years⁶⁹• 10 years⁷⁰• 10 years⁷⁰• 10 year⁷⁰• 3 years⁷¹• 3 years⁷¹

Dispensing Prescription Items

Final Check



VALIDATING & CHECKING PRESCRIPTIONS School of Pharmacy

1. Does the prescription meet the legal requirements¹?

The information supplied on a prescription must be legible and indelible (cannot be erased or removed - written in pencil is NOT acceptable). It must include **ALL** of the following:

- Prescriber's usual signature in their own handwriting (*NOT being a facsimile or other stamp. Exception if received by secure fax or NZePS AND for a non-controlled drug or exempt Class C controlled drug AND a NZePS barcoded AND scanned and downloaded from NZePS at the pharmacy.*)
- Date on which the prescription was signed (*Must be dispensed within 6 months and only funded if within 3 months. Exceptions oral contraceptives must be dispensed within 9 months and class A or B controlled drugs must be dispensed within 7 days.*)

Prescriber details:

- Full name
- Physical work address, or postal address for those who do not have a place of work
- Telephone number
- Registration number (*Not a legal requirement. Needed for funding & auditing.*)

Patient details:

- Surname and each given name
- Physical address
- Date of birth if the prescription is for a child under 13 years for prescription medicines or 12 years for controlled² drug medicines.

Medicine details:

- Name
- Strength (*where appropriate*)
- Total amount of medicine OR total period of supply
- Dose and frequency of dose for internal medicines
- Method and frequency of use for external medicines
- Duration (*Max 3 month supply or 6 month for oral contraceptives. For controlled drugs, max varies from 3 days to 3 months depending on the class of the drug and prescriber's authority.*)

Prescriber Authority:

- Is the prescriber authorized to prescribe the medicine?
- Is the prescriber authorized to prescribe the duration written?

2. Is the prescription clinically appropriate?

Will it be safe for the person?

- Dose and frequency
 - Considering their age, weight, kidney and/or liver function.
- Interactions with other medicines (prescription, over-the-counter, complementary)
- Interactions with other medical conditions
- Contraindications
 - Considering allergy history, cultural practices, religious practices, adverse effect history, and pregnancy/ breastfeeding status.

Will it be effective for the person?

- Medicine
- Route
- Formulation
- Duration
- Affordable

3. Has the prescription been filled accurately?

Label – Does it match the original prescription?

- Prescriber details
- Patient details
- Medicine details
 - Has the quantity been calculated correctly (if applicable)?

Label – Does it include special use conditions (if applicable)?

- Expiry date
- Maximum dose
- Precautions
- Storage conditions

Label – Is it user friendly?

- Readable font size
- Plain language
- Clear instructions

Contents – Does it match the label AND the original prescription?

- Medicine
- Strength
- Formulation
- Quantity

Contents – Is the bulk stock or patient pack within its expiry date?

- Not expired

Annotations – Does it have the general prescription annotations?

- Pharmacy name and address (stamp)
- Date of dispensing (stamp & square)

Annotations - Is EACH item on the prescription annotated correctly?

- Annotation is close to the prescription item
- Quantity of the medicine dispensed
- Strength of the medicine dispensed (where appropriate)
- Prescription number (unique identifying number; square)
- Initials of individual dispensing³
- Initials of checking Pharmacist for completeness and accuracy

The name PHARMSI itself is the mnemonic code for the final safety check.

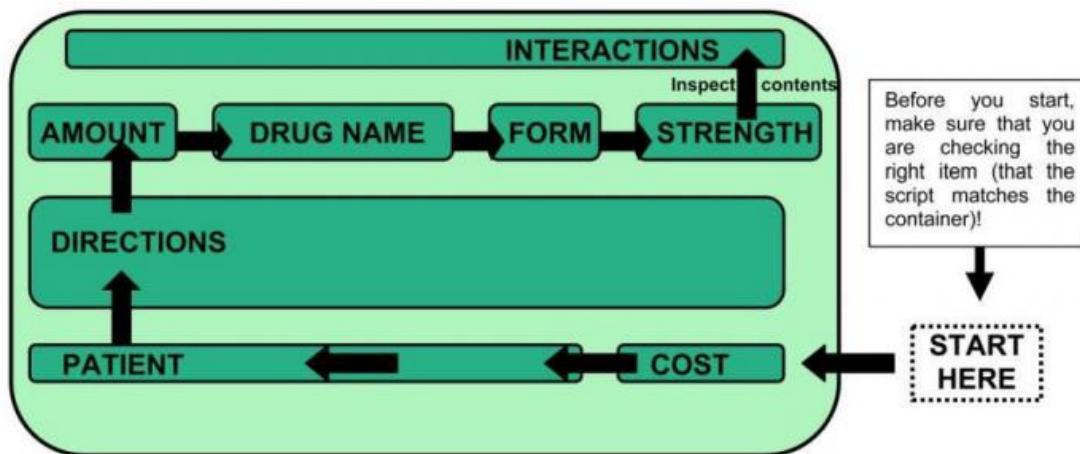
P	=	Patient
H	=	How to take = Directions
A	=	Amount total = Quantity
R	=	Route = Form
M	=	Medicine Name = Drug
S	=	Strength
I	=	Interactions (<i>and other notes</i>)

Do not drink alcohol during treatment and for at least 24 hours after finishing.

21 Metronidazole Tablets 200mg (MET)

Take ONE tablet THREE times daily with food until finished.

Ms Carla Dillon	\$5.00
16Feb21	Dr A Smith



References:

1. [Medicines Regulations 1984; Regulation 41](#)
2. [Misuse of Drugs Regulations 1977; Regulation 29](#)
3. New Zealand Health and Disability Pharmacy Service Standards 5.2.3(f)
4. [Fraser J, Fraser D. The “PHARMSI” Check. 4th ed, Oct 2015, Dunedin, NZ](#)
5. [Pharmacy Procedures Manual: A guide to payment and claiming, Version 8.0. Effective August 2019](#)

Dispensing Antibiotics

Oral Antibiotic Liquids

Where a prescriber has written a Prescription Item for a reconstitutable oral liquid antibiotic indicated in the Pharmaceutical Schedule, and the Dispensing of which would require the Provider to reconstitute another pack, the Provider should reduce the amount Dispensed to the quantity contained in a whole pack provided that the reduction in the amount Dispensed is **less than 10%** of the pack, and in the reasonable opinion of the Provider will not affect the efficacy of the course of treatment.

For Example: 5mL tds for 7 days = 105mL → Dispense 100mL

For Example: 10mL stat, 5mL tds for 7 days = 110mL → Dispense 110mL

Dispensing Eye Drops

Eye Drops

At least one original pack will be subsidised per month; **discard eye drops 30 days after first opening**.

Where the manufacturer states a longer than 30 day expiry date once the eye drops are unsealed, such as Poly-TearsTM, this data can be used to calculate the number of original packs to dispense.

Dispensing Insulin

Insulin Vials and Cartridges

At least one vial or one cartridge will be subsidised per month; **discard insulin vials or cartridges 30 days after first opening (intermediate acting insulin is 42 days)**

Dispensing Inhalers

Bronchodilator Asthma Inhalers

Prescribed PRN: up to **1,200 doses** (i.e. 6 inhalers if 200 actuations per inhaler) supplied every 3 months.

Prescribed Without PRN: supply quantity related to the total number of doses ordered.

Steroid Asthma Inhalers

If no specified definitive dosing and frequency instruction: only **one** inhaler in each **monthly** dispensing.

If dose and frequency of dose specified: supply maximum number of inhalers per prescriber's instructions.

Dispensing Compounded Preparations

Extemporaneously Compounded Preparations (ECP)

Must contain two or more subsidised component Pharmaceuticals listed in the Pharmaceutical Schedule of subsidy.

Labelling: "Caution: Not to be Taken" OR "External Use Only"

Supply Orders (PSO, RPSO, Bulk)

Types of Supply Orders

- Practitioner's supply order (PSO)
- Rural PSO
- Bulk Supply Order

	Types of Supply Orders		
	Practitioner's Supply Order (PSO)	Rural PSO	Bulk Supply Order
Definition	A written order made by a prescriber on a form supplied or approved by the MoH for the supply of community pharmaceuticals to the prescriber.	Designated rural practices may supply any community pharmaceutical on a PSO provided that all the funding requirements are met.	A written order for the supply of community pharmaceuticals on a form supplied or approved by the MoH.
Purpose	<p><i>PHARMAC Rule 1.3.2</i></p> <ul style="list-style-type: none"> • Emergency use • Teaching and demonstration purposes • For provision to certain patient groups where an individual prescription is not practicable 	<i>PHARMAC Rule 1.3.2</i>	<i>PHARMAC Rule 1.3.2</i>
Who can order	Any prescriber but must be within their scope of practice	<ul style="list-style-type: none"> • A prescriber who's normal practice is in a rural area • A locum prescriber for a rural prescriber 	<ul style="list-style-type: none"> • Registered private hospitals • For rest homes and other facilities that are not registered as hospitals, practitioners should use an individual prescription or PSO.
Special Requirements	Class B CD or buprenorphine must be written on a triplicate PSO controlled drug form supplied by MoH		
Quantity of Supply	Quantities as set out in the <u>Schedule</u>	1 month	1 month
Exceptions	<p>Pharmaceuticals will not be subsidised when supplied on a PSO to:</p> <ul style="list-style-type: none"> • Armed Forces or Prisons unless specified in Section B of the Schedule • Health NZ Hospitals or clinics, with the exception of antipsychotic injections for Health NZ Hospital mental health day clinics 	If the listing states 'only on a prescription' or the product requires Special Authority, then it is NOT funded on a rural PSO	<p>If the listing states 'only on a prescription', not on a 'BSO', has a retail pharmacy specialist restriction, or the pharmaceutical requires Special Authority, it is NOT funded on BSO — the only exception is ivermectin which can be obtained on a BSO with a valid Special Authority for one patient</p>

Note: If **unfunded medicines**, or funded medicines of **unfunded quantities** are being requested, pharmacists must apply their professional judgement to each NSS item being requested and ensures it complies with authorised request for medicines under s.25 of the MA 1981 and s.9 of the MDA 1977, and within the scope of practice of the practitioner.

Practitioner's Supply Orders (PSO)

Description

Prescribers can order medicines from a pharmacy that is **not** for a specific patient. PHARMAC will **fund** medicines on PSO's for those uses as long as:

1. *The medicine(s) is:*

- Ordered on a form supplied/approved by the MoH for the supply of community pharmaceuticals to the prescriber (see table below for forms for Class B drugs)
- For the purposes of emergency use, teaching and demonstration purposes, and for provision to certain patient groups where an individual prescription is not practicable.
- Identified in the PHARMAC Schedule as being subsidised on a PSO — see [Schedule List](#)
- In a written quantity dose that does exceed the amount indicated by PHARMAC

2. *The form is:*

- Is personally signed and dated by the prescriber
- Includes the prescriber's address
- Specifies the community pharmaceuticals and quantities
- Prescriptions are coded as 'PS'

Rural Practitioner's Supply Orders (RPSO's)

Description

Designated rural practices can order **any** product listed in the Pharmaceutical Schedule, provided that:

- All the funding requirements of the listing are met (rule 1.3.2) and
- The Prescriber's (or locum prescriber for that prescriber) normal practice is in a Rural Area,
- The quantities ordered are reasonable for up to 1 Month's supply under the conditions normally existing in the practice. DHBs decide what practices are designated rural.

If the listing states 'only on a prescription', or the product requires a Special Authority, then it is **not** funded on a rural PSO.

Bulk Supply Order

Description

Bulk Supply Order (BSO) means a written order for the supply of Community Pharmaceuticals, on a form supplied by the Ministry of Health, or approved by the Ministry of Health.

- **Registered private hospitals** can use a BSO for bulk supplies of funded medicines and related products. For rest homes and other facilities that are not registered as hospitals, practitioners should use an individual prescription or practitioners supply order (PSO).
- Any reasonable **monthly** quantity of any pharmaceutical, provided all requirements in the listing are met.
- If the listing states 'only on a prescription', 'not on a BSO', has a Retail Pharmacy Specialist restriction, or the pharmaceutical requires a Special Authority, it is **not** funded on a BSO.
- The **only exception** to this is ivermectin which can be obtained on a BSO with a valid Special Authority for one patient.

What if unfunded medicines or funded medicines in unfunded quantities are being requested?

In practise, pharmacists must **apply their professional judgement to each NSS item** being requested and ensure it complies with authorised request for medicines under [Section 25 of the Medicines Act 1981](#) and [Section 9 of the Misuse of Drugs Act 1977](#) and within the scope of practice of the practitioner.

GENERAL SALE MEDICINES

Introduction

The medicines—also called 'general sales list (GSL) medicines'—are also available for self-selection in pharmacies. General sale medicines are taken for common, easily recognised ailments which usually last around 2–3 days. These medicines cause few troublesome side effects in normal use.

Complementary & Alternative Medicines

Complementary Alternative Medicines (CAM)

The term complementary and alternative medicine (CAM) is usually used to describe a medical product or practice that is not standard medical care. When this is used together with conventional medicine, it's considered complementary and when it is used instead of conventional medicine, it's considered alternative. Complementary and alternative medicine are **not** required to meet pharmaceutical quality standards.

We need to be aware of cultural beliefs and practices, and how these may impact medication. As pharmacists, we are expected to provide accurate and unbiased information to patients. If there is no current evidence of efficacy, we must ensure patients are informed about the degree to which treatment has been evaluated (and therefore must advise where scientific support is lacking).

Note: The definition of a medicine is as follows: — [M.A s.3](#)

A medicine is a substance or article that is sold/supplied for administering to human beings for a therapeutic purpose AND

- Achieves (or is likely to) its intended action by pharmacological, immunological, or metabolic means.
- Any product making a therapeutic claim

Traditional Medicines

Alternative Medical Systems	Māori (Rongoā), Ayurveda, Chinese, Native American, Aboriginal, African, Middle Eastern, Tibetan, Central and South American cultures, Homeopathy, Naturopathy
Mind-Body Interventions	Cognitive-behavioral approaches, meditation, hypnosis, dance, music, art therapy, prayer, mental healing
Biological Based Therapies	Dietary supplements, herbs, orthomolecular (varying concentrations of chemicals, such as, magnesium, melatonin, and mega-doses of vitamins), individual biological therapies (use of laetrile, shark cartilage, bee pollen).
Manipulative And Body-Based Methods	Chiropractic, osteopathic manipulation, massage
Energy Therapies	Qi gong, Reiki, therapeutic touch, bioelectromagnetic-based therapies (pulsed fields, magnetic fields, or alternating current or direct current fields)

Herbal Remedies

Definition - M.A.s.2

- Herbal remedy means a medicine (not being or containing a prescription medicine, or a restricted medicine, or a pharmacy-only medicine) consisting of—
 - (a) any substance produced by subjecting a plant to drying, crushing, or any other similar process; or
 - (b) a mixture comprising 2 or more such substances only; or
 - (c) a mixture comprising 1 or more such substances with water or ethyl alcohol or any inert substance

Dietary Supplements

Dietary Supplement Regulations 1985 R.2A

- A dietary supplement includes amino acids, edible substance, herbs, minerals, synthetic nutrients, vitamins.
 - Note that some minerals & vitamin have a maximum quantity allowed in dietary supplements. Above these limits, these are classified as medicines
- These are sold:
 - By itself **or** in a mixture
 - In a controlled dosage form (liquid, powder, tablet)
- Intentions:
 - To be orally ingested
 - To supplement that normally derived from food

Note: Reliable sources of information include NZF, National centre for CAM, Medicines Complete, Office of Dietary Supplements

ADVERTISING

Legislation

[**PCNZ PSNZ Advertising Guidelines**](#)

[**PCNZ CAM Statement**](#)

[**PCNZ Code of Ethics 2018**](#)

[**Pharmacy Law Guidebook**](#)

[**Dietary Supplements Regulations 1985**](#)

[**Fair Trading Act 1986**](#)

[**Medicines Act 1981**](#)

[**Medicines Regulations 1984**](#)

[**Misuse of Drugs Regulations 1977**](#)

Introduction

Advertising is the attempt to influence the buying behaviour of customers or clients with a persuasive selling message about products and/or services. There are many different types of advertising. Some common advertising methods include online advertising, newspaper advertising, direct mail, TV, radio, vehicle advertising etc.

Medical advertisements need to be regulated as medicines are not ordinary articles of commerce. The sale of medicine needs to be regulated to ensure patient safety and appropriate use of medicine.

Legal Definitions of Advertisement — [M.A s.56](#)

1. *Advertisement*: any words (written, printed, spoken) and any pictorial representation or design, used to promote the sale of medicines/medical devices/method of treatment and includes any trade circular, label, advertisement in a trade journal and **advertising** and **advertised** have corresponding meanings.

2. *Medical Advertisement*: an advertisement relating, or likely to cause any person to believe that it relates to any medicine/medical device/ingredient or component thereof or to any method of treatment

General PCNZ & PSNZ Advertising Guidelines — [PCNZ PSNZ Advertising Guidelines](#)

Restrictions on Advertisement - [MA s.57](#)

When advertising or promoting any medicine, complementary therapy, herbal remedy, service or intervention or other healthcare product, pharmacists are expected to exercise professional judgement in order to maintain the professional image of pharmacy.

The Pharmacy Council and Pharmaceutical Society of NZ provide a set advertising guidelines. These guidelines include a range of legal requirements, codes and practice standards that pharmacists must comply with when promoting or advertising services or medicines.

- Focus must be on benefits of product/service rather than price
- Should be displayed where staff can supervise selection of the medicine
- Medicine quantity must be appropriate to the clinical needs of patients (i.e. not excessive amounts such as multi-buy offers, competitions (loyalty systems), 2 for 1 deals).
 - No incentives for buying additional quantities
 - Only smaller packs should be advertised
 - Should not be offered for sale via internet
- Comparative pricing of medicines, pharmacy services, or prescription charges is **not** permitted - [PCNZ Ad Guidelines 12](#)
 - It is acceptable for an advertisement to display the selling price or to state “our price”
 - Not acceptable to state “was \$xx”, “elsewhere \$xx” or “normal price” or “30% reduction” or discount on normal price as a comparison.
 - [PCNZ Ad Guidelines 6](#) reinforces that the focus of the ad must be on the benefits of the product or service rather than its price.
- Advertising of controlled drugs is restricted to practitioners, dentists, and pharmacists.
- The Medicine Ad cannot state to the public that the medicine is no habit forming - [MA s.57\(1\)\(g\)](#)

Complementary & Alternative Medicines Advertising

Sales of Herbal Remedies — [M.A s.28](#)

- Does not have to be registered to be sold — any person can manufacture, pack, and label any herbal remedy to sell or supply
- **No** advertisements are allowed! — There are no exemptions in the Medicines Act for advertising of “natural health products”, products traditionally used, homeopathic products, rongoa, or any other “complementary health care products”.
- No written recommendation for their use

Sales of Dietary Supplements — [M.A s.4](#) & [Dietary Supplement Regulations 1985 R.11](#)

No dietary supplement or package or container containing a dietary supplement shall be advertised or labelled with a statement relating to any of the following matters. i.e. a therapeutic claim **can't** be made

- a) treating or preventing disease:
- b) diagnosing disease or ascertaining the existence, degree, or extent of a physiological condition:
- c) altering the shape, structure, size, or weight of the human body:
- d) otherwise preventing or interfering with the normal operation of a physiological function, whether permanently or temporarily, and whether by way of terminating or reducing or postponing, or increasing or accelerating, the operation of that function, or in any other way.

However, a **health** claim which *supports* physiological function can be made:

- *Examples:* Aids healthy digestion, Helps normal bowel regularity, Support joint mobility and flexibility, For overall health and well-being, Supports the cardiovascular system

ETHICS IN PHARMACY PRACTICE

Relevant Legislations - [Pharmacy Competency Standards](#)

Code of Ethics

Principles - [Pharmacy Code of Ethics](#)

1. Make the health and well-being of the patient your first priority.
2. Promote patient self-determination, respect patients' rights, autonomy and freedom of choice.
3. Use your professional judgement in the interests of patients and the public and promote family, whanau and community health.
4. Show respect for others and exercise your duties with professionalism.
5. Actively seek and apply contemporary pharmacy knowledge and skills to ensure a high standard of professional competence.
6. Act in a manner that promotes public trust and confidence in pharmacists and enhances the reputation of the profession.
7. Practise in a manner that does not compromise your professional independence, judgement or integrity, or that of other pharmacists.

Code of Rights

Principles - [HDC Consumers Code of Rights](#)

- Right 1 - The right to be treated with respect.
- Right 2 - The right to freedom from discrimination, coercion, harassment, and exploitation.
- Right 3 - The right to dignity and independence.
- Right 4 - The right to services of an appropriate standard.
- Right 5 - The right to effective communication.
- Right 6 - The right to be fully informed.
- Right 7 - The right to make an informed choice and give informed consent.
- Right 8 - The right to support.
- Right 9 - Rights in respect of teaching or research.
- Right 10 - The right to complain.

Health Information Privacy Code (HIPC)

Principles — [Health Information Privacy Code 1994 \(HIPC\)](#)

Rule 1: Purpose of collection of health information

- Describes that health information must not be collected by agencies unless it is necessary (e.g. legal reasons, a specific purpose) or it doesn't require the individual's identifying information.

Rule 2: Source of health information

- Information collected by a health agency must be from the individual concerned, except if the agency believes it is not applicable to do so in the specific situation.

Rule 3: Collection of health information from individual

- If information is to be collected, the individual needs to be aware of this, plus why it is being collected, who is it going to, is it voluntary or mandatory, what the consequences would be if they don't provide that information and who will have access to this information.

Rule 4: Manner of collection of health information

- Health information must only be collected in a manner that is lawful, fair and not intrusive.

Rule 5: Storage and security of health information

- Information held by a health agency must be protected against loss, access, use, modification, disclosure, or other misuse that is not authorised by the agency.

Rule 6: Access to personal health information

- Individuals are entitled to receiving their health information upon request.

Rule 7: Correction of health information

- Individuals are entitled to request correction of their health information.

Rule 8: Accuracy etc of health information to be checked before use or disclosure

- Health agencies must check the validity of the health information before disclosing it to the approved people.

Rule 9: Retention of health information

- Health information must not be kept by health agencies for longer than is required.

Rule 10: Limits on use of health information

- Health agencies may only disclose health information to approved people or on certain reasonable grounds (e.g. concern for safety)

Rule 11: Limits on disclosure of health information

- Health information must not be disclosed unless the agency believes it is suitable for a specific case

Rule 12: Disclosure of health information outside New Zealand

- A health agency may only disclose information to a foreign person or entity under certain conditions (e.g. individual is dead)

Rule 13: Unique identifiers

- Health agencies may assign individuals with a specific unique identifier to carry out certain functions more efficiently.

Legal Issues In Consent

Relevant Legislations

- Substance Addiction (Compulsory Assessment and Treatment) Act 2017
- Mental Health (Compulsory Assessment and Treatment Act) 1992

Minors — when can children consent?

Care of Children Act 2004

- From age 16, can consent, or refuse to consent, to blood donation and medical, surgical, or dental procedures
- Younger, if the child is married or living in a de facto relationship (“mature minors”)
- Specifically allows female children of any age to consent to, or refuse, pregnancy termination (abortion).



PLUS

The Code and common law emphasise that children younger than 16 **can** provide valid consent depending on the child and the treatment decision (a leading common law case is about contraception).

Adults

- Treatment without consent
- Exceptions for emergencies, unreasonable to delay (necessity)
- Exception under Right 7(4) of the Code

Under Protection of Personal and Property Rights Act 1988:

- Treatment with the permission of others
- Enduring power of attorney
- Court appointed welfare guardian
- Court order

Under Mental Health (Compulsory Assessment and Treatment) Act 1992

Sometimes patients are not permitted to consent or refuse (e.g. substance addition or mental health)

Health Practitioners Competence Assurance Act (HPCAA)

Introduction

Prior to 2003, each profession (medical, nursing and pharmacy councils) was supplied with their own acts. However this was problematic for many reasons, to name a few:

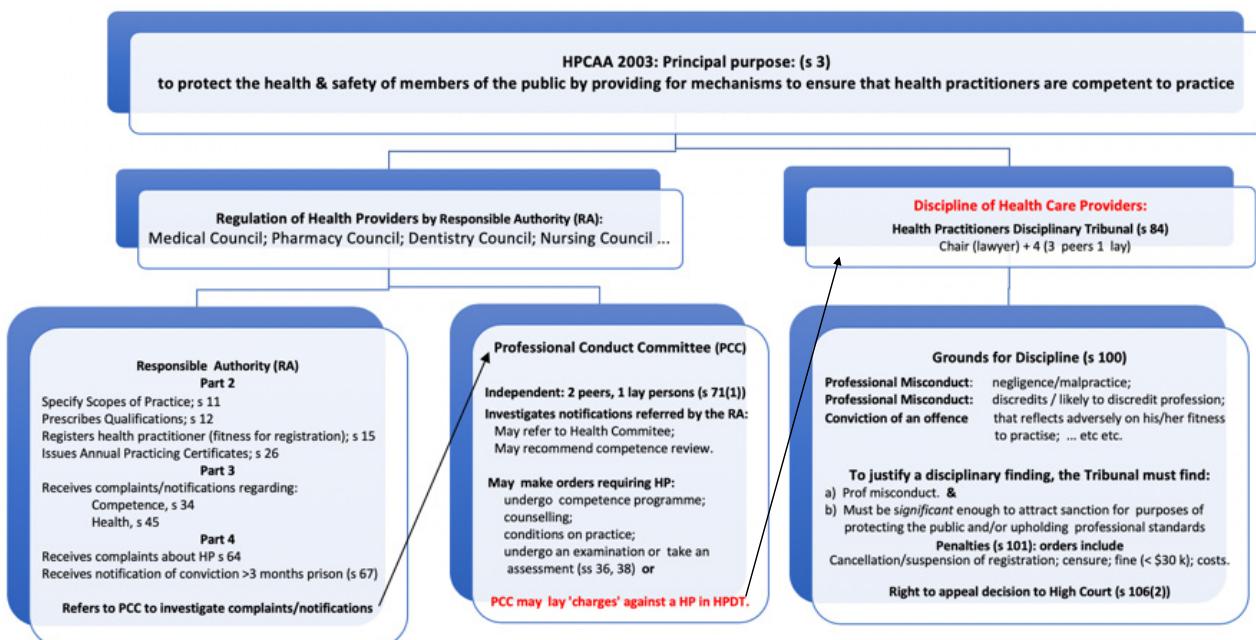
1. Consequences for the same mistake would be awarded differently depending on the profession
2. The process was not transparent, criminal conduct and outraging behaviours were not appropriately responded to and many things would be hidden.
3. Professions would look after their own.

In order to protect the health and safety of the members of the public and thus resolve the complaints, reporting and investigation process of adverse medical events — the HPCAA act aimed to bring all health care professionals under one act.

Components of the Act

The act consists of two parts, which are respectively subdivided further.

1. *The Regulation Part: promotes and encourages good practice*
 - a. The Responsible Authority (RA)
 - b. Professional Conduct Committee (PCC)
2. *The Discipline Part: puts people in their place when they don't.*
 - a. The Health Practitioners Disciplinary Tribunal (HPDT)



1. Regulation Part of the HPCAA Act

a. The Responsible Authority (RA) — e.g. Pharmacy Council

- The Pharmacy Council is our responsible authority. It specifies the following:
- Our scope of practice, our prescribing qualifications, registers APCs as well as HPs
- Receives complaints/notifications from the public regarding competence and health as well as if HP has been convicted to prison for more than 3 months. In the event of the latter, a referral to the PCC is made to investigate those complaints/notifications.

b. Professional Conduct Committee (PCC)

Following the complaint/notification investigation submitted by the RA. The PCC may:

- Refer to the Health Committee to recommend a competence review
- May make orders that require the HP to undergo counselling, competence programme
- May choose to lay charges against the HP in the HPDT (Health Practitioners Disciplinary Tribunal). This is where we engage the second part of the act: the discipline.
- This way the HPCAA Act allows a process to happen before serious harm occurs due to poor practice.

NOTIFICATION – PHARMACY COUNCIL (PC)

Reason to believe a HCP may pose a risk of harm by practicing below required standard of competence (s 34 HPCAA)

- Health Practitioner may give written notice to the registrar of the PC detailing reasons for belief;
- HP who gives notice in good faith protected;
- PC must assess – may refer notice to the PCC;
- After investigating the PCC must provide recommendations, eg
 - that the PC reviews persons competence (s 36(2),
 - the PC counsel the practitioner;
 - no further steps be taken;
 - a charge be laid against the HP in the HPDT (s 80(3).

Reason to believe a HCP is unable to perform required functions due to a mental or physical condition (s 45)

e.g. substance abuse disorders; mood disorders; dementia; anxiety disorders ...

- HP or an employer must give written notice to the PC;
- HP who gives notice in good faith is protected (defamation);
- PC may require HP to submit to medical examination (s 49);
- If determine HP unable to perform function – may suspend;
- If satisfied the person can perform functions, but only if conditions are imposed – may order those conditions be included in HCP scope of practice (s 50(4))

2. Discipline Part of the HPCAA Act

a. The Health Practitioners Disciplinary Tribunal (HPDT)

There are certain offences/charges that can be laid. People can be charged with:

- Professional misconduct in the context negligence/malpractice
- Professional misconduct in the context of discrediting the profession
- HP has been convicted of an offence that reflects adversely on their fitness to practice.

However, a breach finding is not determinative, simple negligence or carelessness is not sufficient to justify a disciplinary finding – given the Code of Rights and the much higher threshold of the HPDT.

To justify an action worth of disciplinary consequences, the tribunal needs to find:

1. The professional misconduct +
2. That misconduct must be significant enough to attract sanctions for the purpose of protecting the public.

The outcome of the Disciplinary Tribunal:

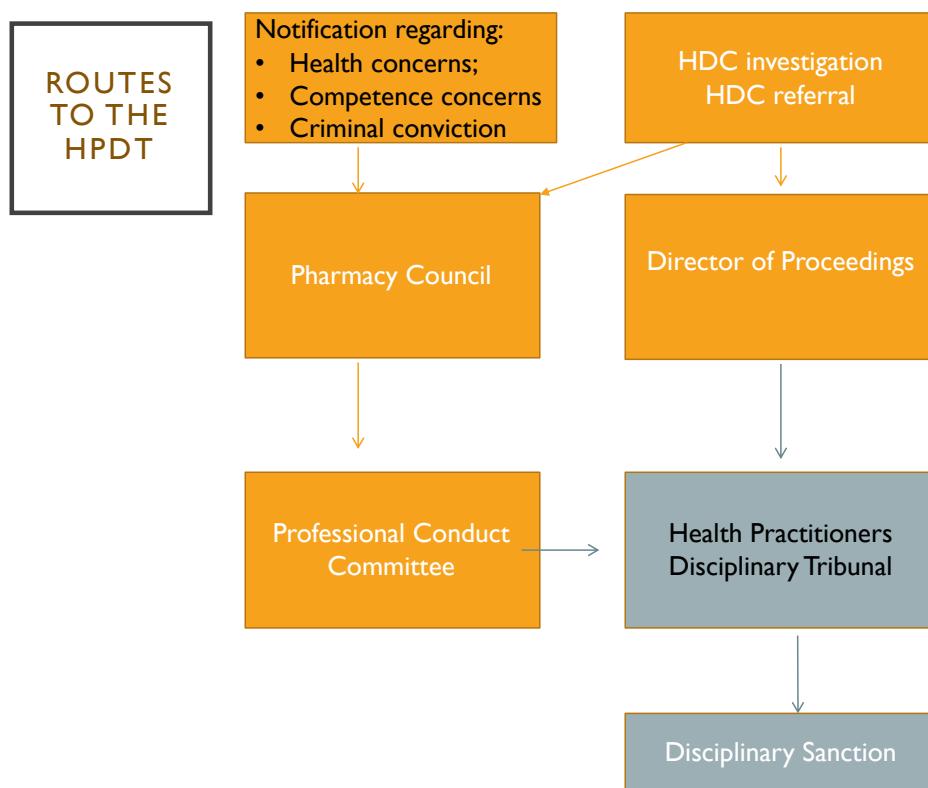
1. Cancelling or suspension of registration
2. Censure
3. Fine of more than 30k
4. Paying of partial or full hearing costs

Summary

So how does a practitioner end up at the Health Practitioners Disciplinary Tribunal? Well there are 2 routes, both beginning at a notification regarding health concerns, competence concerns, criminal conviction.

1. PC (RA) is notified, goes to PCC which goes to HPDT which can result in discipline.
2. Person complaining goes to HDC (health & disability commissioner), which goes to director of proceedings which goes to HPDT.

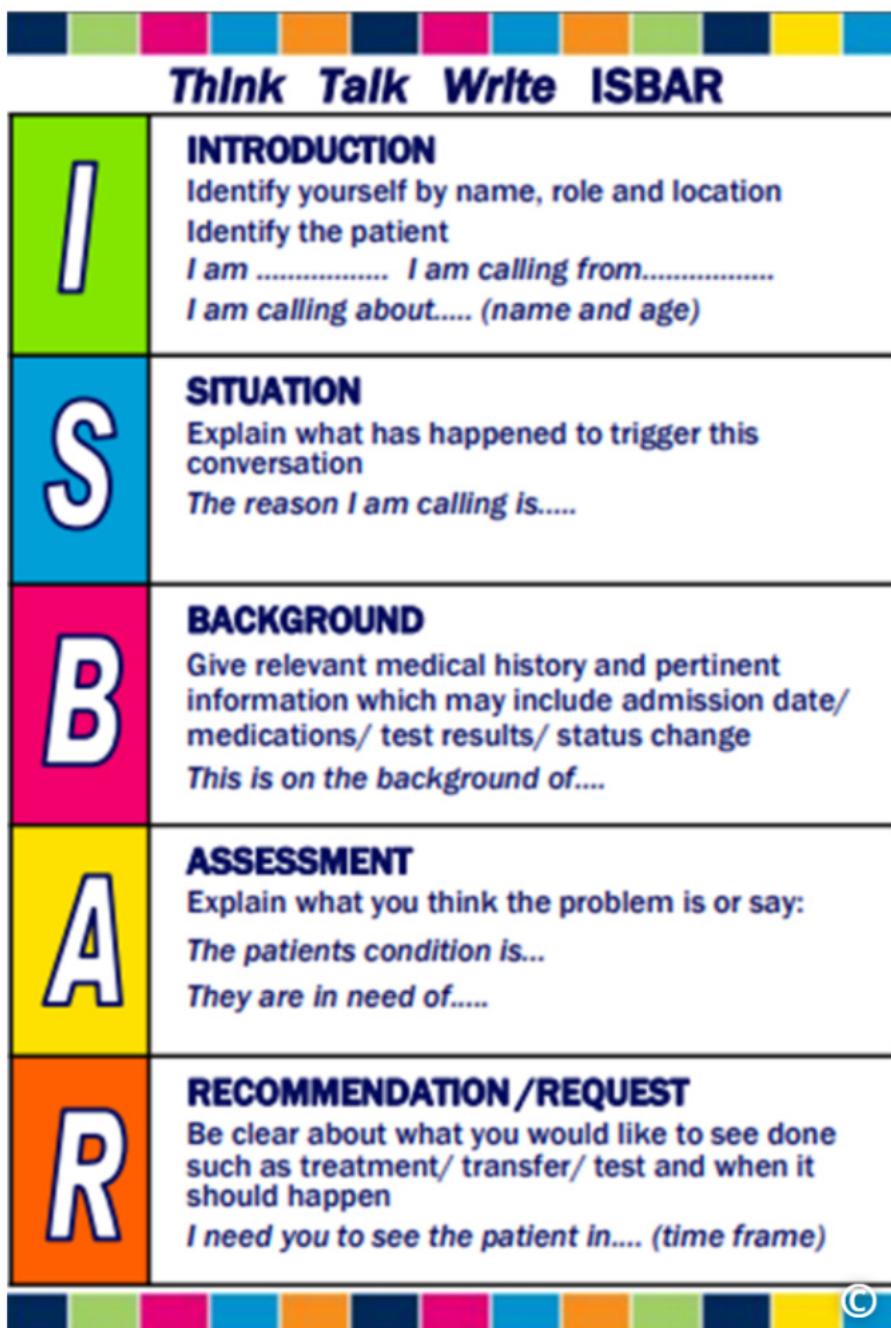
When a health practitioner is convicted of any offence carrying a possible penalty of imprisonment for 3 months or longer, a Court Registrar must send a notice of conviction to the PC (part of the HPCA act). PC must refer the notice to a professional conduct committee.



Contacting HCPs - ISBAR

ISBAR

- Identify: identify yourself and what you are calling about
- Situation: What is going on with the prescription?
- Background: The context, what background information is available that is relevant?
- Assessment: Analysis and consideration of the options
- Recommendation: An agreement on what needs to be done, by whom and when



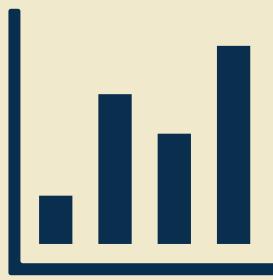
End of Life Choice Bill

Meaning of a person who is eligible for assisted dying (must meet all of the following)

1. Aged 18+
2. Is a NZ Citizen/Permanent Resident
3. Suffers from a terminal illness that is likely to end the person's life within 6 months
4. Is in an advanced state of irreversible decline in physical capability
5. Experiences unbearable suffering that cannot be relieved in a manner that is considered tolerable to the person
6. Is competent to make an informed decision about assisted dying

A person is not eligible for assisted dying if

1. They are suffering from any form of mental disorder/mental illness
2. Have a disability of any age
3. Are of advanced age



CHAPTER 22

PHARMACY BUSINESS



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Chapter 22

Pharmacy Business

Informatics

Assessable Tasks Informatics

1. Define Big Data in healthcare, health informatics and digital health
2. Apply big data, health informatics, digital health to a healthcare context i.e. give some examples of these in healthcare (especially for pharmacy)
3. Describe who can benefit from the use of big data, digital health, health informatics in healthcare
4. Describe some challenges to using Big Data in healthcare, health informatics and digital health
5. Identify aspects of big data, health informatics and digital health that could be applied in the future

Term	Big Data in Healthcare	Integrated Data	Health Informatics	Digital Health
Definition	A term used to describe large amounts of data of patient records by the adoption of digital technologies.	Process of combining data from different sources into a single, unified view.	Describes the acquisition, storage, retrieval and use of healthcare information to foster better collaboration among a patient's various healthcare providers.	The use of digital technologies and accessible data to improve health and wellness
Application in Healthcare (e.g. pharmacy)	<p>Large amounts of data can be analysed (which would otherwise be too complex for traditional technologies e.g. paper) to determine insights and allow strategic planning for better decisions.</p> <ul style="list-style-type: none"> • Improve healthcare performance and quality of care • More efficiency and accuracy with diagnoses and treatments. • Increase rate of new drug development can be discovered 	<p>Clinicians can now have access to a complete patient electronic record across different health care system, improving provision/delivery of health care services.</p> <p>Integrated data can also improve socioeconomic outcomes in NZ by guiding investments where they are needed the most (e.g. rheumatic fever in high risk group)</p>	<p>Use of AI</p> <ul style="list-style-type: none"> • Dispensing robots • Patient Management Systems 	<ul style="list-style-type: none"> • Telehealth • Patient portals • Hira • COVID Tracer App • e-prescriptions • INR Systems • Other diagnostic health tools
Benefits	Analysis can provide reference to future business strategies	Provide better healthcare by being able to seamlessly search across many healthcare systems to retrieve complete patient background	Provide better healthcare by using collective of information specific to the patient	<ul style="list-style-type: none"> • Patients can access their own health records (reduced health care burden) • Reduce error when transferring point of care • Allow easy communication between HCP
Challenges	<ul style="list-style-type: none"> • Retrieval of relevant data • High volume of data 	<ul style="list-style-type: none"> • Breach of patient privacy • Is it necessary? 	<ul style="list-style-type: none"> • Expensive • People may not like change • Susceptibility to network hackers • Unable to retrieve data 	<ul style="list-style-type: none"> • Safety & Privacy issues • Overwhelming amounts of personal data that is easily accessible can stress patient • Patients may prefer being seen by a human than a AI (e.g. can cause health inequities in Māori/Pasifika)
Future Perspective				<ul style="list-style-type: none"> • Allows pharmacists to focus more on patient interaction • Be able to provide more services in pharmacy • Allow treatments to be tailored and specific to individuals • Improve accessibility

Big Data in Health

Big data describes the vast amount of information collected using digital means, that is otherwise too large and complex for traditional data-processing technologies to handle. Data is stored and analysed for strategic planning and decision-making to improve healthcare via:

- Predicting and preventing events by analysing patterns and trends
- Driving innovation by identifying inconsistencies and gaps
- Reducing costs, and improving treatment efficacy by gaining clinical insight

Note that it is not the amount of data that is important, it is what businesses do with the data and how smartly it is managed that is.

Sources of Big Data

Patient portals, research studies, electronic health records, wearable devices, search engines, staffing schedules

Uses of Big Data

1. Product Development

Allows research teams to find useful data much faster and more efficiently (e.g. data collected and organized using search engines), therefore reducing the time and cost needed to develop the product and get it to market.

2. Driving Innovation (biggest healthcare big data use)

Analysis recognises inconsistencies and patterns which drives new drug development and platforms to further improve the quality of healthcare.

3. Predicting Analytics in Healthcare

Insight into clinical data allows prediction of trends and patterns, allowing:

a) Improved Patient Outcomes

- HCPs will be more effective and accurate when diagnosis/treating conditions
- Prevention of future events i.e. epidemics
- Reduction of treatment cost

b) Operational Efficiency

Big data such as workforce data means that healthcare organisations such as hospitals and pharma companies can improve the employee output. For example, managers can redesign workflows to be more efficient and redirect resources to where they are most needed

Integrated Data

Data integration is the process of combining/drawing data from different sources into a single, unified view to provide a range of different services to New Zealand.

- Allows ease access to a particular area of interest which helps to e.g. educate, quickly identify treatment guidelines, statistics etc.

• *Examples:* StatsNZ, HealthOne, Dynamed

Benefits of Integrated Data

From a general point of view:

- Improves **socioeconomic outcomes** in NZ (by identifying where improvement is needed and where investment matters the most)

Improves healthcare provision

With the integration of data in healthcare, clinicians can now benefit from the ability to seamlessly search across healthcare systems to get the whole picture of an individual **patient's electronic health records**. This could include:

1. Allergies
2. End-of-life decisions
3. Medications
4. Medical history

Health problems that can be investigated using NZ-integrated data

- Vaccination records / reminders: vaccination rates
- RF risks in high-risk groups
- Addiction rates
- Health literacy
- Adherence: Regional prescription fill rates
- Scope of practice for pharmacists
- Public health prevention

Health data that pharmacy could benefit from

- Statistics on common ailments e.g. most wanted/best products
- Patients submitting scripts to multiple pharmacies
- Population trends to ensure better forecasting: minimise supply/demand issues
- Patient demands can influence appropriate staffing
- Complete patient background and records
- Medicines usage trends

Health Informatics

Health informatics is a term that describes the acquisition, storage, retrieval and use of healthcare information to foster better collaboration among a patient's various healthcare providers. Health informatics plays a critical role in the push toward healthcare reform.

The integration of computer science, health science, and healthcare to incorporate/recycling information into platforms that allow for integrated care and easy handling by the user.

Examples

- COVID tracer app
- Electronic records
- Healthcare apps
- Telehealth

Pharmacy Informatics

Pharmacy Informatics is a subset of health informatics that leverages clinical expertise and information technology knowledge to improve medication management processes and drug administration safety.

Pharmacy informatics can include various aspects of medication management, from a drug use review, to the use of barcoding technology during product dispensing, to the development of alert systems to improve prescribing and dispensing of medications.

Examples:

- Data, information, and knowledge management
- Information and knowledge delivery
- Practice analytics
- Applied clinical informatics
- Leadership and management of change

AIs in Healthcare

- AI assisted surgeries
- Virtual Nursing Assistants
- AI-guided clinical judgment and diagnosis for clinicians
- AI automated workflow and administrative tasks
- AI sped image analysis
- Dispensing or blister-packing robots
- BenevolentAI aided in discovering which drugs would work well in stopping the progression of COVID. In this case, it was discovered that Baricitinib was a strong candidate

AI in COVID pandemic

- Contactless screening Chatbots and contactless screening of COVID-19 symptoms and to answer questions from the public e.g Clevy.io
- COVID-tracing app: tracking
- e-prescriptions with barcode
- Data analysis to provide stats on: immunisations, PCR/RAT testing & follow up checks

Digital Health & Health Technology

Digital health describes the use of information and digital communications technologies to help manage an individual's health and wellbeing. Such an intervention helps prevent disease, monitor patients and manage chronic conditions - in turn lowering the cost of healthcare provision and making medicines more tailored to individual needs.

Examples

- Wearable gadgets e.g. GoogleFit, Apple Watch
- Ingestible sensors
- Mobile health apps e.g. weight loss trackers, period trackers
- Robotic carers
- Electronic Records
- Artificial intelligence (AI)

Digital Health in NZ

- Telehealth
- Patient portals: toniq, RxOne, HealthOne, Eclair, Testsafe?
- Digital health portfolio reports
- eMedicine
- Assessment framework for safe e-mental health tools

Hira

Hira is a health information system that aims to act as the connector of people's health and wellbeing information – like the medicines they are on, the vaccinations they have had, and their lab results. It will enable information to be pulled from different systems to create a single view.

What does it address?

- Currently, health and wellbeing information is stored in different places, in different formats, and can be difficult to access and use effectively.
- People and whānau often have to repeat their health information and history a number of times to different service providers and cannot easily access that information themselves.
- Health care providers can't always get a full picture of a person's health to enable them and the consumer to make the best treatment decisions.
- It can be difficult for policy makers, researchers and planners to get the latest information to base their advice and thinking on.

How could pharmacy benefit from Hira?

- Hira will enable health information to be delivered to all New Zealanders where and when they need it, and allow people to have better access to their own health information. (Allow patients to take initiative of their own health)
- Health care providers will be better supported to make care decisions, because they will have access to a person's virtual health record, when they need it.
- The digital health industry will have opportunities to use information and services in new and innovative ways, and to trial new approaches to delivering health services.
- Better information will help policy makers, planners and researchers to improve equity and system performance.

How is Hira different from a patient portal?

- Information on Hira can be accessed both by patients and by health care professionals.
- Hira is being co-designed with Māori in a way that embraces te ao Māori ideals and practices.

Benefits of Digital Health

- Fast responses
- Integrated model of care through multidisciplinary workforce
- Automatic notification
- Easy access to secure information
- Increased accessibility
- Reduced human error
- Manage chronic conditions

Digital Healthcare in 2027

- Patient: telehealth, digital platform of avatars that can access patient health, digital monitoring alerts and reminders, chatbots.
- HCP: Automatic systems, automatic appointment management and changes, vocal narration which automatically translates to words on the patient profile and is visible to the whole care team, connectedness to the whole healthcare team, authorisation of medicine changes through AI software, AI algorithms to monitor patients, virtual clinics, relay from wearable devices of patients

IoMT

The Internet of Medical Things (IoMT) is the network of **Internet-connected medical devices**, hardware infrastructure, and software applications used to connect healthcare information technology. IoMT allows wireless and remote devices to securely communicate over the Internet to allow rapid and flexible analysis of medical data.

Advantages of Digital Health/IoMT

- *Improved Efficiency*: digital devices are more accurate due to reduced human error
- *Low Per-Patient Cost*: allows patients to connect with physicians remotely, cutting down costs of visits
- *Fast-Per-Patient Implementation*: fitness devices and sensors integrated with mobile apps allows patients to quickly monitor their health status by saving a lot of time and allowing fast per-patient implementation.

Challenges associated with Digital Health/IoMT

- *Standardization Issues* - many people who manufacture medical devices are looking to gain scalability and minimize the time consumed - however it is difficult to do that with IoMT devices. Currently, only 51% of medical device manufacturers and 44% of healthcare organizations follow the set FDA rules and guidelines which affects the overall efficiency of IoMT.
- *Regulatory Challenges* - new medical devices or updates must be cleared by the FDA. Currently, the collection and storage of patient data are taken care of by regulations like HIPAA but new flexible laws for medical devices are the need of the hour.
- *High Infrastructure Cost* - IoMT aims at reducing the overall healthcare costs but the implementation of the same costs a lot. Hardware costs, building an app, storage and maintenance costs require a high initial investment which acts as a barrier for IoMT
- *Security Vulnerabilities* - Patient data is prone to cyber-attacks and various data breaches. The healthcare industry encounters 340% more security issues than any other industry and it's 200% more susceptible to data theft.

The strain on existing networks - many healthcare institutions don't have an advanced and robust enough network to integrate IoMT devices and use them. They need to emerge in order to make use of it.

How could AI cause health inequities?

Different groups require different needs from the healthcare system (equity). AI takes away a lot of factors that promote good health in particular groups.

For example, in Maori and Pacifica groups, connectedness and being present in the environment make a huge difference in the healthcare they receive. Therefore, if AI takes away this in-person connection, the healthcare system will not work for some groups, thereby promoting health inequities.

Quality Assurance & Improvement

Assessable Tasks Quality Improvement

1. Define and differentiate Quality Assurance (QA) and Quality Improvement (QI)
2. Identify audits that are used in QA and QI processes
3. Identify examples of Quality Improvement tool
4. Identify a QA/QI tool specific to professional development for life-long learning
5. Describe the roles that pharmacists have as leaders, managers and practitioners in improving health care quality, using examples.

Description

Many healthcare systems suffer from poor quality leading to preventable deaths, reduced quality of life or serious adverse events such as medication errors. This is where quality assurance and quality improvement come in.

	Quality ASSURANCE	Quality IMPROVEMENT
Definition	Quality assurance comprises the set of activities used to ensure that the processes under study leads to products that meet predetermined standards of quality.	Quality Improvement is defined as the ‘combined and unceasing efforts of everyone’ to make changes that will lead to better health, patient, system performance and professional development outcomes.
Aim	Aims to conform to standards	Aims for improved performance
Timeline	Relies on inspection of the final product, the service, or a step in the process Reactive Retrospective Process Happens after an event	Ongoing/occurs repeatedly over time Passive Prospective Process Happens before an event
Example	Near miss log, pharmacy incidence form	Pharmacy-Specific CQIs
Problem	Usually completed to address a problem or avoid future problems	Can be completed without identifying problems
Focus	Focuses on what went wrong	Focuses on systems and their interactions
Involvement	Punitive May involve determining fault after something goes wrong Individual assignment or departmental function	Non-Judgmental Involves fixing or improving processes Interdisciplinary function
Benefit	Primary benefit from QA is an improvement in future service/products.	Primary benefit from QI is an improvement in future service/products.
Tools	QI/QA Tool 1. Professional Development: PCNZ/PSNZ e.g. APC 2. Plan-Do-Check-Act (PDSA) cycle 3. Benchmarking: e.g. KPIs, surveys 4. HPCAA 5. Audits 6. KPIs	

Figure 1: The Plan-Do-Check-Act Cycle



Quality Improvement/Accuracy Tools

1. *Benchmarking*: “The practice of comparing business processes and performance metrics to industry bests and best practices from other companies”
 - Determines what improvements are called for i.e. finds gaps in services
 - Use information to improve performance
 - Compare pharmacy’s performance to average
2. *Plan-Do-Study-Act Cycle (PDSA)*
3. *Auditing*: Pharmacy premises in New Zealand are audited by [Medsafe](#) to ensure pharmacy services to the public meet the required standards. Results are reported to the Ministry of Health.
 - Partial: 10 criteria
 - Full: 67 criteria

Quality Improvement/Accuracy Indicators

1. *Key Performance Indicators*: a measurable value that demonstrates how effectively a company is achieving key business objectives.

Pharmacist Roles (as leaders, managers, practitioners) in Quality Improvement

The Pharmacist's Role in Quality Improvement

Pharmacists are able to predict and anticipate the likely effects of medications on patients and would be able to recognise an opportunity to standardise a process that might improve quality of care.

1. PDSA cycle to improve systems (e.g. medication ordering, distribution, and administration processes)
2. Provide a high level, comprehensive and professional clinical pharmacy service to a specified group of patients, as per service requirements
3. Conduct patient surveys, assessment and reviews in regards to the provided service
4. Practice in a proactive manner, forming positive working relationships with key nursing, medical and business personnel within areas of responsibility.
5. Undertake medicines reconciliation to the national standard (Health Quality and Safety Commission) on admission, at transfer and at discharge. Provide a medication optimisation service to patients in clinical areas
6. Implement guidance pertaining to the Hospital Medicines List (HML)
7. Resolve medication related discharge issues for Welcome Haere Mai | Respect Manaaki | Together Tūhono | Aim High Angamua patients (e.g. s.29 medicines, specials authority, Named Patient Pharmaceutical Assessments (NPPA) applications)
8. Provide medicines information to patients, carers and other healthcare professionals
9. Facilitate the supply of pharmaceutical products to ensure timely medication supply to patients
10. Work proactively within a team of clinical pharmacists and technicians, to cover, assist and support others within the team so objectives can be achieved

11. Document clinical interventions and contributions on regular basis and in accordance with departmental requirements
12. Document clinical metrics and other work activities on a regular basis and in accordance with departmental requirements
13. Act as a clinical role model for staff in accordance with the purpose statement and guiding principles of the Pharmacy Department

New Zealand Triple Aim for Quality Improvement

1. Improved quality, safety and experience of care
2. Improved health and equity for all populations
3. Best value for public health system resources



Questions:

What steps does PCNZ suggest pharmacists, as leaders, undertake in terms of reviewing the quality of their services?

- APC: upon renewing, evidence must be shown of continual professional development (CPD)
- Long life learning: keeping up to date with new guidelines
- Patient surveys for feedback

Risk Management

Assessable Tasks Risk Management

1. Identify how Risk Management is applied to pharmacist competence, Standard Operating Procedures, and Pharmacy Quality Audit Standards
2. Create a Standard Operating Procedure for COVID Infection Control in Pharmacy
3. Identify examples of types of risks that can occur both professionally, financially and physically for pharmacists in the course of their work.
4. Describe the steps required in a risk management process
5. Apply a risk management process addressing near miss and error occurrences
6. Consider if we are risk-aversive as a profession and what are possible consequences

Description

Risk Management is an approach to prevent or mitigate a potential risk through identification, analysis, mitigation, planning and tracking of root causes and their consequences. This is **integral to quality improvement and clinical governance**. This may be as simple as recording and analysing ‘near misses’ in the dispensary and taking steps to mitigate their recurrence, or as complex as re-designing the dispensary to create a more logical and less confusing workflow.

Risk Management — Standard Operating Procedures (SOPs)

Relevant Legislation: [Health and Safety at Work Act 2015](#)

SOPs: [An overview of SOPs](#)

Purpose

SOPs are specific to a pharmacy and are necessary to ensure the continuity of processes to achieve quality performance and quality products/preparations. They serve to implement risk management systems in the pharmacy which cover all aspects of the pharmacy business to ensure the safety of staff and customers, in order to comply with the **Health & Safety at Work Act 2015**. The responsibility lies upon the **Pharmacist Manager**.

Benefits of using SOPs in pharmacy

- Induction of new staff
- Role clarification
- Identify training and development needs for current staff
- Enables the pharmacy to be run according to a set system
- Clearly define the processes and procedures within the pharmacy to ensure good practice is achieved at all times (Assures quality and consistency of services)
- Help to assure quality and consistency of service
- Help to ensure that good practice is achieved at all times
- Provide an opportunity to fully utilise the expertise of all team members

- Enable pharmacists to delegate
- Help to avoid confusion over who does what (role clarification)
- Provide advice and guidance to locums and part-time staff
- They are useful tools for training new members of staff
- Provide a contribution to the audit process

SOPs & Risk management:

- They are necessary to clearly define the processes and procedures within your pharmacy to ensure that good practice is achieved at all times. They form part of clinical governance, and in particular, show that pharmacists are putting in place strategies for **risk management and harm minimisation**.

Review of SOPs:

- All pharmacies operate differently and SOPs should be regularly reviewed (every 2 years at least) to ensure they are fit for purpose and reflect the day-to-day running of the specific pharmacy premises.

SOPs must specify the responsible pharmacist **who** created or amended the procedure, the **date of preparation**, and the **date it is due for review**. Separate versions of the old and new SOPs should be referenced and **retained**. Any changes in SOPs should be brought to the attention of relevant staff.

1. General review every **2 years**
2. When procedures change in the pharmacy
3. If legislative changes occur
4. Incidents that led to a compromise in patient safety
5. Breaching of any SOPs

Who is involved:

All relevant staff members should be involved in developing and reviewing SOPs to engage staff and provide an opportunity for **role clarification**. SOPs provide a useful tool for the **induction of new staff** and help **identify training and development needs for current members** of the pharmacy team. Pharmacies will have SOPs in place for all aspects of dispensing and services provided within the pharmacy and these should be readily available to relevant staff at all times, including **locums**.

Elements Found in an SOP	
Purpose	Describe what your SOP is trying to achieve
Scope	Specify exactly what areas of work your SOP will cover and what it won't
Procedure	Describe in detail exactly how the tasks are carried out in your pharmacy in a step by step format
Responsibility	SOP needs to specify who is responsible for different steps in the process. It must ensure that staff responsibilities are clear and that staff members involved are competent to do whatever tasks have been designated to them. This should be based on an assessment of each person's competence and level of qualification
Known Risks	Should contain a description of anything you are aware of that can make the procedure more high risk than usual. These are circumstances that you know can increase the likelihood of mistakes and where you believe extra attention should be paid

	Elements Found in an SOP
Staff Signatures	All staff members should read and sign each SOP to confirm they understand and accept the responsibilities assigned to them
Review Procedure	SOPs should be reviewed regularly (at least every two years, or sooner) due to a legislative change or if an incident occurs which may potentially have led to a compromise of patient safety. Each SOP must specify the responsible pharmacist who created or amended the procedure, the date of preparation and the date it is due for review. Separate versions of the old and new SOPs should be referenced and retained. Any changes in SOPs should be brought to the attention of relevant staff.

Types of SOPs that would form part of the Risk Management Portfolio

1. Fridge temperature management e.g. vaccines, fridge medications
2. Cold chain management e.g. vaccines
3. Controlled drugs recording
4. Staff injury: lifting heavy orders
5. Reporting near misses, and/or recording errors made
6. Fire/emergency evacuation plan
7. Dangerous encounters with customers/thieves or security breach
8. Enquiry or complaint procedures
9. Natural disasters management
10. Infection control

Incidences where staff should document an incident/complaint form at their workspace

1. Near misses: dispensing errors
2. Medicines Errors
3. Fridge temperatures non-compliant practice
4. Cold chain breaches
5. Any forms submitted to PDA (Pharmacy Defense Association)
6. ADRs (CARM)
7. Personal grievances within the workplace (workplace conflict)

Types of reporting that should be escalated to the appropriate authority

1. Staff Misbehaviour
2. Cold chain breaches/failure should be escalated to cold chain clinical leads as certain patients may need to be recalled to be re-vaccinated
3. Major dispensing errors especially with neglectful or maleficent practice intent
4. Any patient complaints

Pharmacy Quality Audits and Inspection Audits – Medicines Control (Medsafe)

- A *Pharmacy Quality Audit* assesses all services provided from the premises. This takes 6-8 hours to conduct on average and covers all audit criteria applicable to the pharmacy services provided from the premises (up to 67 criteria)

- An *Inspection Audit* is a risk based audit assessing some of the services provided from the premises. This takes 1-2 hours on average and covers 10 current risk-based criteria.

Medicines Control auditors assign an attainment risk rating to each criterion assessed during an audit:

Attainment risk rating for criterion	Description	Further Actions
Leading Practice	The auditee can clearly demonstrate achievement beyond the expected full attainment and evidence is available of actions taken based on findings from an internal review as part of a robust quality management system	-
Fully Attained	The auditee can clearly demonstrate implementation (such as practice evidence, training, records, visual evidence) of the process, systems or structures in order to meet the criterion	-
Partially Attained	The auditee is able to demonstrate evidence of appropriate process (such as policy/ procedure/ guideline), system or structure implementation without the required supporting documentation; or a documented process (such as policy/ procedure/ guideline), system or structure is evident but the auditee is unable to demonstrate implementation where this is required	When a partially attained (PA) or unattained (UA) level has been assigned, the Medicines Control auditor considers safety and regulatory consequences, and the likelihood of occurrence to determine the risk <ul style="list-style-type: none"> • <i>Worst Safety Consequence:</i> Consumers or service providers are at extreme risk of harm or actual harm is occurring • <i>Worst Regulatory Consequence:</i> Serious and/or significant deviation from regulatory requirements • Likelihood scale: Frequently, likely, occasionally, seldom, rare
Unattained	The auditee is unable to demonstrate appropriate processes, systems or structures to meet the criterion	

Types of Risks (professional, financial, physical) for Pharmacists

Risk	Consequences	Strategy
Customer theft	Stock shrinkage, financial loss, harm or AEs to the patient from inadequate use	Cameras Shop floor monitoring by staff Staff training Insurance cover - quality improvement
Customer violence/ hold up	Staff stress, damage to premises, stock loss, harm to staff (physical and psychological), resignations, other customer reactions	Staff training to deal with these specific situations (i.e. deescalation) Restraining order/trespass notice Insurance cover to pharmacy in case of damage to the pharmacy Panic button (111)
Employee theft	Stock shrinkage, financial loss, Misconduct of the employee, stress of owner and staff - unhappy staff steal.	Cameras Shop floor monitoring by other staff Insurance Cover? Harsh consequences as a deterrent Keep the staff happy
Forged prescriptions	Illegal supply of medicine, repeat occurrence, police involvement	Check with prescriber Staff training to identify forged prescription Cameras
Inadequate supply of medicines - Out of stock	Harm to the patient? Incomplete course of medication - worse outcomes Stress of customers (poor health outcome) and pharmacy.	Is it a PHARMAC restriction, is it wholesaler supply chain problem, stock procurement problem? Contact back up wholesaler, borrow from another pharmacy, reset stock re-order levels. Use another supplier/company
Power cut	Fridge temp, POS (point of sale), loss of business	Reasons? Powercut, electrical fault (call electrician), surge protector, emergency power pack
Computer malfunction	POS	Reasons e.g. virus, old?

Risk	Consequences	Strategy
Valued staff member resigns	Loss of customers, loss of customer relationships, staff morale, upset owner	Rewards for staff performance e.g. bonus, incentives, pay rise after 2-3 years of practicing (performance appraisal), positive workplace culture
Over-confident Intern employed	Near misses, missing information to the patient causing harm to patient's health, pharmacy's reputation affected, staff conflict	Have a word with them - constructive meeting, identify the gap in their knowledge and work together - pharmacist competence standards, setting boundaries
Reputational damage e.g. bad online service review	Loss of customers, possible resignation of staff (no one wants to work at a place with bad reviews)	Keep customers happy, staff training, try to offer acceptable remedies, have complaint procedure.
Landlord sell premises to new owner	Loss of business, increase rent, affect bottom line profit	Discussion with new land lord. What are intentions in owning this building? — some people may want to turn the land to a new building e.g. restaurant
Earthquake (significant)	Damage to the pharmacy/property, customers/staff injured, loss of stock	Insurance: business interruption insurance, disaster SOPs (natural disasters)
COVID-19 lockdown	Reduced income due to lack of customers, operating in restrictions, can get COVID.	Insurance: business interruption insurance, Have procedures in place to maximise pharmacy performance. SOPs: pandemic, PPEs,

The Risk Management Process

RISK MANAGEMENT PROCESS		
	Step	Description
1	Identify the risk problems	What could go wrong here?
2	Prioritise the risk problems and organise the risk management plan	If the manager tries to work on all risks simultaneously, there is a good probability that none will be addressed adequately. It is important to prioritise which risk should be addressed first, which one is most likely to occur, which will affect our operations to the greatest extent. • Prioritise on: frequency (unusual, periodic, and frequent); severity (minor, moderate, severe, catastrophic); time to probable impact and warning (months, days, no warning). • Plan: what do you want to do about it? (avoid, reduce, eliminate, or transfer the risk)
3	Select techniques to manage the risk problems	What do you need to do and how do you carry out the tasks to avoid, reduce, eliminate or transfer the risk?
4	Implement the Plan	Who does that? Timeframes?
5	Monitor/assess and make changes in the plan by returning to Step 1	Monitor and reporting back • Did it work? Will it continue to work? Did anything else make it worse?

The Risk of Not Taking Risks

- Often when considering risk, the pharmacist will be using options seen as ‘safe’ to minimise or eliminate the risk – but as a consequence the action(s) may stifle innovation or opportunity.
- The pharmacists can get a reputation of always saying ‘no’ or being too cautious.
- There are risks in not taking risks. The failure to innovate may have an equally negative impact on the business. The job therefore is to balance the true risks of doing something against the risk of not doing it – or doing something different

Questions

What constitutes an optimal environment that would be considered for pharmacists working there in order to maintain a safe dispensing procedure?

- Efficient communication between providers
- Adequate documentation
- Adequate staffing, balanced workload
- Minimised time pressures
- Clean and tidy physical spaces
- Minimised disruptions during medication processes
- Positive work culture and environment
- Adequate policies and procedures; SOPs in place

HDC highlighted a number of complaints arising from errors not picked up in a final self-check. Self checking was mentioned as a poor method of error reduction. How can this be addressed in pharmacy?

- Staff review of training and practice i.e. staff training days
- Temporarily initiate 2 final checkers?
- Encourage pharmacists to keep a diary of near misses

- Staff meetings to generate discussion about how to minimize this and identify what is causing the errors
- SOP review

Identify THREE technology or staff innovations in pharmacy practice that the HDC report would assist with risk reduction in the dispensing process.

- Dispensing robot: reduces dispensing errors/wrong medications and counting
- Counting machine: reduces counting errors
- MIMs: maximizes interactions caught and checked, minimizes CAL errors
- Toniq CAL suggestions
- Toniq check-pop ups/Sundry labels

Discuss various ways that distractions/interruptions might be minimised in the dispensing environment.

- Having a designated break room for staff
- Keep dispensing area away from other specialised areas e.g. blister packing, customer service, retail area, vaccinating area
- Keep dispensing bench clean at all times, and clear of any unnecessary items
- Baskets for items so that they stay with their prescriptions.
- Have a system in place regulating medicines orders
- Leave notes for pharmacists regarding consultations waiting, or have a board with required tasks so they can be undertaken organized without interruptions

What part of the dispensing process is often regarded as the last opportunity to prevent a medication error to the patient in community pharmacy and what TWO things does it achieve if carried out?

- The checking process: achieves a final clinical check of the medications to avoid interaction, a legal check to make sure that the prescription meets all legal requirements and is not fraudulent, and corrects any possible dispensing errors.
- The handing out process: checks patient's name and address and confirms that medications are going to the correct patient. Opening the bag at hand out can help minimize any errors.

Provide examples of Compliant Practice and Non-compliant Practice identified in the [Pharmacy Quality Audit Report](#) relating to Fridge temperatures.

Examples of Compliant Practice

- ⌚ Pharmacies held an appropriate fridge for the activities undertaken. Pharmacies providing immunisation services had a pharmaceutical grade fridge that was regularly serviced (annually) and maintained cold chain accreditation.
- ⌚ Temperatures were monitored on a daily basis from an appropriate thermometer, and data-loggers were downloaded weekly.
- ⌚ Documentation was seen demonstrating that where temperatures had deviated from the acceptable range, corrective actions had been implemented where necessary.

Examples of Non-compliant Practice

- ⌚ Fridge temperature records demonstrated that medicines were stored at temperatures consistently out of the required range (including below 0 degrees Celsius) for extended periods of time.
- ⌚ Fridge temperature records were not available.
- ⌚ When temperature deviations had been identified, the pharmacy could not demonstrate that corrective actions had been implemented to ensure the products remained of an appropriate quality for dispensing to patients.

Sustainability of Practice

Assessable Tasks Sustainability of Practice

1. Discuss how the Pharmacy Action Plan assists pharmacists in providing sustainable high-quality services
2. Consider strategies and activities that community pharmacies employ to keep themselves sustainable
3. Identify ways that pharmacy and the pharmaceutical industry impact both positively and negatively on the environment
4. Discuss ways local community and hospital pharmacies can action environmental sustainability

The Sustainability of the Pharmacy Profession

Pharmacy Action Plan 2016 to 2020

This Action Plan was developed as a way of addressing the need to provide sustainable, high-quality pharmacist services in a complex and evolving environment. There is general agreement that we face complex challenges that make it more difficult to use pharmacists' skills more effectively.

Although the pharmacist workforce is young and highly qualified, their skills remain underused in the wider health setting. Yet good evidence shows that making better use of these skills will improve health outcomes and make the use of medicines safer.

The aim of the Pharmacy Action Plan is to unlock pharmacists' full potential so that they can deliver maximum value to the health system and contribute to the objectives of the New Zealand Health Strategy.

Funders will need to work closely with primary, secondary and community health care service providers to develop new, flexible ways of purchasing and contracting services so that these new people-centred, collaborative models of care operate in practice. To get new funding, service providers will need to develop a robust business case detailing proposed service changes and the net benefits of those changes to the wider health system. Such funding will also depend on whether it is made available by reprioritising funding across the health sector.

Focus Area 1: Population & Personal Health

Internationally, pharmacists are increasingly providing an extended range of accessible, high-quality, coordinated services that focus on patient care and population health.

What does success look like?

Improved health outcomes because pharmacists, as part of the wider health care team, are providing a broader range of high-quality health promotion and preventive services that meet local health needs.

Focus Area 2: Medicine Management Services

Growing evidence shows that when pharmacists have a greater role in medicines management, medicines can be used more safely and effectively.

What does success look like?

Pharmacists are working in a broader range of settings. These settings may include (for example) community pharmacy, primary care, aged residential care and hospitals; new business models may also be developed to suit these more diverse settings. The medicines management expertise of pharmacists and pharmacist prescribers is fully used across the health and social sectors, as part of health care teams who may be working virtually or in the same physical location. In particular, these pharmacists play an important role in managing the care of people with complex medicine regimens.

The focus is on a collaborative approach to delivering higher-level clinical services, as part of a seamless continuum of people-centred care. Supporting this approach are fully integrated information technology (IT) systems that enable health professionals to share relevant patient information.

Focus Area 3: Minor Ailments and Referral

Community pharmacists already play a key role in managing acute demand by using their clinical training to ‘triage then treat or refer’; that is, assess symptoms, refer people to other health care providers where appropriate, or provide medicines and/or advice for managing minor ailments. This contribution provides timely access to care and reduces the burden on general practices and secondary care services. However, the cost of medicines can be a barrier for some populations and means that many people with minor, self-limiting conditions may present to acute care settings as the first line of treatment.

What does success look like?

Pharmacists are part of an integrated team providing people with improved access to a minor ailments and referral service. The service is cost-effective to the whole system, materially reducing daily pressure on general practice teams and other acute care settings so that clinicians can prioritise people with more complex needs.

Focus area 4: Dispensing and Supply Services

Redesigning the dispensing process will help to achieve efficiencies in the supply of medicines (dispensing) and free up pharmacists to spend more time on providing people-centred care (counselling, CPAMs, MURs)

What does success look like?

- Robots: useful for large quantity that need to be dispensed
- PACTs (Pharmacy Accuracy Checking Technicians): final accuracy check on a dispensed item, but still requires clinical check by pharmacist i.e. process Rx through, pack medicine → shift in liability?
- Good workflow in dispensary: avoid workplace accidents, consistent smooth workflow for sufficient and effective services delivery, comfortable environment (e.g. temperature/AC)

Pharmacy Financial Sustainability

Pharmacy practice worldwide faces an uncertain future. Pharmacists and technicians are faced with working increasingly longer hours with less staff overlap, and ever increasing operating costs. Governments and health system funders are cutting health care spending and reducing compensation for drug costs. In many countries, there is a critical shortage of pharmacists and pharmacy support staff. **This creates an environment which poses a serious threat to the very sustainability of the profession of pharmacy.**

Pharmacy margins in all areas are narrowing, and economic sustainability is becoming an issue. In a number of countries, patients are incentivised (by price) to use internet and mail order pharmacy services that do not allow pharmacist/patient contact. Simultaneously, governments are placing increasing pressures on pharmacists to focus on their cognitive skills, drive down healthcare costs and generate better patient outcomes. These pressures combine to frustrate pharmacists and lead them to question their place in this cost pressured healthcare environment.

The challenge for the profession of pharmacy is to retain relevance in a health system that faces competing pressures of continually increasing demand for services in a cost constrained funding system.

Environmental Sustainability

A large proportion of carbon dioxide emissions can be attributed to pharmaceutical companies. In addition to the carbon footprint of pharmaceutical companies, inappropriate pharmaceutical disposal leads to contamination of water and bioaccumulation in wildlife.

Historically, waste treatment was expected to degrade any active pharmaceutical compounds to an acceptable risk level. More recently, however, reports of feminised fish have been attributed to water contaminated with estrogen-containing contraceptives.

Increased pharmaceutical consumption will only amplify the environmental consequences of the pharmaceutical lifecycle. It is imperative for healthcare trainees and professionals worldwide to be aware of these issues and to advocate for ‘greener’ pharmaceutical production and disposal.

Pharmacists have significant potential to mitigate the environmental risks of pharmaceuticals. In Sweden, a drug database has been developed to classify the environmental risk of medications. The data are provided voluntarily by pharmaceutical companies and then reviewed by the Swedish Environmental Research Institute, an independent organisation. Each drug is evaluated on environmental hazard, persistence, and bioaccumulation risk. For example, data from AstraZeneca reveal that amoxicillin causes moderate environmental risk, is potentially persistent, and has low potential for bioaccumulation. This information is publicly available and could be incorporated into the therapeutic decision-making process. In fact, we used this database during our otitis media case to discuss the value of such a tool in the prescribing process. All other things being equal, selecting a drug with reduced environmental impact is preferred.

Questions

What is the business strategy these discounters (e.g. Countdown, bargain chemist) typically follow?

Will the same strategy work for independent community pharmacies?

- These discounters are “**loss leaders**”. They reduce dispensing costs (the cheaper, the better) and increase retail prices.
- *Supermarket example*: petrol drives higher grocery sales i.e. they are losing money for one thing to make money from another.
- This strategy won’t work the same for independent community pharmacies as they don’t have the capacity for a large retail front or the demand for it, and are often limited by financial capabilities.

What has been the impact reported for some city and suburban pharmacies in Auckland for example?

- Value of pharmacies dropping
- Pharmacies losing their purpose (patient-centred care) and becoming more retail-focused
- Small pharmacies closing down or merging since patients migrate to bigger pharmacies

Are consumers/patients/customers the winners? Why/why not?

- Price-driven society (capitalism)
- *Pros (of discounted pharmacies)*: cheaper, more range, longer opening hours (close late), convenient, free prescription increases access
- *Cons (of discounted pharmacies)*: compromised patient-pharmacist relationship (no / lack of personalised service), decreased quality of care, long waiting time, may not be able to do compounding prescriptions, stock issues, lose the local pharmacist (pharmacy shuts down)

What are some pharmacies doing to address competition from discount pharmacy chains?

- Lower prices of retail items
- Providing additional services e.g. ear piercing services, CPAMs, vaccinations, methadone
- Pharmacist prescribers: more range of services
- Add value to services i.e. triage, participating in vaccinations, LTC, COVID supervised rat tests

Discuss the employment opportunities and threats this competition raises

- Better pay for employees
- Increase in services offered means more and greater experience for pharmacists and staff
- Large franchise pharmacies offer a wide range of jobs from multiple shop staff, security, pharmacists, few technicians
- Threat: become less qualified in patient care, become more business driven - have ‘franchise’ mindset

What is your wish list if you could be heard by the MoH to make pharmacy more sustainable in the next ten years?

- Have a maximum number of franchise pharmacies in one area

- State that some smaller pharmacies must stay open, or that these larger pharmacies must start to offer consultation services more regularly and increase staff as needed.
- Improve opportunities and success for pharmacy owners, especially of younger age to motivate them to stay in NZ
- Recognise our scope of practice i.e. minor ailments
- Re-evaluate compensation and resources - this will also attract people to enter the profession and those who are in there, to stay in it

What does successful co-existence look like between types of community pharmacies in terms of services and funding models?

All pharmacies want enough funding and competition to keep them popular and running for the good of the people in the community. Funding for different services being shared around - not everyone to have the same services in the same area

Using the article by Wick, identify problems pharmacy is facing under cradle-to-grave stewardship requiring consideration to ensure that future generations are unharmed by our actions. <https://www.pharmacytimes.com/view/getting-to-green-hows-pharmacy-doing>

- Cradle-to-grave (C2G) stewardship (or regenerative design): looks at products' and services' entire life cycle to determine the best way to ensure that future generations will be unharmed by our actions.
 - Production issues: chemicals, synthesis process, life cycle engineering, **packaging**, emission management
 - Transportation of products
 - Healthcare environmental footprint
 - Use of pharmaceuticals
 - Ultimate drug disposal

Discuss ways that local community and hospital pharmacies can act on environmental sustainability.

- Use of e-prescriptions (but still need to print it out lol), decrease paperwork
- Use more sustainable packaging: biodegradable
- Encourage safe drug disposal: dispose at pharmacy (unused and/or expired)
- Package recycling and reuse (reuse is better as recycling takes energy) but also balance out practicality
- Using motion sensors for light switches: reduce light use
- Reusable blister pack → pill boxes
- Only pick up repeats if needed
- Reuse of inhaler containers

Assessable Tasks Change Management

1. Discuss techniques that managers may use to improve staff attitudes to culture change in their workplaces
2. Identify the management stages of transformation in the workplace and apply it to a task requiring significant change
3. Discuss characteristics of a transformational leader with application to changes in workplace impacting on staff

Introduction to Workplace Culture

The culture of an organisation is essentially its personality, it can influence its success or failures. Workplace culture is a collective of people's values, goals, habits, behaviours and shared beliefs. The gap between what organisation truly values as opposed to what it says it values is called 'rhetoric-reality gap.' This is often because statements about values are always easier than living them. A winning company culture creates a culture of competence — they foster employees to develop and encourage them to meet their full potential.

Resistance to change

It is claimed that most failures (i.e. failure to achieve the desired change or unsuccessful in sustaining the change) result from a lack of understanding of certain predictable elements of human nature by leaders. One overwhelming topic surrounding structure reorganisation is change; people do not like change.

Various workplace culture types have been identified (from article)

TYPES OF WORKPLACE CULTURES	
Culture	Description
Power Culture	Dominance & Control A power culture is based on control and dominance of one or a few individuals in an organisation, who make key decisions. This culture is characterised as being competitive, power orientated and political.
Role Culture	Procedure & Rules In a role driven culture, individuals have clear functions to perform and tend to stick closely to their job descriptions. Work in this type of culture is driven by procedures and rules and power is linked to positions rather than people.
Person Culture	Autonomy & Fairness A person culture allows individuals to operate in a fair autonomous manner and make decisions for themselves.
Task Culture	Expertise A task culture revolves around teams and tasks. Teams have tasks to complete and do so with a reasonable degree of autonomy for decision-making. This type of culture is based more on expert power than on position or personal power.

Events that trigger change

EVENT THAT TRIGGER CHANGE	
Events	Description
Rapid Technology Change	Electronic prescriptions, barcode system, robotics
Innovations	New products, software development
Political or economic trends	DHB service contracts & funding (e.g. LTC), election of a new government
Threats from competitors	New pharmacy opening, competitive tendering for services, free prescriptions, online services
Emergent opportunities	Request partnerships
Competitive strategies	Strategies which emphasise unique, cutting-edge technology, product or services.
Customer or patient requirements/ preference	Delivery services, compliance packaging
Stakeholder Demands	Insurers, PHARMAC requirements
Regulatory Demands	Accreditation standards, medicine reclassifications, legislation changes
Globalisation of markets and competition	Product supply continuity, new suppliers/product lines, customer international market choice

Eight Stages of Transformation of Change

EIGHT STAGES OF TRANSFORMATION		
	Stage	Description
1	Establishing a sense of urgency	<ul style="list-style-type: none"> • Examining the market and competitive realities. • Identifying and discussing crises, potential crises or major opportunities
2	Creating the guiding coalition	<ul style="list-style-type: none"> • Putting together a group with enough power to lead the change • Getting the group to work together like a team
3	Developing a vision and strategy	<ul style="list-style-type: none"> • Creating a vision to help direct the change effort • Developing strategies for achieving that vision
4	Communicating the change vision	<ul style="list-style-type: none"> • Using every vehicle possible to constantly communicate the new vision and strategies • Having the guiding coalition role model the behaviour expected of employees
5	Empowering broad-based action	<ul style="list-style-type: none"> • Getting rid of obstacles • Changing systems or structure that undermine the change vision • Encouraging risk taking and non traditional ideas, activities and actions
6	Generating short term wins	<ul style="list-style-type: none"> • Planning for visible improvements in performance or wins • Creating those wins • Visibly recognising and rewarding people who made the wins possible
7	Consolidating gains and producing more change	<ul style="list-style-type: none"> • Using increased credibility to change systems, structures and policies that do not fit together and do not fit the transformation vision • Hiring, promoting and developing people who can implement the change vision • Reinvigorating the process with new projects, themes and change agents.
8	Anchoring new approaches in the culture	<ul style="list-style-type: none"> • Creating better performance through customer and productivity orientated behaviour, more and better leadership and more efficient management • Articulating the connections between new behaviours and organisational success • Developing means to ensure leadership development and succession

Transformational Leadership

Transformational leaders influence and direct the process of change and are assisted by managers and others who carry out the day-to-day operations associated with implementing change.

THE MAIN CHARACTERISTICS OF TRANSFORMATIONAL LEADERS	
Qualities	Description
Inspire motivation	The leader assigns significance to the team
Exemplify influence	The leader is a positive role model who is committed to executing change that will help the organisation proper
Provide individualised attention and equitable treatment	The leader is attentive to individual needs, dedicated to fair treatment and committed to fostering the success of others
Have the courage and initiative to challenge existing normals and boundaries	The leader rises above failures and setbacks and strives to succeed. They work with others to resolve problems and break through the status quo.
Facilitate intellectual excitement	The leader encourages new and creative ways to solve problems
Encourage discussions about future possibilities	The leader promotes new ideas for change and stimulates new projects and methods

Leadership

Assessable Tasks Leadership

1. Recognise the importance of leadership to the pharmacy profession from stakeholders including PCNZ and FIP
2. Describe Golman's six main leadership styles and be able to apply it to pharmacy workplace situations
3. Identify behaviours or traits commonly associated with either leadership or management
4. Describe the role and characteristics of a mentor
5. Describe the role and characteristics of a preceptor

Leadership Styles

A leader is expected to inspire, to motivate and to think and act strategically. Whether or not there is a difference between management and leadership is debatable. Some experts dislike the separation of the two but others think that there is a marked distinction between those who manage and those who lead.

- **Leadership:** change, vision, communication, proactive, high risk, aligning, motivational
- **Management:** organising, planning, budgeting, rationality, control, reactive, risk avoidance
- Inclusive Leadership: relationship between collective leadership and compassionate and inclusive leadership behaviours

Characteristics of a Leader

- Passion for change
- Hardworking
- Giving back to the community
- Humble
- Understanding/compassionate
- Business driven
- Cares for the community and patients

GOLMAN'S SIX STYLES OF LEADERSHIPS

Leadership Style	Behaviour	Pros	Cons
Authoritative	<p>Authoritative leaders: inspire people to fulfil a vision</p> <ul style="list-style-type: none">• Make time to find new and better ways of doing things• Show people the part they play in bringing the business vision to life• Rally people to achieve their goals• Take a step back to work on the big picture	<ul style="list-style-type: none">• Useful when you need vision and a clear path for getting there• Works well in almost any business situation — especially effective when the business is entering new territory (markets, products)• Most effective for getting people behind ideas, to perform well and act with integrity• Motivates employees by giving their work a sense of worth• Gives employees flexibility — the business vision and goals are clear and employees are free to find their own way to meet them	<ul style="list-style-type: none">• Less effective if you're working with a team of experts, or with people who are more experienced than you

GOLMAN'S SIX STYLES OF LEADERSHIPS			
Leadership Style	Behaviour	Pros	Cons
Pace-Setting	Pace-setting leaders: expecting excellence, hard work and self-direction <ul style="list-style-type: none"> Expect immediate results Work quickly and to a high standard, and expect others to do the same Are quick to point out weaknesses: in people and processes, and demand more Are more likely to set employees new goals to work on than stop to offer feedback or rewards 	<ul style="list-style-type: none"> Can work well when people are highly motivated and competent. Well suited to times when you have a lofty goal and very short timeframe to achieve it Useful for situations when competition is fierce or when decisions and actions need to be made quickly. 	<ul style="list-style-type: none"> Can only be sustained for relatively short periods — employees can feel overwhelmed by demands and burn out trying to keep pace Tends to hurt culture, motivation and employee performance There's no room for employees to develop People can feel lost if the leader leaves
Affiliative	Affiliative leaders: focusing on relationships and team bonds <ul style="list-style-type: none"> Put people first Focus on building strong emotional relationships and trust Make sure they have processes in place to support their teams Create teams who get on well and look out for one another 	<ul style="list-style-type: none"> This style works when you're facing conflict or turbulent times Builds strong team relationships and trust Employees feel loyal to the business People feel confident experimenting and are more likely to be innovative 	<ul style="list-style-type: none"> Always looking for agreement can mean you avoid conflict or making hard decisions Focusing on relationships can leave employees wondering what tasks they're meant to be doing This style isn't helpful when you just need to get things done May not work well in a time of crisis or when something is urgent
Democratic	Democratic leaders: asking what people think <ul style="list-style-type: none"> Listen first, act second Encourage their people to work together Solve problems by consensus. Make sure everyone's voice is heard Won't impose their own decisions Make sure no-one dominates meetings 	<ul style="list-style-type: none"> Helps people take ownership of projects. People are more likely to have a vested interest in the project Talking things through helps you uncover ways to keep staff motivated Helps shape or establish a collective vision Ensures people have a voice 	<ul style="list-style-type: none"> May be difficult for people who aren't used to having a say in things People can end up frustrated and unclear what they're responsible for doing Meetings can go on with no clear outcome Can be time-consuming especially if it involves multiple stakeholders Employees with limited communication and interpersonal skills may feel left out
Coaching	Coaching leaders: Helping people develop and grow <ul style="list-style-type: none"> Recognise employees' strengths and weaknesses Support their personal and professional development Readily delegate and give people constructive feedback on how they've done Encourage people to establish long term goals and plan how to get there 	<ul style="list-style-type: none"> Encourages employees to take ownership of how they perform Creates an environment where people are supportive and happy to give each other constructive feedback Ongoing dialogue helps build relationships and communicate your expectations and purpose Good for developing employees' skills as it helps them to perform well long-term Positively affects your business long-term Eventually frees up your time 	<ul style="list-style-type: none"> May be problematic when the person is unskilled and has never done the task Not useful in a time of crisis or when things need to be done quickly Feedback needs to be motivating and positive to avoid micromanaging May not work when people are resistant to change You need to be ready to accept short term failure to achieve long term learning
Coercive	Coercive leaders: Demanding people do what you say <ul style="list-style-type: none"> Give a lot of orders Tend to take charge Tell team members exactly how to do tasks Make decisions without consulting the team 	<ul style="list-style-type: none"> Benefits employees who need close supervision and direction Highly effective in an emergency or crisis Useful when working towards tight deadlines Allows the leader to demonstrate their talents and expertise 	<ul style="list-style-type: none"> Needs to be used with caution as can alienate employees May stifle creativity and stop employees from expressing their own opinions and ideas Can stop people from using their initiative May make employees feel they have no independence in their work Can negatively affect motivation

Mentorship

The word “mentor” implies a wise guide or protector.

The term “mentoring” can be defined as the **“naturally formed, one-on-one, mutual, committed, nonsexual relationship between a junior and senior person designed to promote personal and professional development beyond any particular curricular or institutional goals.”** The relationship is often **long-term** and constantly changing to meet the needs of the person being mentored, unlike a preceptor-student relationship, which is often prearranged and is a short-term commitment.

Mentoring in the pharmacy profession

Mentoring is a very important component, in that it can be used to increase awareness and ease of access to leadership opportunities. This awareness can help impact junior pharmacists recognize and achieve their

potential contributions to the pharmacy profession. In effect, the encouragement and support of a mentor might increase the confidence of his or her junior colleague to take on leadership roles, which otherwise he or she might not have been interested in. Furthermore, mentoring could also be used as a means of passing undocumented professional knowledge, which is not part of the Doctor of Pharmacy curriculum, from generation to generation.

In order to maximise the benefits of a mentor, select someone in your respective field. It should also not be overlooked that the relationship between students and preceptors can be cultivated into that of a mentorship. Rotations are an excellent opportunity to network and meet different members of the pharmacy profession. Mentoring relationships can also be established through joining and attending meetings and conferences of pharmacy organisations such as the ASHP, the American Pharmacists Association, the American College of Clinical Pharmacy, and others.

Pharmacy students about to set out into the professional arena need to understand the value of mentoring. It's a positive activity that should be encouraged, because it benefits the mentor, mentee, and the progression of the pharmacy profession as a whole.

Note: Honesty is key! Quality is more important than quantity.

Mentee

- Most benefit: receives professional guidance, aid in promoting self-confidence, and knowledge about the mentor's real-world experiences
- Receives opportunity for networking i.e. when looking for job
- Important to overcome fear of approaching mentor (relationship building)
- Can have more than 1 mentor

Mentor

- Usually an established pharmacist within pharmacy field of practice
- Usually has been out of pharmacy school for many years so can get up to date information from mentee (recent graduate)
- Can provide knowledge concerning mentee's questions
- Provides the mentee an opportunity for networking
- Has the mentee's best interests at heart and will give **honest** opinions (even in areas outside professional limitations i.e. managing complexities of balancing family and career)
- Passes down knowledge, experiences, and skills with the hope that the mentee will also pass them on in the future (hopes that this will not be lost and forgotten)
- Mentee's success will be a good reflection on the mentor
- Can assist more than 1 junior colleague

MENTOR vs PRECEPTOR towards MENTEE/INTERN		
Factors	Mentor (Mentee)	Preceptor (Intern)
Goals	Not goal orientated	Goal orientated (cause they want us to qualify)
Time	Not time bound, usually long term	Time bound (10 month → site change), short term
Formation	Naturally formed	Prearranged
Interprofessional	Can be different professions	From the profession
Ratio	1 mentor → 3-4 mentees (no set limit) <i>and vice versa</i>	1 preceptor → 1-2 interns max
Qualifications	Qualifications or experience not required	Need qualifications (registered pharmacists of at least 3 years current APC) & no HDC complaints of proceedings with your name
Qualities	Listener → advice role	Teacher, role model, guide, facilitator, safety net, authentic, evaluator (can't be friends with preceptor because of evaluator role)
Networking	Networking outside the pharmacy profession	Network within the pharmacy industry
Role Responsibility	No commitment to action	Responsibility to pass, give feedback for learning, facilitate learning goals i.e. commitment to action
Benefits	<p><i>Mentor:</i> Up-to-date information from the mentee (e.g. recent graduate), mentee's success provides a good reflection of mentor</p> <p><i>Mentee:</i> provided an opportunity for networking by the mentor, passing down of knowledge, experiences, skills from the mentor</p>	

Preceptorship

A preceptor is a registered pharmacist who has been approved by the Society to take responsibility for, and oversee the training of, an intern pharmacist. Approval of pharmacists as preceptors is the responsibility of the Society as provider of the EVOLVE programme. The Society must ensure a prospective preceptor meets, at a minimum, the following Council requirements prior to approving. Where the Society does not have sufficient information, it must seek advice from Council. The preceptor is responsible for socialising the student to the values of the profession through **teaching, supporting, role modelling, facilitating, guiding, evaluating and by being authentic.**

1. At least 3 years' experience in practice after registration as a Pharmacist. For pharmacists from overseas, at least one year of the required experience must be subsequent to Pharmacist registration in NZ
2. A current APC without conditions
3. Council does not have concerns relating to health, conduct, or competence that may affect a pharmacist's ability to undertake the preceptor role
4. Undertake Society preceptor training within two months of becoming a preceptor.

	Description
Role model	<ul style="list-style-type: none"> • Provides patient care in accordance with established, EBP standards; • Fulfils responsibilities according to the standards and ethics of practice while adhering to the clinical site's policies and procedures; • Maintains professional working relationships with other healthcare team members; • Uses resources safely, effectively and appropriately.
Teacher	<ul style="list-style-type: none"> • Identifies learning needs; • sets goals in congruence with curricular expectations and in collaboration with the faculty member; • provides feedback; • plans the learning experiences to assist the student in meeting weekly professional and clinical learning goals

Guide	<ul style="list-style-type: none"> • showing them the way to provide safe, competent and optimal care; • tailoring experiences so that the learning objectives can be achieved; • optimizing all learning opportunities in the clinical practice setting
Facilitator	<ul style="list-style-type: none"> • helping the student connect with others in the institution and in the health care system who have different expertise; • encouraging the student to check and assess their own patient care so that they develop an awareness of their progress, rather than opinion of others; • socializing the student into the unit culture by making them feel welcomed by peers and coworkers; • assisting the student in establishing relationships and becoming familiar with the written and unwritten norms of the clinical setting
Evaluator	Provides ongoing feedback to assist students to integrate work and educational values to improve their psychomotor skills. Evaluating the attitudes, professional values, and competence that are to be developed; giving feedback in a constructive manner, avoiding any embarrassment of the student in front of patients, other students, staff, or health professionals; and by being objective.
Safety net	The preceptor also serves as a safety net as the student adapts to professional practice. Continuous and consistent support is a key responsibility. The responsibilities are perceived in the role of teacher and facilitator.
Authentic	You truly teach who you are (Brookfield, 2006). Each preceptor has a personal style. They inspire trust and encourage students to express their thoughts and feelings openly in a safe learning environment. By being authentically and genuinely who they are, they will connect with the student and have a positive influence on both their learning and strengthen the preceptorship experience.

Management Tips

Management Tips from the Community Sector

- Bring managers of a similar level together to share experiences about how they have dealt with specific problems and challenges
- Be straightforward, honest and fair with people (authoritative)
- Keep to the point when reasoning with your colleagues - do not waffle (pace-setting)(pace-setting)
- Always listen to other people's point of view (democratic)
- Try to get to the root cause of an issue otherwise you will only temporarily fix it (authoritative)
- Often your staff will have the solution to a problem – just let them talk it through with you (democratic)

Management Tips from the Hospital Sector

- Look after yourself and manage your personal boundaries
- Do not be afraid of making mistakes, but do ensure that if you make a mistake or change your mind, you are open about it – do not pretend otherwise
- Do not work too many hours unless you are happy with this choice. No one will thank you and your boundaries and personal confidence will founder if you let yourself get too tired.
- Do not be afraid to say no when required (to yourself, your staff, your colleagues and your boss) but do be prepared to say why
- Study your boss – adapting and delivering in a way that suits their management style will make life easier

Management Tips from the Pharmaceutical Sector

- Try to identify your own natural management styles
- Expose yourself to early training
- Be aware that your natural management style may not be as effective as other styles in some situations
- Be aware of the differences between being a manager and being a leader

Entrepreneurship

Assessable Tasks Entrepreneurship

1. To identify drivers for becoming innovative and/or an entrepreneur
2. To describe roles where entrepreneurship occurs within pharmacy practice
3. To describe skills, knowledge and attitudes associated with entrepreneurship
4. To identify where aspects of (2) and (3) fit into the development of your Health Care Initiative (HCI) Business Case
5. To describe similarities and differences between intrapreneurship and entrepreneurship
6. To apply aspects of (2) and (3) to a recognised health related business or service in New Zealand demonstrating characteristics of intrapreneurship or entrepreneurship
7. To describe the challenges facing the pharmacy and health sector when considering innovation, entrepreneurship or intrapreneurship.

DRIVERS TO BE AN ENTREPRENEUR/INNOVATOR

Improved human condition

To resolve societal problems and promote the human condition - address issues that undermine human well being

Economic Growth

To promote economic growth. May result in new business with new opportunities for employment, financial, independence and self-sustainability.

Organisational survival and competitive advantage.

Organisations that become stagnant may be at a greater risk for failure.

Improved performance

May break up boredom, monotony and inertia experienced by organisations and their employees.

Accumulation of wealth

Likely to generate higher revenues (sales) and earn greater profits and encourage self-sustainability.

DRIVERS TO NOT BE AN ENTREPRENEUR/INNOVATOR

While being an entrepreneur comes with much freedom, certain factors prevent many employees to make the jump to being a boss:

Willingness to balance risk

Especially with recent funding cuts to community pharmacy)

Time requirements

E.g. difficult to find time for your family

What leads to development of innovative patient-care services:

- Escalating healthcare costs
- Increasing burden of chronic diseases
- Primary care provider shortages
- Uneven affordability of healthcare (disparities)
- Poor health outcomes

Roles for Entrepreneurship in Pharmacy Practice	
Role	Description
Pharmacy Practice Innovation	Entrepreneurship identified with innovation, creativity and new opportunities/ideas. Need to be versatile — encourage adaptability to a variety of situations.
Service Development	Entrepreneurship related to the process of developing a new pharmacy service e.g. proposal development such as pitching in order to raise capital.
Problem-Solving	Entrepreneurship tied to problem solving, critical thinking and addressing problems in pharmacy. There is a need to develop a 'self starter attitude and a sense of autonomy/responsibility.'
Benefiting Society	Entrepreneurship in the context of improving public health, the quality of care, or social entrepreneurship. Need to have a 'social responsibility' — skills addressing moral/ethical decisions and the importance of serving the community.
Service Promotion	An entrepreneur as an effective communicator to promote services to multiple stakeholders. Traditional communication skills including written, oral, public speaking, interpersonal, negotiation and networking. Need to have good marketing skills.
Risk Taking	Courage or willingness to take risks and tolerate ambiguity/uncertainty
Pro-Activity	Taking action in anticipation of events rather than passively reacting to issues. Focus on assertiveness and taking initiative e.g. competitiveness aggressiveness. Need work ethic and persistence to succeed.
Job Satisfaction	The intrinsic motivation described by some entrepreneurs could improve pharmacist job satisfaction. Need to be positive, build confidence and a positive attitude. Need to identify to self personal strengths and weaknesses.
Evaluating Sustainability	Entrepreneur's role in assessing the financial benefits of a new program or service. Ability to develop a strategic plan or conduct a SWOT analysis. Ability to make decisions and establish priorities for effective resource allocation.

Frequent Skills, Knowledge and Attitudes for Entrepreneurship	
	Description
Risk-taking	Tolerance of uncertainty and the willingness to take calculated risks
Creativity/innovation	Developing new ideas
Self-starter	Developing a self-starter attitude and sense of autonomy/responsibility
Management	Traditional business management knowledge and skills taught in business schools
Proactivity	Focussing on assertiveness and taking initiative
Communication	Traditional communication skills including written, oral, public speaking, interpersonal, negotiation, networking etc.
Strategic Planning	Ability to develop a strategic plan or conduct a SWOT analysis
Positivity	Building confidence and a positive attitude
Decision-making	Ability to establish priorities for effective resource allocation
Teamwork	Effective work in small groups or teams to achieve goals
Versatility	Encouraging adaptability for a variety of situations
Marketing	Traditional marketing and sales knowledge and skills
Critical thinking	Improving critical thinking skills to solve problems
Competitiveness	Encouraging competitive aggressiveness
Proposal Development	Knowledge and skills pertaining to raising capital (business plan, proposal, pitch)
Numeracy	Traditional mathematics and working with numbers
Technology	Effectively using new technology
Self-reflection	Identifying personal strengths and weaknesses
Persistence	Work ethic and persistence to succeed
Social Responsibility	Skills addressing moral and ethical decisions and the importance of serving the community
Cultural Competence	Developing a basic understanding of other cultures and perspectives

Intrapreneurship and Entrepreneurship

INTRAPRENEURSHIP VS ENTREPRENEURSHIP		
	Intrapreneur	Entrepreneur
Definition and Risks	Responsible for innovating within an existing organisation	Runs their own company
	Both need autonomy and freedom — but the intrapreneur must work within the existing corporate hierarchy.	Owns the organisation and takes complete responsibility of the risk of possible financial failure
Attitude towards business ownership	Less inclined towards business ownership. They believe in entrepreneurship but lack the necessary resources to engage in such activities, but may still be able to capitalise on their unique entrepreneurial abilities and understanding/promoting entrepreneurship.	More inclined towards business ownership
Support networks	Intrapreneurs have an existing support network	Entrepreneurs often start without them.
Risks in the event of failure	Intrapreneurs face a career risk	Entrepreneurs face a personal financial risk
When creating a new venture	Intrapreneurs can lend the business name/reputation to make way for a new venture	Entrepreneurs have to create the image/reputation of the business over time.
	Intrapreneurs can often rely on existing organisational funds and resources	Entrepreneurs have to locate and obtain resources for new ventures

The workforce and ownership changes in the last 30 years have led to an increase in the number of employee pharmacists. This has made the term intrapreneurship highly relevant to the pharmacy profession today – to describe those who develop innovative patient-care services within institutional or business settings.

Stages of Intrapreneurship process

1. Defining opportunity or problem (including considerable data collection and analysis)
2. Building support
3. Mobilising resources
4. Executing the project (focusing on the start-up of the internal corporate venture)
5. Completing the venture: if the venture is successful, the intrapreneur may secure a position of continued project oversight within the corporation.

Workplace Conflict

Assessable Tasks Workplace Conflict

1. Define workplace conflict and identify factors that contribute to conflict within a pharmacy workplace.
2. Identify interpersonal reasons that conflict in the workplace commonly occurs from.
3. Recognise the direct and indirect cost of conflict to the workplace.
4. Identify what a collaborative approach requires from managers when meeting with parties in conflict.
5. Identify helpful mediation techniques that can be employed when raising conflict issues with staff.
6. Provide examples of conflict-diffusing conversation starters that can be used when meeting staff.
7. Describe steps that management can use to prevent or reduce conflict occurrences in the workplace.

Definitions

Definitions	
Term	Description
Conflict	Begins when one person makes a claim or demand on another who rejects it
Workplace conflict	A condition between or among workers whose jobs are interdependent (impacts on the job), who feel angry, who perceive the other(s) as being at fault, and/or who act in ways that cause a business problem. <ul style="list-style-type: none">• Notice that this definition includes feelings (emotions), perceptions (thoughts), and actions (behaviours). Not necessarily all at the same time but at least one of them.
Conflict Management	The practice of identifying and handling conflict in a sensible, fair and efficient manner
Not Conflict Resolution	It is not feasible to expect that all problems will be solved, accommodated, or settled

Introduction

Many people work in very complex, demanding and fast paced environments — a pharmacy is no exception. While these kind of complexities can challenge employees to meet new challenges they can also inspire workplace conflicts.

Conflict is a healthy and necessary part of any work environment. When bright, diverse, highly skilled employees work closely together, they are bound to bump into each other, not only on a physical level but intellectual and emotional levels as well. Conflict can divide people or bring them together (as ideas, perspectives and values are being shared). This is not necessarily a bad thing — the importance is that while you do not have to like everyone, you have to respect differences.

	Factors within pharmacy workplaces that are recognised for prompting conflict situations	
Examples	1. Conflict with the public	Frustrated and sick patients
	2. Conflict with prescribers	Finding errors in prescriptions
	3. Conflict with colleagues	Taking your frustration out on one another
	3. Conflict with emotional input	Discussion spills over to a fight
	3. Conflict with communication style	More efficient to be direct than to be polite/beat around the bush

Factors that may prompt conflict within a pharmacy setting

1. Heavier than normal workloads
2. Being understaffed
3. The introduction of new staff members and/or leaders
4. Scheduling disagreements
5. High noise levels
6. Introduction of new protocols or procedures
7. Inadequate understanding of job duties
8. Impression that pharmacist makes the money but technician does the work
9. After a medication error has occurred

Types of Conflict

Conflict can be classified into good or bad; either improving or creating problems in workplace & workflow

TYPES of Conflict		
	Good Workplace Conflict	Bad Workplace Conflict
Description	Conflict is a healthy, constructive and necessary part of work that has value when: <ul style="list-style-type: none"> • It effectively resolves the problem by bringing people together e.g. to share ideas on how to solve it. • Maintains relationships in the process by enhancing the ability of people to understand one another. • People feel heard and respected • The focus is on the issues and not the personalities. 	Conflict becomes destructive when it is not adequately dealt with and left to fester: <ul style="list-style-type: none"> • It does not effectively resolve the problem e.g. the fight goes on and on with no end. • It damages relationships and divides the team - making the work environment toxic. • People do not feel heard or respected, instead they feel overpowered, harassed or bullied. • The fight gets personal and leads to the point where emotions, words, and/or behaviour are out of control.

Symptoms of Conflict

- Negative body language: eye-rolling, turning away, closed postures, facial expressions of anger / hurt
- Repetition of story or requests
- Disruptive behaviour, angry outbursts, aggressive actions (throwing objects, slamming doors)
- Avoidance behaviours: not following through, showing up late, frequent sick calls, indirect or no communication
- Sabotage, intentional misinformation, harmful gossip
- Turnover, compensation claims, disability
- Apathy, disengagement, hopelessness

Costs of Conflict

We want to prevent conflict because of the severe consequences it can have.

COSTS of Conflict		
Description	The Cost of Good Conflict	The Cost of Bad Conflict
	The Cost of Good Conflict It is important to note that conflict is the result of people feeling passionate about their work. When conflict is dealt with early and effectively, this passion is harnessed to maintain a productive, vibrant and healthy environment.	The Cost of Bad Conflict When conflict (unresolved or destructive) in the workplace is not managed effectively (due to either inability or a lack of willingness) — it can cost employees in terms of:
COSTS of BAD Conflict		

Direct Costs of Conflicts		Indirect Costs of Conflicts	
Productivity	<ul style="list-style-type: none"> Conflict is difficult to deal with and can cause a great deal of distress. Employees will have decreased a job satisfaction and motivation to work (work itself takes a backseat to make place for interpersonal dynamics) 	Emotional costs	<ul style="list-style-type: none"> Pain Turmoil for those involved
Sick leave/Long term disability & stress claims	<ul style="list-style-type: none"> Employee mental/physical health deterioration 	Relationships	<ul style="list-style-type: none"> Poor workplace relationship
Employee Resourcefulness/ Turnover	<ul style="list-style-type: none"> Co-workers can sabotage (e.g. theft, damage) the efforts of others Workers may simply quit to look for a better place to work 	Pharmacy cost	<ul style="list-style-type: none"> Cost to patient service Reputation (e.g. negative publicity) Lost opportunity to develop staff and leadership
Financial	<ul style="list-style-type: none"> Legal costs Training/recruitment of new staff 		

Indirect cost describe the effect on people who are not involved and/or subsequent consequences.

Direct cost describe the immediate consequences

Conflict Prevention

Factors of Conflict

In order to prevent conflict, we have to effectively understand how it comes about. Its development and resolution can be narrowed down to two contributing factors: organisational factors and individual factors.

FACTORS of Conflict		
Factor	Organisational Factors	Individual Factors
Development	Lack of effective leadership, respect and fairness in the workplace Are often the reason behind destructive conflict stemming from organisation factors.	Poor individual conflict management skills Individual employees also have a responsibility in dealing with conflict in the workplace. However they are likely to contribute to destructive conflict when they have poor communication skills, engage in passive/aggressive behaviour (competitive rather than co-operative styles)
Resolution	1. Strong Leader A strong leader recognises that conflict is a vital aspect of a dynamic team and does not avoid dealing with it. They will explicitly define those norms such as expected behavioural expectations and how to meet them e.g. effective communication, assertive skills, respectful professional behaviour, zero tolerance for bullying. 2. Work Environment Assessment A work environment assessment can be conducted if the team leader finds it difficult to get to the bottom of a problem or manage it.	1. Conflict Resolution Process To resolve a conflict, you can use the conflict resolution process established by the employer, or escalate the situation to a supervisor or mediator. Professional help can also be sought. 2. Quit At worst, you can let go and walk away. Nothing is more important than taking care of your personal well being.

Enhancing Collaboration in Pharmacy Teams

Recommendations for Enhancing Collaboration in Pharmacy Teams	
Causes of INTERPERSONAL Conflict	Resolution/Prevention Proposed
Role Ambiguity or Incompatibility When individuals do not have a clear understanding of their responsibilities vis-à-vis others, they can interpret others' behaviours as turf encroachment (intrusion)	Establish Role Clarity Role clarity can prevent such clashes and can be established such as through a job description. Additionally, there needs to be mechanism for ongoing discussion of workflow so it is clear who is responsible for what.
Environmental Stressors Competition for scarce resources (time, money, praise, promotion, physical constraints such as tight, confined, crowded dispensaries) leads to emotional/ psychological stress and uncertainty, which primes us to interpret events more emotionally than may be warranted. They can breed interpersonal stress and conflict regardless of other factors.	Recognise and value the contribution of all pharmacy team members While experience, educational qualifications and titles may differ - each team member plays a valuable role in the patient care process. Explicit acknowledgement of these roles, no matter how different they may be, needs to happen on a regular basis.
Informational deficiencies Lack of sufficient, accurate or up-to-date information relevant to a situation that produces knowledge gaps, leading to misunderstanding. Addressed through information sharing	Pay attention to the physical constraints of the workplace Addressing environmental problems before they become interpersonal ones is recommended.
Personal differences	Learn conflict management skills Do not avoid or ignore early-warning signals of disagreement or conflict.

Recommendations for Enhancing Collaboration in Pharmacy Teams	
Causes of INTERPERSONAL Conflict	Resolution/Prevention Proposed
Fundamental values, morals or beliefs that produce a world view and behaviours that are difficult/impossible to challenge or change. Address through agree to disagree.	Learning how to appropriately use direct and indirect communication skills can prevent small problems from escalating.
Disagreement over methods rather than outcomes When method is more about personal choice than substantive difference in the outcome. Addressed through attempts to find common ground and focus on outcomes	Conflict = Intellectual disagreement + Emotional involvement De-escalating conflict is everyone's role and can be achieved through either parts of that equation. Moreover, addressing conflict while it is still logical can prevent it from escalating to having an emotional component (which is much more difficult to manage and often too late by then)

Conflict Management (Within Organisations) — **Collaborative Approach**

Pharmacist managers are often called on to manage conflict within their organisations when employees or patients are unable or unwilling to resolve conflict themselves. In some cases, something that began as a simple misunderstanding may escalate into a team-dividing conflict. Levels of team conflict can take many forms, ranging from generalised complaints that the warring sides have with each other to specific issues regarding specific employees.

Effectively Dealing with Conflict	
Recognition	Recognising It <ul style="list-style-type: none"> • Seeing and experiencing emotions escalating • Tone of communication is increasing in intensity or volume • Individuals may withdraw in silence and non verbal behaviours may be more aimed, closed or aggressive as opinions are expressed • As ideas and underlying values are shared, people may start to take sides • Perspectives become more narrow or rigid • You know you are in conflict when you feel personally involved in the issue and the outcome of discussion matters to you.
Intervention	Intervene When emotions interfere and become more important than the work, then there is a problem that needs to be resolved.

Collaborative Approach

Collaborative Conflict Management (CCM) involves a group session in which each individual is provided with the opportunity to express his or her concern — this can generate useful ideas

1. All participants are expected to voice their desired outcomes
2. All parties are committed to resolving the issues under discussion
3. Ground rules for facilitation should be established (suggestions will not be judged or evaluated until all ideas are presented; there will be no interruptions)

A neutral facilitator often can assist in fostering a helpful atmosphere. The facilitator should remind participants about the importance of separating interests from positions. When interests are voiced, it is much easier to develop potential options to address them. e.g: a position might be “we need more staff”, while an interest might be “we want to ensure that we don’t make errors as a result of time pressures”

While CCM is effective is not always easy – it takes time and effort from all parties and requires that participants be sensitive to the needs and feelings of others. However, this approach is preferred by many because it focuses energy on attacking a problem instead of the individuals involved.

1. Separate the person from the problem
2. Focus on the issue, not the intent or personal problems
3. Generating a variety of options
4. Base agreement on objective criteria e.g. don't assume someone has to win or lose..

5. Prepare for failure before it happens

COLLABORATIVE CONFLICT MANAGEMENT IN A TEAM SETTING	
Before the Meeting	
<ul style="list-style-type: none">• Analysing your own interests and those of others• Defining your desired outcome• Considering natural points of agreement and intersection between your interest and others• Listing factors that might derail the conversation and developing strategies to keep the conversation on track• Paying attention to timing	
During the Meeting	
Identify the problem Participants must identify and define the problem. Equally important, those involved must also identify who “owns” the problem	
Identify all possible solutions This is the time for brainstorming. This stage may take some time. Although a variety of solutions will be advanced, none should be criticised or discounted. However, participants are encouraged to improve on submitted ideas and even suggest ways in which these solutions can be combined.	
Decide which solution is best Now that all ideas are on the table, revisit the problem and identify which solution is the best fit. Does this solution appeal to the parties involved?	
Determine how to implement the solution Devise a plan for implementing it.	
Assess the outcome of the solution Did the chosen solution result in a win-win outcome? Were all parties equally satisfied with the results?	

Mediation Techniques

MEDIATION TECHNIQUES		
Technique	Description	Purpose
Listening for understanding	Listening openly without interrupting, giving advice, judging, or asking immediate questions	Allows speaker to feel heard and control content of information. Allows listener to hear issues, show empathy, and make assessments without jumping to conclusions
Reframing	A statement or response acknowledges the emotion, removes the inflammatory language, restates the problem or issue, and seek validation from speaker	Can neutralise issues, inform the speaker that you understand what they are saying, and redirect conversation from a confrontational mode to a problem solving mode.
Elevate the definition of the problem	A statement or response that composes opposing positions by reflecting back to an issue that is common to everyone involved	To acknowledge issues that are important to each person while establishing common ground. To encourage each person to work toward a common goal, to regain trust
Clear Agreements	A mutually acceptable agreement that is specific, clear and represents an attempt to meet the needs and interests of the parties.	Guide future behaviour, provide a foundation for trust.

Strategies to Building Conflict Competence

In the event group conflict occurs, a pharmacist manager/owner can employ a number of strategies to manage group conflict:

- Establish organisational protocols for managing conflict i.e. agree as a group how conflict will be managed
- Equip employees with the tools and confidence necessary to manage their own conflict
- Screen for conflict competence during hiring and promotion processes
- As a manager, refuse to hear arguments until the parties in conflict have exhausted their ability to reach consensus by themselves
- Establish a conflict escalation protocol – require those who cannot reach agreement by themselves to jointly present their disagreement to management
- Make the process of conflict resolution transparent – if your employees bring conflict to you, explain the factors that led to your eventual decision so that employees will understand the criteria for making decisions in the future

Labels or Inaccurate Assumptions that can Block Resolution

- | | |
|--|--|
| <ul style="list-style-type: none"> • Difficulty individual or family • Passive-aggressive co-worker • Not a team player • Power-hungry • Control freak • Arrogant • Intellectual snob • Thinks she is better than anyone else • Just wants to be the centre of attention • He just wants everyone else to be miserable too | <ul style="list-style-type: none"> • Uncooperative • She wants to get even • Doesn't care • Disengaged • Lazy • Incompetent • Bully • He is just an angry person • Irresponsible • Dangerous |
|--|--|

Conflict-Diffusing Conversation Starters

CONFLICT DIFFUSING CONVERSATION STARTERS	
Strategy	Conversation Points
Discuss each other's perceptions	"What happened from your perspective?" "May I share how I see things?"
Acknowledge how you might have contributed to the conflict	"I assumed you knew that I wanted extra syringes ordered. I wasn't explicit about that, so I can understand why they weren't ordered"
Let people talk	"I'm interested in your view of what happened" "Tell me more about that."
Consider interest rather than position	"Help me understand what you hope to achieve"
Collect data to understand the perspective	"You say that you disagree with how I manage the pharmacy. Can you give me specific examples of things that need to be different?"
Establish objective standards for making decisions	"Let's agree to use regional salary data to determine a fair rate of pay for your new position."
Partner in problem solving	"Let's work together to propose some potential solutions." "Why don't we make a list of possible options and then review the pros and cons of each?"

Questions

What is workplace conflict?

- Where two or more employees/colleagues in a workplace cannot agree. They have thoughts, feelings, or actions that cause a **business problem**.
- A condition between or among workers whose jobs are interdependent, who feel angry, who perceive the other(s) as being at fault, and/or who act in ways that cause a business problem.
- Notice that this definition includes feelings (emotions), perceptions (thoughts), and actions (behaviours). Not necessarily all at the same time but at least one of them.

Provide FIVE factors within pharmacy workplaces that are recognised for prompting conflict situations.

- Pay
- Workload
- New staff/understaffed
- Noise levels
- Errors

Interpersonal conflict in the workplace can occur for many reasons, stemming from differences, deficiencies, ambiguity and stressors. Provide FOUR common causes of such conflict and give an example of each one within a pharmacy workplace environment.

- *Personal differences* such as moral or religious differences → in pharmacy this could be related to proving contraception or abortion products, one staff member may have a moral/religious issue with this service while another thinks it is necessary. Another example is antivaxxers.

- *Informational deficiencies* such as lack of up-to-date SOPs/knowledge → in pharmacy if someone needs to rely on an SOP for an issue and they are not up to date then can cause conflict between staff who need to decide what is best to be done.
- *Environmental stressors* such as low money or resources → could be relevant to new pharmacies coming in for competition, money issues due to inflation, promotion up for grabs or anything that could cause emotional stress.
- *Role ambiguity* if a person is not sure of what their role entails → relevant to pharmacy if someone gets a promotion to retail manager, how is this different from their previous role? What are their further expectations etc?

**State EIGHT examples of either DIRECT or INDIRECT costs that can occur from workplace conflict.
(Identify each example as being a direct or indirect cost).**

- Loss of staff/labour- direct
- Loss of business due to reputation reductions - indirect
- Training new staff (relevant to first one) - direct
- Cost to patient - indirect
- Loss of pharmacy reputation - indirect
- Legal costs - direct
- team morale and relationships - indirect
- Emotional costs - pain, stress - in/direct
- Disability and stress claims - direct
- Increased incidence of disruptive behaviour - in/direct

When a pharmacy manager wishes to meet with staff in conflict, using a collaborative approach, outline considerations that he or she should make prior to the meeting, then discuss key steps in identifying problems with appropriate management outcomes during the meeting.

Prior to meeting:

- Analyse own interest and interests of others
- Plan for time management
- Define desired outcome
- Consider natural points of agreement and intersection between your interest and others
- Listing factors that might derail the conversation and developing strategies to keep the convo on track

During the meeting:

- Identify the problem
- Plan different solutions
- Decide on the best solution
- Implement the solution
- Monitor and assess outcome

Provide FOUR key mediation steps that can be employed by a manager to bring optimal outcomes from meeting staff in conflict with each other.

- Listen for understanding
- Reframe the problem
- Elevate the definition of the problem
- Clear agreements

If you were a pharmacy owner or manager, discuss what strategies (competence) you could use for addressing future conflict in the workplace by way of procedure or training to you and staff.

1. Establish organisational protocols for managing conflict. i.e. agree as a group on how conflicts will be managed.
2. Equip employees with the tools and confidence necessary to manage their own conflict.
3. Screen for conflict competence during **hiring** and promotion processes.
4. As a manager, refuse to hear arguments until the parties in conflict have exhausted their ability to reach a consensus by themselves.
5. Establish a conflict escalation **protocol** – require those who cannot reach an agreement by themselves to jointly present their disagreement to management.
6. Make the process of conflict resolution **transparent** – if your employees bring the conflict to you, explain the factors that led to your eventual decision so that employees will understand the criteria for making decisions in the future.

Give examples of ‘labels’ that staff might use when criticising other colleagues when in conflict that are barriers to any resolution. What is a technique you can employ in a meeting of such parties that will neutralise such terms?

- Irresponsible, unreliable...
- Reframing?

Provide FOUR examples of conflict-diffusing conversation starters and state what such a starter was hoping to achieve.

- Discuss each others perceptions
- Acknowledge how you might have contributed to the conflict
- Let people talk
- Consider interest rather than position
- Collect data to understand the perspective
- Establish objective standards for making decisions
- Partner in problem-solving

Describe steps you could take as a pharmacy manager that can enhance collaboration with your team to prevent or reduce conflict

- *Role clarity/definition:* Develop a mechanism for ongoing discussion of workflow so it is clear who is responsible for what.
- *Learn conflict management skills:* Do not simply avoid or ignore early-warning signals of disagreement or conflict. Learning how to appropriately use direct and indirect communication skills and prevent small problems from escalating.
- *Recognise and value the contributions of all pharmacy team members:* While experience, educational qualifications and titles may differ, each team member plays an important role in the patient care process. Explicit acknowledgement of these roles, different though they may be, needs to happen on a regular basis.
- *Pay attention to the physical constraints of the workplace:* These can contribute to the stress that escalates conflict: tight, confined, crowded dispensaries will breed interpersonal stress and conflict regardless of other factors.
- *Conflict = intellectual disagreement + emotional involvement:* De-escalating conflict is everyone's role and can be achieved through either part of that equation.

Pharmacy Ownership & Consumer Law

Assessable Tasks Ownership

1. To apply the legislation to pharmacy practice scenarios, focusing on pharmacy ownership and consumer guarantees

Definitions

GLOSSARY	
Holding an interest in a pharmacy	MA s5A Hold an interest in a pharmacy if have/acquire any direct/indirect estate or interest in the pharmacy (by way of shares in a company or otherwise) that affects ownership, management, or control of the pharmacy practice carried on in the pharmacy
Operating a pharmacy	MA s5B Establishes or carries on business in a pharmacy
A company	Companies Act 1993 & MA s10 • A company must have: <ul style="list-style-type: none">• A name,• One or more shares,• One or more shareholders having limited/unlimited liability for the obligations of the company,• One or more directors
Limited/Unlimited Liability	A ‘ limited liability ’ company offers protection to its shareholders, as once the company is formed it is regarded as a separate legal entity from its shareholders. This means that if a company is unable to pay its debts and a liquidator is appointed, the shareholders are not liable for the business debts (in most circumstances).
Shares	Companies Act 1993 & MA s36 These are received in return for money invested in the company
Shareholders	Companies Act 1993 & MA s36 An investor in the company (owns shares) Rights and powers attaching to shares — MA s36 A share in a company confers on the holder (shareholder) the right to vote on a poll at a company meeting to: <ul style="list-style-type: none">• Appoint or remove a director (most powerful vote as directors are involved in the day-to-day running of the business)• Adopt a constitution• Alter the company’s constitution, if it has one• Approve a major transaction such as the sale of the business• Shareholders have certain rights which can be altered in the company’s constitution. If a company does not have a constitution, then shareholders have all of the rights provided in the Companies Act 1993• Note: Under the Companies Act, one share in a company confers the right to one vote.
Director	Companies Act 1993 & MA s36 Responsible for managing the company’s day-to-day business and may, or may not, be shareholders Shareholders vs Directors <ul style="list-style-type: none">• In many smaller New Zealand companies, the shareholders are also the directors of the company. Often the largest shareholder is the managing director.• In larger companies, most shareholders have no say in its daily operations.• However, all shareholders that hold voting shares in a company may participate in the election and removal of directors. This gives shareholders the collective right to elect the directors and have the ultimate control of the company without necessarily being concerned in its day-to-day affairs.
Urgent Pharmacy	Urgent pharmacy is a pharmacy that is open outside normal business hours – extended shopping hours have reduced the need for urgent pharmacies however.
Consumers Guarantee Act	<ul style="list-style-type: none">• Goods must be of acceptable quality, must be fit for purpose (that consumer makes known and that supplier represents).• Failure of guarantee means supplier has to either replace, repair or refund.• Failure of the supplier to remedy this means the consumer can claim costs from suppliers or reject goods.

Introduction

The laws surrounding pharmacy ownership change over time!

	Past (<i>Pharmacy Act</i>)	Present (<i>MA & MR</i>)	Future (<i>Therapeutics Products Bill</i>)
If pharmacy is owned by pharmacist	Under the Pharmacy Act 1970: <ul style="list-style-type: none"> Pharmacist(s) could own one pharmacy (exemptions for urgent pharmacies) — with the ownership including at least a 75% share capital. 	Repealed in 2004 & MA s55D/E/F <ul style="list-style-type: none"> Pharmacist(s) can now own 5 pharmacies (exemptions for urgent pharmacies) — with the ownership in each of those pharmacies being the majority interest (>50% value of business) No restriction on the number of pharmacies for minor shareholders — so can have minor shares in many pharmacies. 	
If pharmacy is owned by a company	<ul style="list-style-type: none"> If the pharmacy is owned by a company, the pharmacist(s) must have at least 75% of share capital AND have effective control of the company. 	<ul style="list-style-type: none"> MA s55D(2): If the pharmacy owned by a company, the company can own up to 5 pharmacies and the pharmacist(s) must own at least 50% of share capital AND have effective control of the company. Cannot be a major shareholder in two companies which each own 5 pharmacies 	Replacing MA & MR with Therapeutic Products Bill <p>However, recently new changes have been proposed:</p> <ul style="list-style-type: none"> 'Fit and proper' (non-pharmacists) people can now own pharmacies But there must have Supervisory Pharmacist responsible for compliance with licence conditions & implementation of professional standards
Access with other business	<p>Pharmacy had to be enclosed by 4 walls (had to be a separate area):</p> <ul style="list-style-type: none"> No direct access to a medical centre Not allowed to operate in conjunction with other businesses or have direct access to them 	<ul style="list-style-type: none"> No such restrictions — pharmacies can now be located within supermarkets, medical centres, hospitals, etc... 	<p>This change was proposed to be implemented as it is no longer believed that the old pharmacy ownership laws are necessary for safe ad proper services to be provided.</p>
Who can hold interest?	<p>Pharmacy Act prevented wholesalers from holding an interest in a pharmacy.</p>	<p>This restriction has been omitted from MA. Instead, MA s42c restricts authorised prescribers from holding an interest in pharmacies (but does not restrict access between pharmacies and medical centres like in Pharmacy Act)</p>	
Effective control of a company	<ul style="list-style-type: none"> The purpose of the pharmacist holding majority shares (particularly the majority voting shares) is so that their decisions could not be overridden by other members on the company's board. If the company does not have a constitution, then this may not be an issue as the pharmacist/s are required to own the majority of voting shares (75% in the past, >50% now) If the company has a constitution which allows for voting and non-voting shares then the pharmacist/s must have >75% (in the past) or >50% (now) of the voting shares. <p><i>Retaining effective control of the pharmacy means — MA s55D(2)(a)</i> Pharmacist/s shareholders are able to appoint the majority of the company's board of directors (which dictate how the business runs day-to-day)</p> <p><i>Mandatory condition of licence to operate pharmacy — MA s55C</i> It is a condition of every licence to operate a pharmacy that the holder of the licence must not request or require any pharmacist who is employed or engaged in duties at a pharmacy to act in a way that is inconsistent with the applicable professional or ethical standards of pharmacy practice.</p>		

Security of Pharmacy & Medicines — MA s42A, MA s42B, MA s47

- Pharmacy must be under **immediate supervision & control** of a **pharmacist**
- Every person who operates a pharmacy must ensure:
 - Prescription & restricted medicines must be secured to prevent public gaining ready access to medicine
 - All medicines held in storage must be secured to prevent public gaining access to the medicine



CHAPTER 23

PHARMACY INTERNSHIP

Chapter In Progress
Will be regularly updated this year

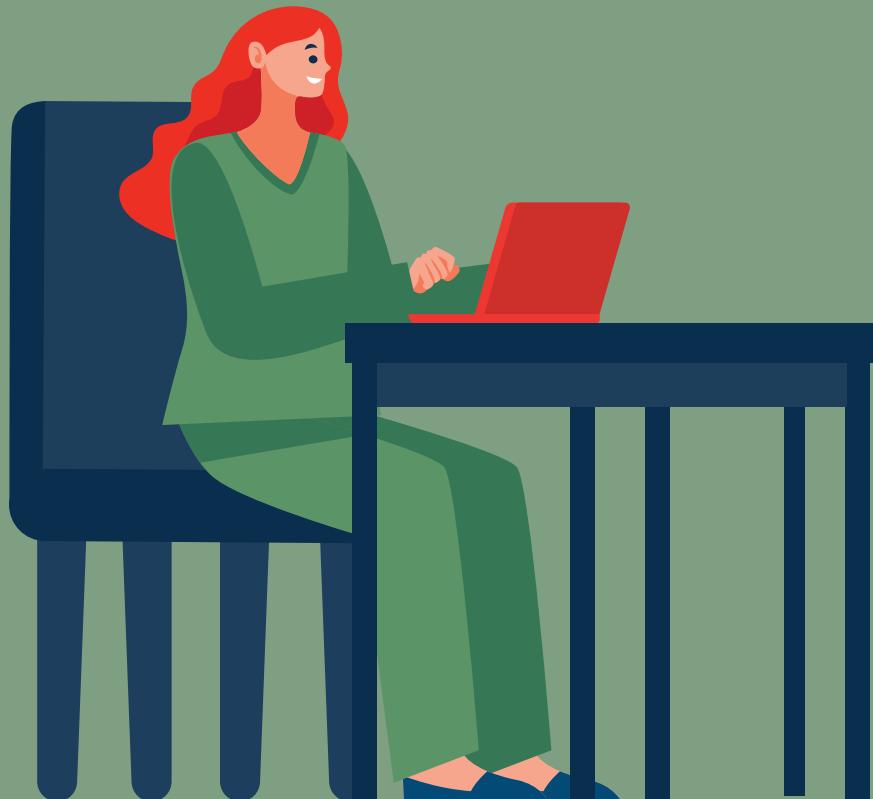


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Chapter 23

Pharmacy Internship

Pharmacist Services

Welcome to the final chapter of this handbook - we presume you are by now intern pharmacists! Please note, a large portion of this chapter builds off what we have covered so far - revisit respective chapters when applicable if needed. Let's look into a few pharmacist services:

- Age-Related Residential Care (ARRC)
- Aseptic Services
- Blister Packing
- Clozapine Dispensing (monitored therapy medicine services)
- Community Pharmacy Anti-Coagulation Monitoring Service (CPAMS)
- Compounding
- Community Residential Care (CRC)
- Controlled Drugs
- Emergency Contraceptive Pill (ECP)
- Influenza Immunisation
- Locally commissioned services
- Long Term Care (LTC)
- Medicines Reconciliation (MedRec)
- Methadone Dispensing (OST)
- Needle Exchange Programme (NEP)
- Nicotine Replacement Therapy (NRT): patch, gum, lozenges
- Oral Contraceptives (OC)
- Opioid Substitution Treatment including Co-Dispensing (CDOS)
- Repeats Collection
- Sildenafil
- Smoking Cessation
- Sumagran
- Sterile manufacturing services
- Trimethoprim
- Vaccinations
- Wound Care

Self Care Cards

Introduction

These are the self-care cards available to you in a pharmacy to give to patients. We are in the process of building custom self-care cards matching the theme of the Handbook! Please see the next page for an example. We appreciate your patience regarding this matter.

Acne	High Blood Pressure
Alcohol and pregnancy	Indigestion and Heartburn
Anxiety	Influenza
Arthritis	Maternity Services
Asthma	Migraine
Children's Illnesses	Mouth Ulcers
Children's Pain and Fever	Pain Relief
Chronic back pain & Ankylosing spondylitis	Preparing for Pregnancy
Cold Sores or Herpes Simplex	Prostate Problems
Constipation	Quit Smoking
COPD	Reducing Your Cholesterol
Coughs and Colds	Safe Use of Medicines
CPAMS	Scabies
Depression	Sleeping Well
Diarrhoea and Vomiting	Sprains and Strains
Emergency Contraceptive Pill	Sun Safety and Skin Cancer
Eye Care and Conjunctivitis	Threadworms
Fighting Colds and the Flu	Type 2 Diabetes
Fungal Infections	Urinary Tract Infections
Gout	Vaginal Thrush
Haemorrhoids	Warfarin Management
Hayfever	Weight and Health
Head Lice	

- Cellulitis -

Dermatology | Self-Care Card

What Is It

Cellulitis is a bacterial infection of the deeper layers of the skin such as the fat. While it is not contagious, it is a serious condition that warrants seeing a doctor as quickly as possible - the earlier you are treated, the better!

What Causes It

The bacteria that causes cellulitis exists naturally on our skin without causing problems. However, if it gets through e.g. through a cut, an open wound, dry/cracked skin, it can proliferate and cause this condition.

While anybody can get cellulitis - there are many things that increase your likelihood of getting it:

- You've had it before, you are overweight
- You have a history of skin conditions such as eczema, psoriasis, scabies, acne, fungal infections, insect/animal bites.
- Your immune system is impaired e.g. heart problems, high blood sugar, high blood pressure, being pregnant, you take certain medicines

What Does It Look Like

Cellulitis generally affects one side of the body and usually appears on the legs or arms. The bacteria may make the skin look:

- Red, swollen, with blisters
- Feel hot and/or painful to touch.
- You may feel feverish or unwell a few hours before you see changes in your skin



What Can I Do

You can reduce your chances of getting cellulitis again by:

1. Keeping your skin clean and well moisturised and treating any breaks in your skin.
2. Check everyday the size of the wound and how its healing
3. Get plenty of rest and water - it's important to ensure you are not dehydrated.
4. Elevate the body part affected to reduce swelling - a cold compress can also help!
5. Control any risk factors such as diabetes or fungal infections
6. Ensure your tetanus boosters are up to date

Treatment

Your doctor might trace around the area with a marker to monitor if the infection is spreading.

- *If the area infected is small:* it is usually managed with oral antibiotics and some pain relief e.g. panadol
- *If your case is a bit more complicated:* may need to go to the hospital for intravenous antibiotics.

You will improve within **7-10 days** after treatment. Antibiotics are usually well tolerated but can upset your stomach and cause rashes - please let your pharmacist or GP know **if you have any known allergies**. It is important to finish the whole course even if the infection doesn't look like it's there anymore - there may be remnants of the infection that you cannot see.

When Should I Seek Help

- There is no improvement after 5 days of treatment
- You're having trouble breathing, your throat is swelling up and you have racing heart.

Full Summary of OTC Recommendations

Introduction

Throughout the first few chapters, we discovered diseases for which could be remedied with OTC supplies. Please find a full summary here.

DERMATOLOGY					
Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Dandruff/Seborrhic dermatitis	<ol style="list-style-type: none"> 1. Zinc pyrithione (Head & Shoulders) 2. Antifungal shampoo (ketoconazole — sebizole, Nizoral) 			<ul style="list-style-type: none"> • Ketoconazole 2% shampoo not for children 	<ul style="list-style-type: none"> • Regular hair washing
Head Lice*	<ol style="list-style-type: none"> 1. Dimeticone (apply to dry hair and leave for 8 hours/ overnight; repeat application after 7 days) <p>Note: All affected household members should be treated simultaneously.</p>				<ul style="list-style-type: none"> • Wet hair combing (after conditioner — every 4 days for 2 weeks until no live for 3 consecutive sessions)
Acne*	<ol style="list-style-type: none"> 1. Benzoyl Peroxide 2. Azelaic acid 3. Salicylic acid <p>Do not use these in breast area</p>	<ul style="list-style-type: none"> • <i>Isotretinoin is contraindicated</i> • <i>Doxycycline is teratogenic</i> 			<ul style="list-style-type: none"> • Wash face x2 • Oil-free moisturiser • Limit sugar and dairy • Use sunscreen; avoid too much sunlight • May cause dry skin • May bleach fabrics
Cold Sores*	<ol style="list-style-type: none"> 1. Aciclovir (Viratac, Zovirax, Viraban): q4h (5x daily) for 5-10d 2. Virasolve: q1h for first day then q4h for 5 days 3. Compeed patches 	<ul style="list-style-type: none"> • Virasolve is contraindicated 	<p>Virasolve may make breastmilk taste unpleasant</p>		
Mouth Ulcers*	<ol style="list-style-type: none"> 1. Medijel, Bonjela: q3h 2. Kenalog/Oracort 	<ul style="list-style-type: none"> • Kenalog/ oracort not recommended 			<p>Wipe surface Do not eat or drink after taking</p>
Dermatitis*	<ol style="list-style-type: none"> 1. Moisturiser 2. Hydrocortisone 				<p>Cold compress Loose clothing Cold shower Moisturise liberally</p>
Bites & Stings	<ol style="list-style-type: none"> 1. Stingose 2. Soov Bite Gel (lignocaine) 3. Oral antihistamines 4. Hydrocortisone 			<ul style="list-style-type: none"> • Stingose: >12 months • Soov: >2 years 	<ul style="list-style-type: none"> • Insect repellent
Cuts	<ol style="list-style-type: none"> 1. Crystaderm (hydrogen peroxide) 2. Betadine (iodine) <p>Note: Do not use together</p>	Avoid betadine (due to potential thyroid complications from increased iodine absorption)			<ul style="list-style-type: none"> • Watch out for infection
Athletes Foot*/ fungal infections	<ol style="list-style-type: none"> 1. Miconazole cream 2. Terbinafine cream 3. Clotrimazole cream <p>Can treat but must REFER DIABETICS</p>	<p>Terbinafine is not recommended</p>	<p>Terbinafine is contraindicated</p> <p><i>Oral terbinafine & itraconazole contraindicated</i></p>		
Onychomycosis*	<ol style="list-style-type: none"> 1. Amorolfine Refer if >2/3 toes and covers majority of toe <p>REFER DIABETICS</p>	<ul style="list-style-type: none"> • Amorolfine is contraindicated 			

Nappy rash	1. Barrier cream (Sudocrem) 2. Miconazole +/- hydrocortisone				• Nappy-free period • Change nappies frequently • Use barrier creams after changing nappies
Scabies*	1. Permethrin 2. Itch-soothe				
Shingles	1. Capsaicin cream (Zostrix)				
Warts	1. Duofoam — AVOID IN DIABETICS (can cause ulceration) 2. Salicylic acid				
Threadworms*	1. Mebendazole (Vermox) 2. Pyrantel (Combantrin)	• Mebendazole is contraindicated			
Urticaria	1. Oral antihistamines 2. Corticosteroids (if inflammation)				
OCULAR					
Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Dry eyes	1. Polytears 2. Systane (preservative free)				Avoid rubbing the eye Anything that may have caused it?
Conjunctivitis (Bacterial)*	1. Chloramphenicol (eye drops/ointment) 2. Propamidine (Brolene)		• Chloramphenicol is contraindicated		• Wipe away discharge with warm cloth (consider using disposable wipes) • Avoid infecting babies • Do not share items
Conjunctivitis (Allergic)*	1. Mast cell stabilisers: Cromoglycate (Cromo-Fresh), Lodoxamide (Lomide) 2. Antihistamines: levocabastine (Livostin) 3. Decongestant: naphazoline (Albalon, Clear Eyes, Naphcon-Forte) 4. Oral antihistamines				
Conjunctivitis (Viral)*	Only lubricating eye drops for symptomatic relief • Hylofresh, Systane, Polytears				
OCULAR					
Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Ear Conditions	1. Ear wax removal (Cerumol, Waxsol)				• Warm olive oil • Do not use cotton buds
Otitis Externa & Media	1. Auralgan (pain) 2. Vosol (antiseptic; treats & prevent) 3. Analgesics				Refer if <6 months or <2 months with moderate/severe infection Dry ears - swimmers ear
RESPIRATORY					
Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Allergies	1. Oral antihistamines (loratadine) 2. (Nasal corticosteroids) 3. (Decongestants)				• Check if anaphylaxis • Avoid triggers

Cough (dry)	1. Cough suppressants (dextromethorphan, pholcodine, DHC, codeine)	Dextromethorphan only		• Cough suppressants ≥ 12 years	• Honey • Lozenge
Cough (productive/ chesty)	1. Mucolytic: Bromhexine 2. Expectorant: Guaifenesin			• Bromhexine ≥ 6 years • Guaifenesin ≥ 12 years	• Steam to breakdown mucous
Sore Throat	1. Lozenges 2. Throat spray CHECK FOR RF RISK			• ≥ 6 years	
Runny Nose	1. Antihistamines				
Blocked Nose	1. Nasal Decongestants (Otrivin) 2. Oral Decongestants (phenylephrine) NOTE THE ABOVE IS CONTRAINDICATED IN DIABETICS, heart/eye/prostate problems. 3. Intranasal corticosteroids (fluticasone, budesonide) 4. Intranasal antimuscarinics (ipratropium bromide) 5. Saline	• Oral/nasal decongestants contraindicated	• Xylometazoline contraindicated	• Nasal Decongestants ≥ 6 years • Oral decongestants/ Intranasal corticosteroids/ Intranasal antimuscarinics ≥ 12 years	
Sinusitis	1. Saline rinse 2. Decongestants 3. (Antibiotics)				

GASTROINTESTINAL

Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Oral Thrush	1. Miconazole Oral Gel (apply to affected areas and hold in mouth before swallowing - qid after food). Continue for 1 week 2. Nystatin Oral Drops			• Nystatin Oral Drops (1mL qid after food swirl around mouth). Continue for 48h	• Mouthwashes (non-alcohol)
Indigestion, GORD*	1. Antacids (Mylanta, Gaviscon) - chewable tablets 2. Omeprazole		Gaviscon not recommended Omeprazole not recommended		
IBS	1. Hyoscine (Gastro-soothe)	Hyoscine contraindicated			
Diarrhoea*	1. Loperamide 2. Electrolyte replacement therapy				
Constipation*	1. Osmotic (Lactulose) 2. Faecal softeners (coloxyl) 3. Bulk-Forming (psyllium husk) 4. Stimulants (Senna, bisacodyl)	• Stimulant not recommended		• Lactulose	• Probiotics • Fibre, fluids • Exercise • Smaller, more frequent meals • Don't resist urge to go
Haemorrhoids*	1. Anusol 2. Proctosedyl - pharmacy only 3. (Ultraproct)	Caution with Proctosedyl			• See Constipation • Cold compress • Avoid scratching

RENAL

Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
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UTIs*	<ol style="list-style-type: none"> 1. Trimethoprim 2. Ural sachets 3. Hiprex... <p>REFER DIABETICS</p>	Trimethoprim is contraindicated			<ul style="list-style-type: none"> • Water intake! • Avoid acidic drinks (fruit drinks, fizzy) • Loose-fitting cotton underwear • Correct wiping technique • Avoid feminine products • Ural sachets • Cranberry juice
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NEUROLOGY					
Condition	Normal	Pregnancy	Breastfeeding	Child	Lifestyle
Migraine*	<ol style="list-style-type: none"> 1. Triptan 2. Prochlorperazine for nausea (10 buccal tablets) 	Triptans not recommended			
Motion Sickness	<ol style="list-style-type: none"> 1. Antihistamines (meclozine, promethazine (10 tabs), cyclizine) 2. Hyoscine (scopolamine) Note: these all cause sleepiness 			<ul style="list-style-type: none"> • Promethazine >2 years • Cyclizine >2 years (>6 for tablets) 	<ul style="list-style-type: none"> • Ginger
Sleeping problems	<ol style="list-style-type: none"> 1. 1st gen antihistamines (unisom) 2. Melatonin 				
Vaginal Thrush*	<ol style="list-style-type: none"> 1. Clotrimazole 2. Fluconazole (with food) <p>REFER DIABETICS</p>	<i>Fluconazole contraindicated</i>	<i>Should be alg</i>		Refer <16
STI	Refer for antibiotics and STI check				
Breastfeeding (baby has oral thrush)	<ol style="list-style-type: none"> 1. Miconazole cream on nipple if baby has oral thrush 				

PHARMACIST ONLY MEDICINES

Introduction

Many medications can only be supplied by you! It is important to know the processes around it as well as what you can supply. See the [Protocol for the Sale and Supply of Pharmacist Only Medicines](#) by Pharmacy Council.

Recall from the Law Chapter: Recording of Pharmacist Only Sale

- Name and address of purchaser
- Name of pharmacist
- Date
- Name and quantity of the medicine sold
- Directions for use

Bacterial Conjunctivitis

Revisit *Chapter 2 - The Ocular System* for more information

Introduction

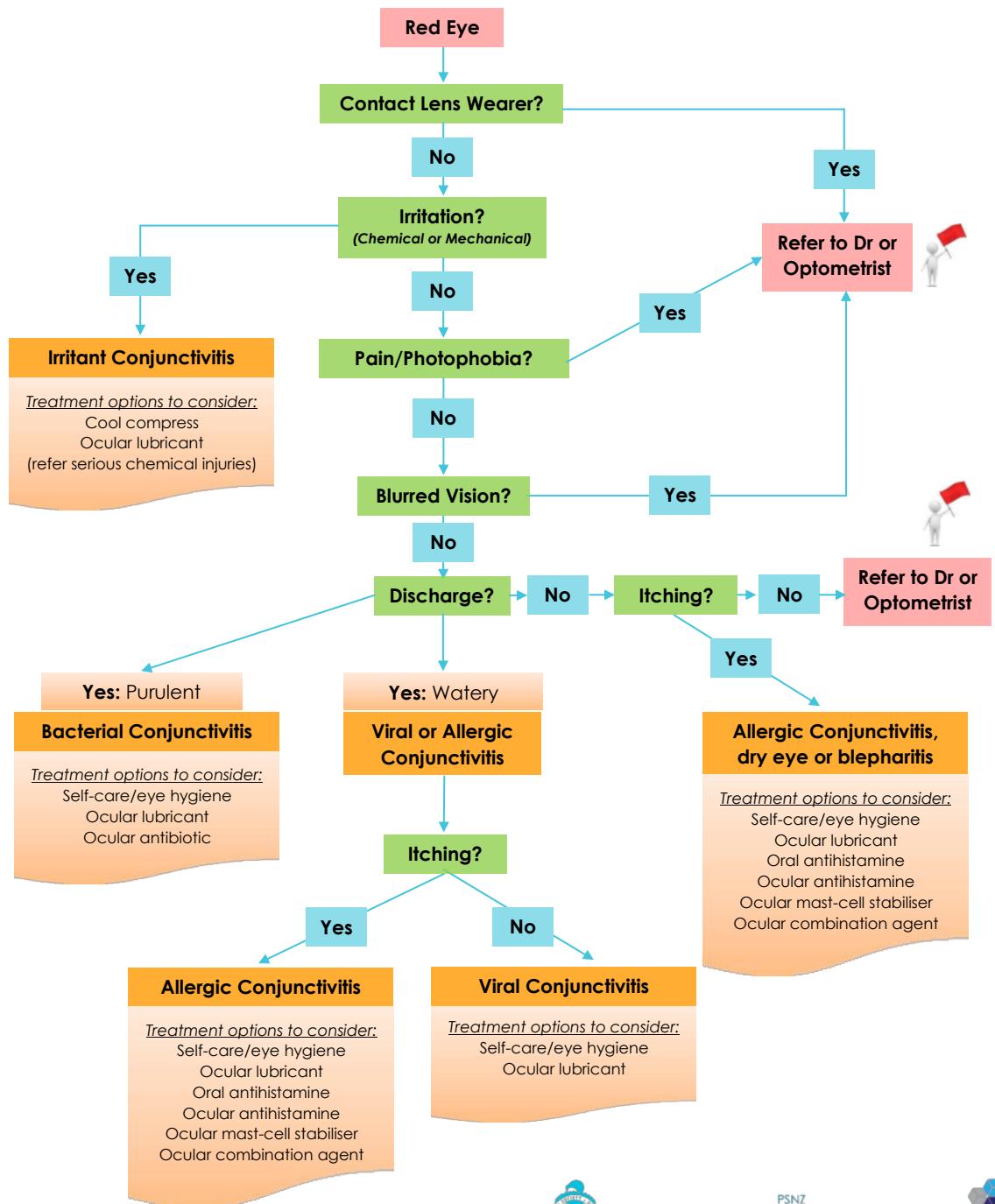
As a pharmacist, there are two pharmacist-only medications you can supply for bacterial conjunctivitis.

Other Options

- Pharmacy only: propamidine (Brolene)

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Chloramphenicol 0.5% Eye Drops	Instil 1-2 drop(s) into the affected eye(s) every 2-6 hours for 2-3 days. Continue treatment for 48 hours after symptoms resolve.	<ul style="list-style-type: none">Ophthalmic use onlyDo not use for children under the age of 2If allergy	<ul style="list-style-type: none">Tighten the cap on the nozzle to pierce the tip.Keep unopened bottles in the fridge — opened bottles do not have to be stored in the fridge.Discard 4 weeks after opening.To minimise contamination, avoid the tip from contacting the surface of the eye.	<ul style="list-style-type: none">If the patient wears contact lenses — avoid wearing of contacts during duration of treatment and 24 hours after treatment
Chloramphenicol 1% Eye Ointment	Apply a thin ribbon (1-1.5cm) of ointment to the lower eyelid of the affected eye(s) every 3 hours for up to 5 days. Continue treatment for 48 hours after symptoms resolve.	Pregnancy <ul style="list-style-type: none">Compatible Breastfeeding <ul style="list-style-type: none">Not recommended	<ul style="list-style-type: none">Discard 4 weeks after opening. This product does not need to be stored in the fridgeIf used with eye drops, use eye drops during day and ointment at night	<ul style="list-style-type: none">If under the age of 2If symptoms do not get better or worsen within 2-3 days, or if the patient becomes systemically unwell

Algorithm for the differential diagnosis and treatment of CONJUNCTIVITIS



January 2022

Oral Thrush (Candidiasis)

Revisit *Chapter 4 - The Gastrointestinal System* for more information

Introduction

There are two products you can supply as a pharmacist: Miconazole Gel and Nystatin Drops.

Other Options

- Prescription Only: fluconazole, itraconazole

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
<i>First line in >6 yo</i> Miconazole Oral Gel Daktarin, Decozol	Frequency: Apply FOUR times daily after food. Use for at least 1 week after symptoms resolve Infants (6-24 months): 1/4 of measuring spoon (or 20mg/kg/day) Adults: 1/2 of measuring spoon	<ul style="list-style-type: none">Warfarin (CYP interaction)Allergy to imidazole antifungalsAvoid in babies due to choking hazard	<ul style="list-style-type: none">Place gel onto the tongue using the measuring spoon supplied. Keep gel in the mouth for as long as possible before swallowing.Avoid placing gel at the back of the throat.In younger children, give dose in smaller amounts in different areas of the mouthIf dentures are a contributing factor, apply directly to the denture and leave overnight	<ul style="list-style-type: none">If no improvement after 2 weeks (symptoms usually improve after 1-2 days)If patient becomes systemically unwell (i.e fever)
<i>First line in <6 yo</i> Nystatin Oral Drops Nilstat	Frequency: Take 1mL FOUR times daily after food, usually for 7 days. Use for at least 2 days after symptoms resolve Infants >1 month old & adults: 1mL four times a day	<ul style="list-style-type: none">Allergy to nystatin Pregnancy & breastfeeding: Compatible	<ul style="list-style-type: none">Use the supplied measuring syringe to drop 1 ml of the medicine under the tongue and swish around for as long as possible before swallowing.	<ul style="list-style-type: none">If no improvement after 7 daysIf patient becomes systemically unwell (i.e fever)

Vaginal Thrush

Revisit Chapter 12 - Men & Women's Health for more information

Introduction

There are 5 pharmacist only products you can supply - generally vaginal creams and fluconazole tablet are pharmacist only.

- Patients should seek medical advice if symptoms return within 2 months or they have had 3 or more fungal infections within the past 6 months.
- Refer to GP if age <16 years or >60 years
- Note: if topical cream contains hydrocortisone (e.g. Micreme H, Canesten Plus) it is for external use (external manifestations of thrush) - do not use vaginally.

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Fluconazole 150mg one-dose capsule	<ul style="list-style-type: none"> One off dose capsule. Must be sold in manufacturer's OP containing 150mg or less as a single dose for the treatment of vaginal candidiasis 	Pregnancy: Contraindicated Breastfeeding: Okay <ul style="list-style-type: none"> Allergy 	<ul style="list-style-type: none"> Relief of symptoms is quicker with oral options Take with food and water Check for allergies Should work within a day Causes N&V 	<ul style="list-style-type: none"> If symptoms do not resolve after a day or get worse e.g. fever, patient becomes systemically unwell Allergic reaction develops e.g. itching, rash, swelling
Miconazole + Hydrocortisone <i>Micreme H</i> Topical Cream			<ul style="list-style-type: none"> <i>For external use only</i> as product contains hydrocortisone 	
Miconazole <i>Micreme</i> Vaginal Cream (2%) with Applicator	<ul style="list-style-type: none"> 1 applicatorful for 7 days before bed (regardless of whether symptoms disappear) 	Cautions <ul style="list-style-type: none"> For vaginal use only Cream reduce effectiveness of latex condoms If pregnant: pessaries may be preferred. If inserting cream with applicator - ensure no contact with the cervix If pregnant: topical clotrimazole is not recommended over oral clotrimazole. Will generally cause itching, swelling and a burning sensation. 	<ul style="list-style-type: none"> Wash hands and insert one applicator filled with cream into the vagina while lying on your back as far as it will comfortably go Slowly press the plunger of the applicator in to apply the cream. Wash applicator thoroughly before reusing Symptoms resolve within a week 	<ul style="list-style-type: none"> If symptoms worsen or persist. Treatment longer than 7 days may be required - refer to doctor
Nystatin <i>Nilstat</i> Vaginal Cream (100,000 IU/5g)	<ul style="list-style-type: none"> 1 applicatorful, TWICE daily for 14 days 		<ul style="list-style-type: none"> Wash hands before use. Similar to Miconazole, fill the applicator up with cream (5g) and insert high into the vagina ONCE or TWICE daily. Applicator can be reused. Wash thoroughly before reusing. 	<ul style="list-style-type: none"> If symptoms worsen or persist after 3 days Treatment longer than 14 days might be required - refer to doctor
Clotrimazole <i>Canesten, Clomazol</i> <ul style="list-style-type: none"> Vaginal Cream (1%); 6 Days Vaginal Cream (2%); 3 Days Vaginal Cream (10%); 1 Day - Canesten 	Depends		<ul style="list-style-type: none"> Wash hands and insert one applicator filled with cream into the vagina while lying on your back as far as it will comfortably go. Slowly press the plunger of the applicator in to apply the cream. DISPOSE applicator after use. 	<ul style="list-style-type: none"> If symptoms worsen or persist after 4 days Longer treatment may be needed.

Influenza Antiviral

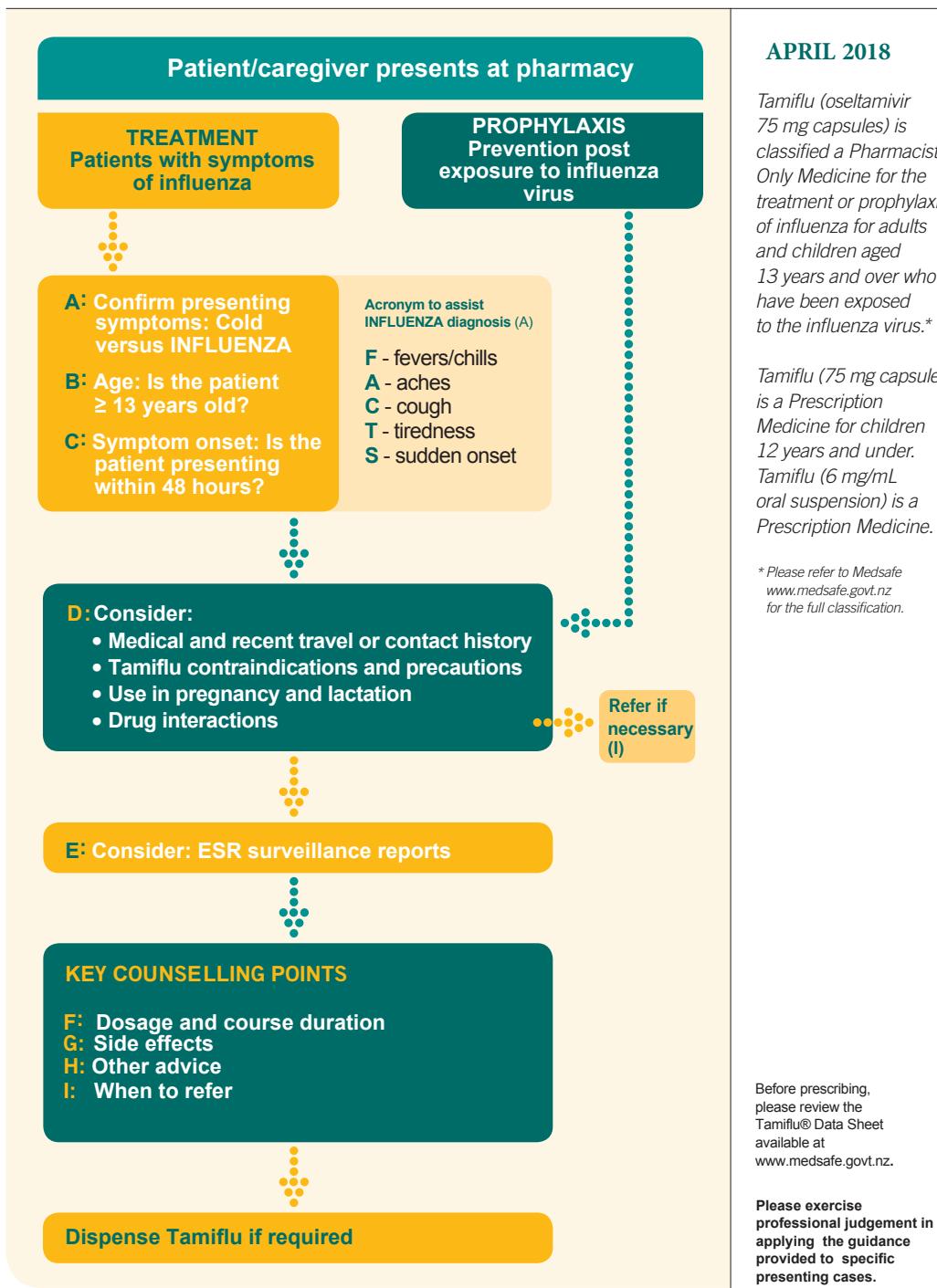
Revisit Chapter 7 - *The Respiratory System* for more information

Introduction

Tamiflu is the pharmacist only product you can supply.



Tamiflu® (oseltamivir) Pharmacist Protocol



Smoking - NRT

Introduction

Please note, NRT requires pharmacist training, not accreditation.

Medications	Eligibility & Dosing	Counselling
Patches (7, 14, 21mg)		<ul style="list-style-type: none"> Apply patch to clean, dry, and hairless skin Remove the old and apply the new patch daily, at alternating sites (hip, chest, upper arm) If pregnant: intermittent therapy (gum/lozenge) is preferred but if patient is experiencing pregnancy related N&V then patches are recommended but should be removed before going to bed
Gums (2, 4mg)	Course training required Funded to provide 3 month's supply in monthly lots	<ul style="list-style-type: none"> Bite to release the peppery taste, then rest in the side of the mouth (between cheek and gum) Chew again when the taste starts to fade Chew for about 30 minutes then discard
Lozenge (1, 2mg)		<ul style="list-style-type: none"> Suck to release the peppery taste, and then rest in the side of the mouth (between the cheek and gum) Suck again when the taste starts to fade



Guide to Prescribing Nicotine Replacement Therapy (NRT)

August 2021

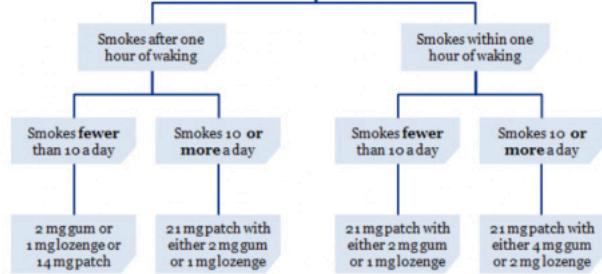
Step 1: Explain how NRT works and the products available

NRT provides some of the nicotine that a person gets from smoking. Nicotine is the addictive part of cigarettes but does not cause the harm associated with smoking. NRT works to reduce craving and other withdrawal symptoms associated with stopping smoking.

Step 2: Assess the time when the first cigarette is smoked (see note 1)

Step 3: Assess how many cigarettes are smoked (see note 2)

Step 4: Recommend which product and dose to use and explain how to use the product (see below)



Subsidised NRT products

Product information	Patch*	Gum*	Lozenge*	Inhalator	Mouth spray
Instructions for correct use	Three strengths (21 mg, 14 mg, and 7 mg) Apply patch to clean, dry and hairless skin. Remove the old and apply new patch daily, alternating sites. Some redness under the patch may occur – this is normal. The patch can be removed overnight if sleep is disturbed.	Two strengths (4 mg and 2 mg) Recommend regular use. Bite to release the peppery taste and then rest in the side of the mouth (between cheek and gum). Chew again when the taste starts to fade. Chew for about 30 minutes then discard.	Two strengths (2 mg and 1 mg) Recommend regular use. Suck to release the peppery taste, and then rest in the side of the mouth (between cheek and gum). Suck again when the taste starts to fade.	15 mg cartridge Recommend regular use. Puff for 20 minutes each hour and replace the cartridge every 3 hours. People tend to under-dose (1 cigarette puff = 10 inhalator puffs).	1 mg nicotine/spray dose Recommend regular use, but it can also be used when craving occurs. Prime the spray and point nozzle into the mouth, spraying towards the side of the mouth. For best results, do not swallow for a few seconds after spraying.

* Patches, gum and lozenges are subsidised if supplied on prescription or via the Quit Card programme. Otherwise, all NRT products (including the inhalator and mouth spray) can be purchased over the counter from supermarkets for the normal retail price. Community pharmacies can also provide subsidised NRT without a prescription and many stop-smoking providers supply NRT at no cost to clients.

ACCREDITATION-REQUIRED PHARMACIST ONLY MEDICINES

Description

These medicines require accreditation for pharmacists to be able to supply. Recording of Pharmacist Only Sale medicines must be taken still:

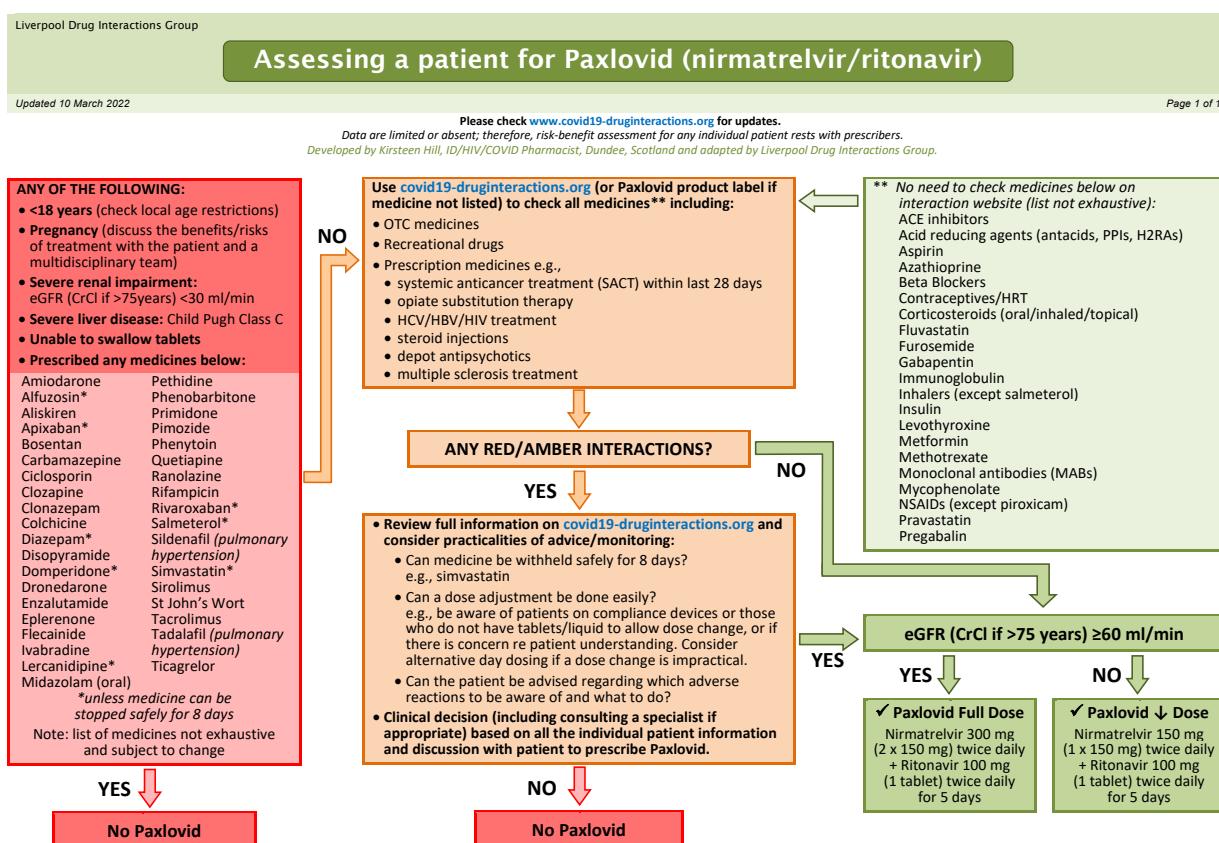
- Name and address of purchaser
 - Name of pharmacist
 - Date
 - Name and quantity of the medicine sold
 - Directions for use

COVID-19 Antivirals

Revisit *Chapter 7 - The Respiratory System* for more information

Introduction

Accredited pharmacists can supply from these 2 COVID-19 antivirals: Paxlovid or Molnupiravir.



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Oral Antiviral Assessment Summary

Name

Address



PHARMACEUTICAL SOCIETY
of New Zealand Incorporated

Phone number (preferably mobile)

Age (over 18 years) NHI

Pregnant (or possibly pregnant) NO / YES = Refer

Confirmed/symptomatic COVID-19, < 5 days AND NO supplemental O₂

YES/ NO = NOT eligible

IF ELIGIBLE FROM ABOVE CRITERIA – THEN USE PHARMAC ACCESS CRITERIA TOOL		
Eligible		Not eligible
ASSESS SYMPTOMS – MUST USE IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
• Patient has mild/moderate symptoms	• no significant clinical concern regarding severity of illness or possibility of a co-existent illness	• Patient referred (GP/Secondary Care)
ASSESS RENAL FUNCTION for nirmatrelvir/ritonavir - IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
• Renal Function eGFR > 60 mL/min	• Renal function eGFR < 30 mL/min	
• Renal function eGFR ≥ 30 to < 60 mL/min	• NO information	
ASSESS LIVER FUNCTION for nirmatrelvir/ritonavir - IN CONJUNCTION WITH CLINICAL DECISION PATHWAY		
No severe liver disease	• Severe liver disease	
REVIEW PATIENT MEDICATION HISTORY/IDENTIFY DRUG INTERACTIONS for nirmatrelvir/ritonavir MUST USE IN CONJUNCTION WITH ALL AVAILABLE CLINICAL RECORDS AND CLINICAL DECISION PATHWAY		
• GREEN - NO Interactions identified	• RED - Interaction cannot be managed	
• AMBER - Interaction can be managed with GP	• Not enough information	
SUPPLY DECISION		
• Nirmatrelvir/ritonavir supplied	• Molnupiravir supplied	• NO supply - referred
• GP Consultation notes (if required)		
PHARMACY DISPENSING SYSTEM DOCUMENTATION (NOT as an OTC product)		
• Label produced	• Actions documented (e.g. GP consultation, supply declined & reasons))	
CCCM DOCUMENTATION		
• Patient found or new patient created (NHI)	• Check timeline	• Send to GP
• Add GP Practice name and Practice ID (EDI)	• Clinical note added	• LOG OUT!
TELEHEALTH COUNSELLING		
• Patient understands how to take the medicine safely and appropriately	• Patient information leaflet supplied	
DELIVERY DETAILS CONFIRMED		
• Pickup (by non-isolating person)	• Delivery required	
Pharmacist	Date	

Insomnia

Revisit *Chapter 16 - The Neurologic System* for more information

Introduction

Accredited pharmacists can supply melatonin and first generation antihistamines.

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Melatonin Immediate release: <3mg Modified releases: <2mg	<ul style="list-style-type: none">• SLEEP Questionnaire <p>Accreditation required</p> <ul style="list-style-type: none">• For primary insomnia• Age ≥ 55 years• Up to 13 week supply• Sold in manufacturers original pack• Take ONE tablet OD, 1-2 hours before bedtime• Take with food	<ul style="list-style-type: none">• Secondary causes of insomnia e.g. underlying mental health, underlying causative medicines	<ul style="list-style-type: none">• Modified release: Swallow whole, do not crush or chew• May take a few days or longer for benefit• Needs to be taken every night to be effective; aids in getting back to a good sleep habit• Do not drink alcohol• ASLEEP sleep hygiene• It is not funded - \$40-\$65 for a pack of 30 tablets (only funded if it is a specialist prescription for insomnia secondary to neurodevelopmental disorders and under 18).	<ul style="list-style-type: none">• Moderate to severe depression or anxiety• Obstructive sleep apnoea• Alcohol misuse• Restless leg syndrome• Shift work• Suspicion of recreational use
First Generation Antihistamines	<ul style="list-style-type: none">• POM for insomnia for >2 years of age (EXCEPT cyclizine)• Max 10 doses <ol style="list-style-type: none">1. Chlorpheniramine (Histafen)2. Cyclizine (Nausicalm)3. Diphenhydramine (Unisom)4. Doxylamine (Dozile)5. Promethazine (Allersoothe)6. Trimeprazine			

Oral Contraceptives

Revisit *Chapter 12 - Men & Women's Health* for more information

Introduction

Accredited pharmacists can supply oral contraceptives.



PRACTICE GUIDELINES

Pharmacist-Supply of Selected Oral Contraceptives (SOCs)

2 Objectives

2 Regulatory Requirements

- | | |
|---|---------------------------------------|
| 2 Medicines Classification | 2 SOC available for Pharmacist Supply |
| 2 "Emergency Supply" of Medicines: Medicines Regulation 44(m) | |

3 Combined Oral Contraceptives (COCs)

3 Progesterone Only Pills (POPs)

4 Service Provision and Professional Obligations

- | | |
|--|----------------------|
| 4 Privacy | 4 GP Notification |
| 4 Informed, Person-Centred Care | 5 Quantity of Supply |
| 4 Documentation of Assessment and Supply | |

5 Assessment Guide for the Pharmacist Provision of SOCs

- | | |
|------------|------------------|
| Background | The Consultation |
|------------|------------------|

6 Checking Eligibility: Is the woman eligible for SOC supply?

- | | |
|---|--|
| 6 Combined Oral Contraceptive Pill (COC) User | 6 Previous medical practitioner initiation |
| 6 Progestogen Only Pill (POP) User | 6 Contraception indication only |
| 6 Switching between SOC formulations | 7 Example Eligibility Scenarios |
| 6 Switching between SOC brands | 7 Special Considerations for Postpartum Oral Contraceptive Use |
| 6 Non-permitted Oral Contraceptives | |

8 Checking Clinical Risk for Continuing or Restarting SOC

- | | |
|---|--|
| 8 Potentially Significant Adverse Events | 10 Body Mass Index (BMI) |
| 8 Current Health Status | 11 Cardiovascular Risk Precautions – when combined |
| 9 Contraindicated Medical Conditions | 11 Smoking |
| 9 Drug Interactions / Contraindicated Medicines | 11 Migraine |
| 10 Cardiovascular and Stroke Risk (COCs) | 11 High cholesterol or other dyslipidaemia |
| 10 Is it safe to continue a COC? | 11 Family History of Heart Disease / Stroke |
| 10 Diabetes | 11 Age |
| 10 Blood Pressure (BP) | |

12 Appropriate Use – Is it safe to supply SOCs?

12 Counselling: information and advice

- | | |
|---|--------------------------|
| 12 Pill Teaching – Checking Understanding | 13 The Missed Pill Rules |
| 12 Starting or Re-starting the POP or COC after a break | 14 Adverse Effects |

14 Sexual Health Screening

14 Resources Supporting Verbal and Written Information

15 Resupplies

- | | |
|--|----------------------------------|
| 15 Is it safe to resupply? | 15 Sexual Health Screening Check |
| 15 Check Compliance and Changes to Health Status | 16 Useful Resources |

16 References



COMBINED ORAL CONTRACEPTIVE (COC) CHECKLIST

Ethinylestradiol (20 µg or 35 µg) + levonorgestrel/norethisterone. Same formulation as prescribed or see guidelines.
Name: _____ DOB: _____ Age: _____ (16-39 years only) NHI: _____

Last doctor visit for o/c: _____ (must be ≤ 3 yrs) Seen a doctor at least twice for an o/c? Yes No

Current user (also ask further questions below)

Current COC: _____ Compliance issues? (Consider pregnancy, LARCs) _____
Any side effects/concerns? _____ Use for contraception: Yes No
 Yes No

Restarting oral contraceptive (also ask further questions below)

Previous o/c: _____ Date when last used: _____
 Discuss contraceptive options. Unexplained vaginal bleeding? Yes No
Possibly pregnant, lactating, ≤42 days post-partum, allergy to o/cs? Yes No

Cardiovascular and stroke risk

Any heart problems/stroke/diabetes? Yes No
Blood pressure: _____ [no supply if systolic ≥140 or diastolic ≥90, or on BP meds]
BMI ≥ 35 Calculation if necessary: weight(kg)/height(m)²: _____ Yes No
Migraine with aura? Yes No

	Yes*	No
Daily smoker current or in the last year?		
Migraines without aura?		
Known high cholesterol or other dyslipidaemia		
BMI 30-34.9		
Heart disease/stroke in father/brother <55 years or mother/sister <65 years?		
Age 35-39		

* More than one "yes" in the table above = no supply.

VTE risk (BMI see above)

Ever had thrombosis/blood clot in veins (DVT) or lungs? Yes No
Mother/father/sister/brother had thrombosis/blood clot in veins or lungs? Yes No
Immobile, planning major surgery? Yes No

Other health

History of breast cancer, liver or gall bladder disease, problems with blood circulation/clotting, organ transplant, lupus, severe Crohn's disease, bariatric surgery? Yes No
Medication taken: _____
[No supply if currently on: BP meds, HIV meds, anti-epileptics, St John's Wort, rifampicin, rifabutin, other CYP3A4 inducers]

Notes from consultation: _____

Appropriate to supply? Yes No Product supplied: _____ Quantity: _____
Woman's address: _____ Phone number: _____
Dr: _____ Inform doctor of supply unless opt out: _____
Pharmacist signature: _____ Name: _____ Date: _____

Advice required: complete next page. Complete this form annually, and resupply form in between. Maximum 6 months' supply. Red/black shaded boxes mean do not supply, refer to doctor as appropriate.

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PROGESTOGEN ONLY PILL (POP) CHECKLIST

(use at first pharmacist supply then annually)

- Supply of levonorgestrel, norethisterone, or desogestrel alone.
- Use the same formulation as prescribed before. However, change is permitted when used for post-partum use or a woman from overseas where the currently used o/c is not available in NZ.

Age: _____ (16-52 years only) Last doctor visit for o/c supply: _____ (must be ≤ 3 yrs)

Seen a doctor at least twice for an oral contraceptive? Yes No

Current user of the same POP (also ask further questions below)

POP used: _____ Any side effects/concerns? _____
Any problems missing or delaying pill taking? (consider pregnancy) _____
New or worsening headaches or migraines with POP use? Yes No
Post-partum? (If post-partum, supply and refer to the doctor for further contraceptive advice.) Yes No

Changed oral contraceptive - only if post-partum or if last prescribed overseas (also ask questions below)

Previous o/c: _____ Date when last used: _____
Any side effects or concerns with previous o/c? _____
Discussed contraceptive options?
Unexplained vaginal bleeding?
Possibly pregnant?
Allergy to progestogens? Yes No
 Yes No
 Yes No
 Yes No

Cardiovascular and stroke risk

History of heart disease or stroke? Yes No

Other
Recently had thrombosis/blood clot in veins (DVT) or lungs? Yes No
History of breast cancer, severe liver problems, lupus, organ transplant, severe Crohn's disease, or bariatric surgery? Yes No
Medication taken: _____
[No supply: anti-epileptics, St John's Wort, CYP3A4 inducers]

Notes from consultation: _____
Appropriate to supply? Yes No Product supplied: _____ Quantity: _____
Woman's name: _____ Address: _____
NHI number: _____ Phone number: _____ Dr: _____
Inform doctor of supply unless opt out: _____
Pharmacist signature: _____ Name: _____ Date: _____
Maximum 6 months' supply.
Advice required: complete next page. Use this form annually, and resupply form in between. Red/black shaded boxes mean do not supply, refer to doctor as appropriate.

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Emergency Contraceptive Pill (ECP)

Revisit *Chapter 12 - Men & Women's Health* for more information

Introduction

Accredited pharmacists can provide the morning after pill.

Other Options

- Prescription: Copper IUD

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Levonorgestrel 1.5mg Postinor-1	Accreditation required ECP Questionnaire <ul style="list-style-type: none">Unprotected sex within 72 hours>70kg or BMI >26: 2 tablets as a single doseCan take with food to reduce N/V	Breastfeeding: Okay, but can express milk prior to feeding	<ul style="list-style-type: none">If vomiting or severe diarrhoea occurs within 3 hours of taking, take a second doseNext period may be late or early(Follow up with GP/family planning within the next 2-3 weeks for STI assessment)	<ul style="list-style-type: none">If >72h after unprotected sex, refer for copper IUDIf next period is >5 days late, pregnancy is a possibility

Consultation Record

Pharmacy Guild of New Zealand (Inc) October 2017

Emergency Contraceptive Pill

NAME: _____ SCRIPT NO. _____

ADDRESS: _____

WEIGHT: _____

HEIGHT: _____

BMI: _____

DISCLAIMER: This document should be used in conjunction with the Practice Guidelines for Pharmacist supply of the Emergency Contraceptive Pill (ECP).

QUESTIONS	RESPONSE	COMMENTS
Is the ECP for your own use? If not, who is it for?		
Have you had unprotected sex or possible contraceptive failure?		
How long ago did this happen?		
When did you have your last period?		
Was it lighter, shorter or different than usual?		
Have you had unprotected sex at any other time since your last period?		
Have you used the ECP already since your last period?		
Are you taking any other medicines or herbal products - prescribed or that you have purchased? Refer to Guidelines if patient is taking any of the below medicines. Enzyme inducers - barbiturates, primidone, phenytoin, carbamazepine, topiramate, rifampicin, rifabutin, ritonavir, nevirapine, neflavav, tacrolimus, griseofulvin, St John's wort. Ciclosporin - toxicity increase		
Do you have, or have you ever had, any medical conditions? e.g. Rovell disease, severe liver disease, high blood pressure, diabetes, heart disease/stroke, breast cancer?		
Have you ever had an allergic reaction to, or vomited after taking, the ECP?		
Are you breastfeeding?		

PHARMACIST RECORD

ECP supplied (1.5mg) ECP supplied (3mg) Patient referred to GP or FPC
 ECP not appropriate Informed consent given to supply ECP YES NO

Pharmacist _____ Date _____



ADVICE CHECKLIST

THE ECP DOES NOT PREVENT PREGNANCY IN EVERY SITUATION

- It is 95% effective if used within 24 hours of unprotected sex.
- It is 85% effective if used within 25 – 40 hours of unprotected sex.
- It is 56% effective if used within 49 – 72 hours of unprotected sex.

TIMING

- The ECP is most effective when it is taken as soon as possible and no later than 72 hours after unprotected sex.

- The ECP is unlikely to be effective in women who weigh more than 70kg or have a BMI greater than 26. If you weigh more than 70kg or have a BMI greater than 26 a copper IUD would provide more effective emergency contraception. Please see your doctor or family planning clinic.

POSSIBLE SIDE EFFECTS

- Nausea, tiredness, headache, dizziness, breast tenderness, vomiting. These should resolve within a few days.
- If vomiting occurs within three hours of taking the ECP, another dose should be taken immediately. You will need to obtain another supply of the ECP.

THE ECP IS FOR EMERGENCY USE ONLY

- It is not a substitute for regular contraception.

USE OF CONTRACEPTION AFTER TAKING THE ECP

- Barrier method recommended until your next period starts and regular method of contraception begins.
- If using the contraceptive pill, keep taking the hormonal pills as normal and use additional barrier protection for seven days.
- If there are less than seven hormonal pills left in the packet, you should continue with the next pack omitting the seven day break or placebo (sugar) tablets.

POSSIBLE CHANGE TO TIMING OF NEXT PERIOD

- It may be a few days earlier or later than usual.

SEE YOUR DOCTOR OR FAMILY PLANNING CLINIC

- If your next period is unusually light or heavy, more than 5 days late or, for those taking oral contraceptives, there is no bleeding in the pill-free interval.
- If you have any lower abdominal pain.

THE ECP DOES NOT PROTECT AGAINST SEXUALLY TRANSMITTED INFECTIONS (STIs)

- If you have any concerns, see your doctor or Family Planning Clinic.

RECOMMEND FOLLOW-UP APPOINTMENT WITH DOCTOR OR FAMILY PLANNING CLINIC

- about two to three weeks after taking the ECP to check that it has worked, to screen for STIs (if indicated) and to discuss regular methods of contraception.

BREASTFEEDING

- While the ECP is not considered harmful, to reduce the amount the baby ingests, either express milk immediately before taking the ECP or take it immediately after feeding the baby.

PATIENT INFORMATION LEAFLET PROVIDED

Erectile Dysfunction (ED)

Revisit Chapter 12 - Men & Women's Health for more information

Introduction

Accredited pharmacists can supply Viagra.

Other Options

- Prescription only: Tadalafil, vardenafil, intracavernosal injection of alprostadil

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Sildenafil & other analogues Viagra, Vedafil	<p>Cardiac Risk Assessment</p> <p>Vedafil Questionnaire</p> <p>Accreditation required</p> <ul style="list-style-type: none"> Males aged 35-70 ≤100mg tablets ≤12 solid dosage units In manufacturer's original pack May increase to 100mg dose if starting dose is ineffective If maximum dose of 100mg doesn't work, try up to 6 different times then see GP <p>Note: Inform GP unless patient declines</p>	<ul style="list-style-type: none"> CV problems (stroke, unstable angina, MI, HTN, hypotension) Concomitant use of nitrates Penile deformity (e.g. Peyronie's disease) 	<ul style="list-style-type: none"> Take dose 1h before sexual activity — sexual stimulation is still required Maximum 1 dose in 24 h Take on an empty stomach — effect may be delayed if taken with food Avoid grapefruit and its juice May take 3-8 attempts (2-8 weeks) to attain maximum effect 	<ul style="list-style-type: none"> If erection maintains longer than 4 hours If priapism (prolonged, painful erection) Sudden loss of vision or hearing

Patient Assessment	Page 2 Supply
21/07/20 15:31	
Date: 21/07/20 15:26 NHI: Pharmacy Name: School of Pharmacy Phone: 03 479 7280	
<p>Vedafil</p> <p>Patient: NHI: DOB: Pharmacy Details: Name: School of Pharmacy Address: 18 Frederick Street Phone: 03 479 7280 Fax: 03 479 7034</p> <p>To enable your pharmacist to correctly assess whether Vedafil® is suitable for you, please tick to confirm that the information you have provided during this assessment is correct and complete</p> <p>To ensure your GP is aware of your health, we would like to contact your GP to advise of this assessment and supply of Vedafil®. If you do not want your GP to be contacted please tick here:</p> <p>GP Name: Phone: Fax: Facility Name:</p> <p>Patient Signature:</p>	
<p>Product Selection</p> <ul style="list-style-type: none"> A starting dose of 25mg is required for patients <ul style="list-style-type: none"> Over 65 years of age Overweight individuals (e.g. doxazosin) Taking erythromycin, ketoconazole or itraconazole and thiazide according to response/tolerance. For all other eligible patients, a starting dose of 50mg is recommended, and 100mg can be offered to established patients requiring a higher dose. A pack size of 4 tablets is recommended for patients using Vedafil® for the first time. Larger pack sizes may be recommended for patients who previously have used Vedafil® successfully. Supply is restricted to maximum of 12 tablets at any one time. <p>Vedafil® to be supplied:</p> <p><input checked="" type="checkbox"/> 25mg <input type="checkbox"/> 50mg <input checked="" type="checkbox"/> 100mg</p> <p>Re-Supply (please tick)</p> <p>Changes in health? Changes in medication? Vedafil® working with no adverse effects?</p> <p>Comments: A full assessment is required every 12 months or sooner if clinical status of the patient has changed since last assessment.</p>	

Patient Assessment	Page 1 Screening
Age between 35 & 70 yrs <input type="checkbox"/> Age: DOB: If < 35 yrs or > 70 yrs <input type="checkbox"/>	
<p>Has erectile dysfunction (ED)? <input type="checkbox"/> Discuss the patient's concerns and consider potential risk factors (e.g. relationship problems, anxiety, depression). Record details.</p> <p>Used ED medication before? <input type="checkbox"/> If previous use of ED medication has not been effective, if significant adverse events occurred. <input type="checkbox"/></p> <p>Did it work? Any adverse effects? <input type="checkbox"/></p>	
<p>Medical History (please tick)</p> <p>Diabetes: High cholesterol (uncontrolled or untreated) <input type="checkbox"/> Unable to walk briskly for 5mins or walk uphill without becoming breathless or getting chest pain; OR advised by Doctor to avoid exercise including sexual activity. <input type="checkbox"/></p> <p>Current smoker: Severe liver dysfunction <input type="checkbox"/> Previous heart attack/stroke/TIA <input type="checkbox"/></p> <p>Severe kidney dysfunction <input type="checkbox"/> History of angina <input type="checkbox"/></p> <p>Blood disorders (sickle cell disease, leukaemia, multiple myeloma) <input type="checkbox"/> Previous coronary intervention (e.g. angioplasty, bypass surgery, valve replacement) <input type="checkbox"/></p> <p>Any deformity of the penis (e.g. Peyronie's disease) <input type="checkbox"/> Personal or family history of low eye disorders, excluding glaucoma and cataracts (e.g. Retinitis pigmentosa) <input type="checkbox"/></p>	
<p>Blood Pressure mmHg / mmHg Restarting heart rate bpm If <110/70 or >160/95 <input type="checkbox"/> If <50bpm or >100bpm <input type="checkbox"/></p>	
<p>Other medicines, either prescribed or purchased?</p> <p>Details: Nitrates, e.g. glyceryl trinitrate, isosorbide salts, amyl nitrates, Pulmonary arterial hypertension (PAH) treatments, ED medications including other PDE5 inhibitors, Nitrofurantoin or saquinavir <input type="checkbox"/></p> <p>Two or more antihypertensives. <input type="checkbox"/></p>	
<p>Any other health concerns or comments?</p> <p>Details: If any of the following are being taken: <input type="checkbox"/> REDUCED DOSE is required. Alpha blockers, erythromycin, ketoconazole, itraconazole <input type="checkbox"/></p>	
<p>Vedafil is a suitable treatment for your patient. You can proceed with supplying Vedafil</p>	

This document was prepared by Dr Natalie Gaud (sponsored by Douglas Pharmaceuticals Ltd) in collaboration with the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and Green Cross Health Limited. For further detail refer to approved training content, associated assessment forms, and relevant data sheet. June 2020

Migraines

Revisit Chapter 16 - The Neurologic System for more information

Introduction

Accredited pharmacists can supply sumatriptan & prochlorperazine:

Other Options

- General: Paracetamol, NSAIDs
- Prescription Only: Rizatriptan, Zolmitriptan, opioids, β -blockers, TCA, anti-epileptics
- N/V: Metoclopramide, domperidone

Medications	Eligibility & Dosing	Counselling	Referral
Sumatriptan Sumagram	Accreditation Required Sumagram Questionnaire Migraine Disability Assessment Test • 2 tablets	<ul style="list-style-type: none"> Take ONE dose at the first sign of a migraine attack If symptoms improve but return, take a second tablet after 2 hours. Do not take more than 2 tablets for the same attack If not effective, do NOT take a second tablet Maximum 300mg in 24 hours May cause tingling, dizziness, drowsiness, flushing, fatigue Swallow whole, do not crush or chew Take with or without food, and a large glass of water May cause sleepiness Effect seen within 30 min 	If frequent migraines i.e. >6 per month Tightness in any part of the body
Prochlorperazine For N/V	Accreditation Required • POM for N/V associated with migraines • 10 buccal tablet pack	<ul style="list-style-type: none"> Take 1-2 tablets twice daily Place tablet between upper lip and gum, and leave to dissolve Best not to eat or drink fluids while the tablet is dissolving as you may swallow portions or all of the tablet Effect seen in 60 min 	

Sumagran Active
Fast effective migraine relief

PHARMACIST NOTES

Sumagran Active is only suitable where there is a clear diagnosis of migraine.

2 If a patient has taken a sumatriptan containing preparation previously, it is likely their doctor has confirmed the diagnosis of migraine.

If the patient answers 'Y' to Q1 or Q2, pharmacist is not required to rely on the answers given to Q3 to confirm diagnosis.

3 To confirm diagnosis of migraine, the criteria in Q3 + must be met:

a. The patient must have reported or recurrent headache attacks lasting 4-72 hours untreated or successfully treated **and**
b. The patient must have answered yes to at least TWO of these to be diagnosed as having a migraine **and**
c. The patient must also answer YES to at least 2 of the following questions to be diagnosed as having a migraine:

Note: Patients who do not answer YES to the headache, headache duration or frequency questions may include mild disturbances such as brilliant flickering lights or blurring of vision or sensory disturbances such as numbness or weakness of the limbs.

If the patient answers 'Y' to Q4, refer to doctor to confirm migraine diagnosis.

4 If the patient can only be referred to a doctor who has a stable, well-established pattern of symptoms.

5 If the patient answers 'Y' to any of Q5, refer to doctor.

a. Refer to doctor if patient complains of any signs and symptoms:
- unilateral motor weakness; double vision; tinnitus; clonic or co-ordinated movements; change in consciousness; or weakness in one part of the body.
- any type of headache, including tension and/or migraine.
b. If the pattern of onset of symptoms has changed, attacks have become more frequent, more persistent, or more severe; or in patients who do not respond completely between attacks.

6 If the patient has answered 'Y' to any of Q6, refer to doctor.

a. Refer to doctor. Safety & effectiveness outside this age group has not been established.
b. Refer to doctor. Category B3. Sumagran Active is not to be used in pregnancy or where breastfeeding unless on the advice of the doctor.
c. Not suitable.
d. Not suitable. Possible cross allergy to sulfer (e.g. sulfonamides).

7 If the patient has answered 'Y' to any of Q7, refer to doctor.

a. Not suitable if answering 'Y' to any of these questions. The use of sumatriptan in these medical conditions is contraindicated. Refer to data sheet for further information.

8 Medicinal Interactions:

a. Ergotamine (including methysergide) containing or ergot-type medication within the past 24 hours. Sumagran Active is not suitable.
b. Serotonin reuptake inhibitor (SSRI) within the past 2 weeks. Sumagran Active is not suitable.
c. Monoamine oxidase inhibitor (MAOI) within the past 2 months. Sumagran Active is not suitable.
d. Oral contraceptive pill: refer to doctor if the onset of the migraine is recent or if there is worsening of attacks (may be at higher risk of stroke).
e. St John's Wort: although there is no evidence, it is possible that an interaction between sumatriptan and the herbal remedy St John's Wort (Hypericum perforatum), which may result in an increase of side effects.
f. SSRI: warn the patient to see their doctor if they develop weakness and uncoordination after taking Sumagran Active.

9 Counselling Points (as per Sumagran Active Data Sheet):

Remind the patient to read the enclosed leaflet for further information.

Dosage:

What at least 2 tablets over the first tablets taken. Do not take any other triptan to treat the same attack. Swallow whole with a glass of water. Take with or without food.

Common side effects (frequency > 1%) are: tingling; dizziness; drowsiness; flushing; fatigue; feelings of weakness. These side effects are usually temporary and may affect any part of the body including the chest; pains; sensations of heaviness, heat, pressure or tightness.

Caution is recommended in patients performing skilled tasks, e.g. driving or operating machinery. Drowsiness may occur as a result of migraine or its treatment with sumatriptan.

Overactive bladder symptoms such as urge incontinence and urinary frequency and sensitivity to light and sound. Clinical response for relief of migraine headache begins around 30 minutes following a 50mg oral dose. Sumatriptan tablets are effective in treating menstrual migraine i.e. migraine without aura that occurs between 3 days prior and up to 5 days post onset of menstruation.

Expectations:

Sumagran Active is a fast acting triptan that relieves symptoms of migraine and sensitivity to light and sound.

TAPS DA 1828FR-75

Sumagran Active
Fast effective migraine relief

Mylan
Sister Health for a Better World

PRIMARICAL SOCIETY OF THE PHARMACEUTICAL INDUSTRY

Patients Name _____
Address _____
Phone _____

Circle or mark as appropriate

1 Have your symptoms been previously diagnosed by a doctor as a migraine Y N

2 Have you ever taken sumatriptan before? Y N

3 To confirm symptoms of migraine:

a. How long have your previous migraine headaches lasted? _____ hours
b. Do you experience any of the following types of headache pain?
- Unilateral (one-sided) headache pain Y N
- Throbbing or pulsating pain Y N
- Pain worsened by movement / physical activity Y N
- Moderate to severe in intensity / interferes with normal daily life Y N
c. Do you have any of the following symptoms?
- Sensitive to light and/or sound Y N

4 Is this the first time you have had these symptoms? Y N

5 Are your symptoms different from your previous migraines? If so, list symptoms in the comment box below:
a. Do you feel that this migraine is worse than your previous migraines? Y N

6 Patient Information:

a. Are you under 18 years or over 65 years of age? Y N
b. Are you pregnant? Is there a possibility that you may be pregnant, or are you breastfeeding? Y N
c. Do you have any other health problems? If so, list symptoms in the comment box below:
d. Do you have an allergy to sulfur, including sulfonamides, aspirin or non-steroidal anti-inflammatory drugs? Y N

7 Medical History. Do you have, or have you ever had any of the following:
a. Heart disease, or any other problems affecting your heart? (Including vascular problems, uncontrolled blood pressure, angina) Y N
b. A stroke or mini-stroke Y N
c. Headaches that are constant or continuous? Y N
d. Gastrointestinal problems? Y N

8 Medicinal Interactions:

What other medicines, including herbal remedies, have you taken in the past 2 weeks (especially medication used for migraine or depression, and the oral contraceptive pill)?

9 Counselling Points - Discuss:

a. Dosage
b. Side effects
c. Patient expectations for product

Comments: _____

The Migraine Disability Assessment Test

The MIDAS (Migraine Disability Assessment) questionnaire was put together to help you measure the impact your headaches have on your life. The information on this questionnaire is also helpful for your primary care provider to determine the level of pain and disability caused by your headaches and to find the best treatment for you.

INSTRUCTIONS

Please answer the following questions about ALL of the headaches that you have had over the last 3 months. Select your answer in the box next to each question. Select zero if you did not have the activity in the last 3 months. Please take the completed form to your healthcare professional.

1. On how many days in the last 3 months did you miss work or school because of your headaches?

2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)

3. On how many days in the last 3 months did you not do household work (such as housework, home repairs and maintenance, shopping, caring for children and relatives) because of your headaches?

4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)

5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

Total (Questions 1-5)

What your Physician will need to know about your headache:

A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.)

B. On a scale of 0 - 10, on average how painful were these headaches? (where 0=no pain at all, and 10+ pain as bad as it can be.)

Scoring: After you have filled out this questionnaire, add the total number of days from questions 1-5 (ignore A and B).

MIDAS Grade	Definition	MIDAS Score
I	Little or No Disability	0-5
II	Mid Disability	6-10
III	Moderate Disability	11-20
IV	Severe Disability	21+

If your MIDAS Score is 6 or more, please discuss this with your doctor.

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UTIs

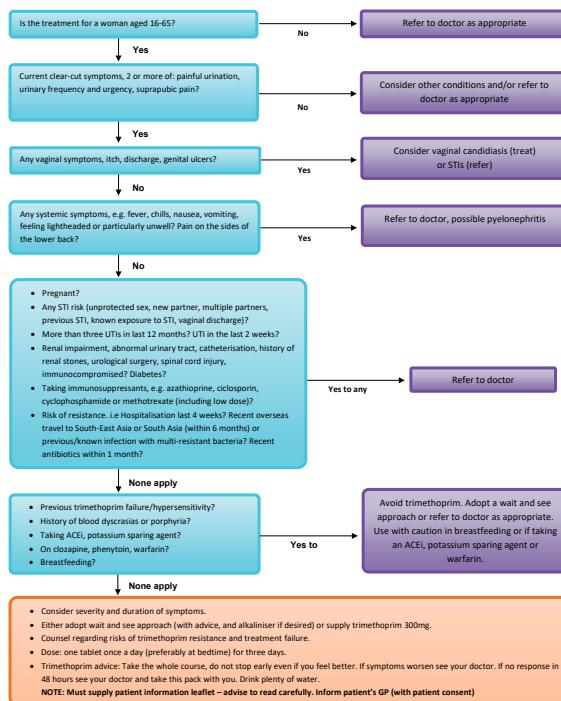
Revisit *Chapter 10 - The Renal System* for more information

Introduction

Accredited pharmacists can supply Trimethoprim for UTIs - and recently, Nitrofurantoin.

Medications	Eligibility & Dosing	Contraindications	Counselling	Referral
Trimethoprim	<p>PSNZ UTI Assessment</p> <p>Accreditation required</p> <ul style="list-style-type: none"> 1 tablet (300mg) once daily for 3 days (preferably at bedtime) <p>(Pregnancy: continue for 7 days in pregnancy, but avoid in first trimester)</p>	• Complicated UTI	• Drink plenty of water	<ul style="list-style-type: none"> If symptoms worsen or no response in 48 hours Signs of pyelonephritis, complicated UTI, antibiotic resistance Male <16 y or >65 y Diabetes TMP allergy Blood disorder STI risk Pregnancy?

Trimethoprim for UTIs Algorithm



Consultation Record – UTI Assessment

Name		Address		PHARMACEUTICAL SOCIETY of New Zealand Incorporated	
Anatomically Female: YES/NO		Age (between 16 and 65 years)		Diabetic NO / YES = refer	
Pregnant (or possibly pregnant) NO/ YES = Refer		Trimethoprim allergy/hypersensitivity NO/ YES = refer			
				YES/NO	Notes
SYMPOTMS: Urinary tract: Two or more of Painful urination, urinary frequency and/or urgency, suprapubic pain Vaginal: Any of Itch/irritation, discharge Consider vaginal candidiasis (treat) or STI – (see criteria for referral below) Systemic: Any of Fever, chills, nausea, vomiting, very unwell, pain in sides or lower back					
CRITERIA FOR REFERRAL: <ul style="list-style-type: none"> UTI in the last 2 weeks or more than three UTIs in last 12 months Immunocompromised Risk of resistance, i.e. <ul style="list-style-type: none"> Recent hospital admission within last 30 days Previous trimethoprim failure Previous/known infection with multi-resistant bacteria Recent overseas travel to South-East Asia or South Asia (within last 6 months) STI (unprotected sex, new partner, multiple partners, previous STI, known exposure to STI) Other renal impairment, abnormal urinary tract, catheterisation, history of renal stones, urological surgery, spinal cord injury 					
				Refer – do not supply	
DRUG INTERACTIONS: Avoid: <ul style="list-style-type: none"> Warfarin - not contraindicated but possible theoretical rise in INR – advice re bleeding possibility ACEI/ARB – theoretical possibility of hyperkalaemia. Avoid TMP if possible, however short course of 3 trimethoprim tablets unlikely to cause this in age group being treated! 					
				May supply – give advice	
CONTROINDICATED: <ul style="list-style-type: none"> Clozapine – risk of blood dyscrasia Immunosuppressants e.g. <ul style="list-style-type: none"> Azathioprine - increased risk of haematological toxicity Cyclosporin - increase serum creatinine levels Methotrexate (including low dose) - bone marrow depression Phenytoin - Phenyltoin serum concentrations can be increased by TMP 					
				Refer – do not supply	
BREASTFEEDING – compatible – refer if baby is premature or otherwise unwell.					
PHARMACIST MANAGEMENT PLAN					
<input type="checkbox"/> 3 x trimethoprim 300mg tablets <input type="checkbox"/> Treated for vaginal candidiasis <input type="checkbox"/> Referred to doctor <input type="checkbox"/> Advice: Self-care measures, follow up with doctor if symptoms persist or worsen (antibiotic resistance – different treatment), provide patient information sheet <input type="checkbox"/> Notify patient's GP (send this form with patient consent)					
Patient consent YES/NO GP Name and Practice					
Pharmacist		Date			

1. Medicines Adverse Reaction Committee. <https://www.medicines.govt.nz/committees/marc/reports/178-32.1%20Use%20of%20trimethoprim.pdf>



Version: November 2021



Summary of Pharmacist Only Medicines

Generic Name	Indication	Restrictions
Adapalene [Rx with exemption] • Differin: cream, gel • Epiduo (+ benzoyl peroxide): gel	Acne	<ul style="list-style-type: none"> • Acne • In medicines containing $\leq 1\text{mg/g}$ or mL • In a pack containing $\leq 30\text{mg}$
Adrenaline [POM]	Anaphylaxis	<ul style="list-style-type: none"> • In medicines containing 0.02%-1%
Brompheniramine [POM]	Cough & Cold	<ul style="list-style-type: none"> • Cough and Cold (Oral use) • $>2\text{yo}$ (unless for insomnia or anxiety) • Original packs containing not more than 10 dosage units <p>Pharmacy Only: For $>6\text{yo}$ when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant) for cough and cold symptoms</p>
Calcipotriol [Rx with exemption]	Psoriasis	<ul style="list-style-type: none"> • Diagnosed mild/moderate psoriasis • If $\leq 50\text{mcg/g}$ or mL • In a pack not more than 30mg or 30mL
Chloramphenicol (antibiotic) [POM]	Conjunctivitis	<ul style="list-style-type: none"> • Ophthalmic use
Chlorpheniramine [POM]	Sedating antihistamine	<ul style="list-style-type: none"> • Oral use • $>2\text{yo}$ (unless for insomnia) • Insomnia: in original pack containing not more than 10 dosage units <p>Pharmacy Only: For $>6\text{yo}$ when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p>
Cholera Vaccine [Rx with exemption]		<ul style="list-style-type: none"> • Oral liquid (Dukoral®)
Ciclopirox [POM] • Discontinued: Ciclopirox 8% (Apo-Ciclopirox Nail Lacquer) • Funded alternative: Amorolfine nail solution 5% (MycoNail)	Fungal nail infection	<ul style="list-style-type: none"> • Fungal nail infection (External use only) • In preparations for applications to the nails, containing 2%-8% <p>Pharmacy Only: External use, containing $\leq 2\%$, for tinea pedis only</p>
Cimetidine [POM] [Rx]	Gastric acid reduction	<ul style="list-style-type: none"> • Symptomatic relief of heartburn, dyspepsia, hyperacidity, or as directed by medical practitioner • Original pack containing not more than 14 days supply
Clobetasone [POM]	Corticosteroid	<ul style="list-style-type: none"> • Dermal use • In medicines containing $\leq 0.05\%$ • In original packs containing not more than 30g that have received consent of the Minister or Director General
Clotrimazole [POM] • Clomazol • Canesten Clotrimazole	Fungal Infection (vaginal, topical)	<ul style="list-style-type: none"> • Vaginal use <p>Pharmacy Only: For external use, except in medicines for tinea pedis only</p> <p>General Sale: External use for tinea pedis only</p>
COVID-19 Vaccine [Rx]		<ul style="list-style-type: none"> • By authorised vaccinator
Cyclizine [POM]	N/V prophylaxis	<ul style="list-style-type: none"> • N/V (oral use): in original pack containing no more than 6 tablets • Insomnia (oral use): in original pack containing no more than 10 tablets
Dexchlorpheniramine [POM]	Sedating Antihistamine	<ul style="list-style-type: none"> • $>2\text{yo}$ (oral use) • Insomnia, $>2\text{yo}$ (oral use): in original pack containing no more than 10 tablets <p>Pharmacy Only: For $>6\text{yo}$ when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p>
Dextromethorphan [POM]	Cough & Cold	<ul style="list-style-type: none"> • Cough and cold (liquid form), $>6\text{yo}$ • Liquid: packs containing not more than 600mg, with a recommended daily dose of not more than 120mg
Diclofenac [POM]	NSAID	<ul style="list-style-type: none"> • Solid dose form containing 12.5mg-25mg per dose form • Pack containing no more than 30 tablets or capsules <p>Pharmacy Only: In solid dose form containing $\leq 12.5\text{mg}$ per dose, with a recommended daily dose of not more than 75mg. Pack containing no more than 30 tablets or capsules</p>
Dimenhydrinate [POM]	Antihistamine	<ul style="list-style-type: none"> • Motion sickness, $>2\text{yo}$ • Not more than 10 tablets or capsules

Diphenhydramine [POM]	Antihistamine	<ul style="list-style-type: none"> >2yo (oral use) (unless for insomnia) Insomnia (oral use): in original pack containing not more than 10 dosage units <p>Pharmacy Only (oral use): For >6yo when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p> <p>Treatment/Prevention of motion sickness in >2yo except when sold at a transport terminal or abroad a ship or aircraft</p>
Doxylamine [POM]	Antihistamine	<ul style="list-style-type: none"> >2yo (oral use) (unless for insomnia) In original pack containing no more than 10 dosage units <p>Pharmacy Only (oral use): For >6yo when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p>
Diphtheria, Tetanus, Pertussis Vaccine [Rx with exemption]		<p>Tdap - Boostrix</p> <ul style="list-style-type: none"> Single dose to ≥18 or a pregnant women ≥13 Authorised vaccinator
Econazole [POM] [Rx]		<ul style="list-style-type: none"> Vaginal Use In original pack <p>Pharmacy Only: For dermal use</p>
Famciclovir [POM]	Antiviral	<ul style="list-style-type: none"> Recurrent herpes labialis forms Oral use, containing 500mg or less Original pack containing up to 3 dosage units
Fluconazole [POM]	Antifungal	<ul style="list-style-type: none"> Vaginal Candidiasis In medicines that have received consent of the Minister or Director General In original pack containing no more than 150mg as a single dose
Fluorides [POM]		<ul style="list-style-type: none"> For external use in: <ul style="list-style-type: none"> Liquid: containing 1g-5.5g/L or kg Non-liquid form: containing 1g-5.5g/L or kg except in medicines containing >1 and ≤1.5g/L or kg Except when supplied to a registered dentist
Glucagon [POM]	Glucagon hormone	<ul style="list-style-type: none"> ≤100mcg/L or kg
Glyceryl Trinitrate [POM]	Vasodilation	<ul style="list-style-type: none"> Oral, sublingual, rectal use
Guaiphenesin [POM]	MAOI	<ul style="list-style-type: none"> Oral use (modified release): maximum recommended daily dose of no more than 2.4g Original pack containing 10-30 days' supply Approved by the Minister or Director-General <p>General Sale: Original pack containing no more than 10 days' supply e.g. <i>Mucinex</i></p>
Hydrocortisone & Hydrocortisone acetate [POM] For dermal use (does not include the inner ear)	Corticosteroid	<ul style="list-style-type: none"> Dermal use Containing 0.5%-1% by weight of hydrocortisone base with no other active ingredient except an antifungal Maximum 30mL or 30g per container <p>Note: May need repackaging and be labelled specifically for the needs of a named individual</p>
Hydrocortisone & Hydrocortisone acetate [POM]	Corticosteroid	<ul style="list-style-type: none"> Rectal use: containing 0.5%-1% by weight of hydrocortisone base, and in combination with a local anaesthetic Maximum 35g or 12 suppositories per container or pack
Hyoscine Butylbromide [POM]	Anticholinergic	<ul style="list-style-type: none"> Oral use: containing not more than 10mg per dose form, and in packs containing not more than 20 tablets or capsules For relief of muscle spasm of the GIT (oral use): not more than 20mg per dose form, and in packs containing not more than 10 tablets or capsules
Ibuprofen [POM]		<ul style="list-style-type: none"> >12yo (oral use): tablets or capsules containing up to 400mg per dose form In original packs containing not more than 50 dose units Received consent of the Minister or Director-General
Influenza Vaccine [Rx]		<ul style="list-style-type: none"> ≥13yo Authorised vaccinator
Ketoprofen [POM] [Rx]		<ul style="list-style-type: none"> Containing 25mg or less per dose form In packs of not more than 30 capsules or tablets

Lansoprazole [POM]		<ul style="list-style-type: none"> Short term symptomatic relief of gastric reflux-like symptoms in ≥ 18yo, or relief of heartburn Original pack Oral dosage forms containing ≤ 15mg with a maximum daily dose of 15mg, containing not more than 14 dosage units
Levonorgestrel [POM]		<ul style="list-style-type: none"> Emergency post coital contraception, in packs not more than 1.5mg ECP Accreditation
Macrogols [POM] (polyethyleneglycols)		<ul style="list-style-type: none"> In oral preparations for bowel cleansing prior to diagnostic, medical, or surgical procedures <p>Pharmacy Only: in preparations for oral use as a liquid concentrate for laxatives</p>
Measles, Mumps, Rubella Vaccine • Screening, consent form		
Melatonin [Rx]	Melatonin hormone	<ul style="list-style-type: none"> Treatment of primary insomnia for ≤ 13 weeks in ≥ 55yo Oral use: ≤ 3mg (immediate release) or ≤ 2mg (modified release) Original pack Received consent from Minister or Director-General
Metoclopramide [POM]	Antiemetic (dopamine receptor antagonist)	<ul style="list-style-type: none"> Only when compounded with paracetamol for the treatment of nausea associated with migraine In packs of not more than 10 tablets or capsules
Miconazole [POM]	Antifungal	<ul style="list-style-type: none"> Oral use: Oral candidiasis Vaginal use: Vaginal thrush <p>Pharmacy Only: External use General Sale: Tinea pedis (topical use)</p>
Meningococcal Vaccine [Rx]		<ul style="list-style-type: none"> ≥ 16yo Authorised vaccinator
Nicotinic acid Except nicotinamide	Vitamin B3	<p>Pharmacy Only: In medicines containing 100-250mg per dose form General Sale: <100mg per dose form</p>
Nystatin [POM]	Antifungal	<ul style="list-style-type: none"> Buccal use: oral candidiasis Vaginal use
Orlistat [POMCC] - for chronic conditions XENICAL Guidelines	Lipase inhibitor	<ul style="list-style-type: none"> In medicines for weight control containing ≤ 120mg per dose form
Oseltamivir [POM] TAMIFLU Guidelines	Antiviral	<ul style="list-style-type: none"> Treatment/prophylaxis of influenza, ≥ 13yo who have been exposed to the influenza virus Solid oral dosage forms containing 75mg in a pack size of up to 10 dosage units
Paracetamol [POM]	Analgesic	<ul style="list-style-type: none"> In modified release forms containing ≤ 665mg
Pantoprazole [POM] [Rx]	PPI	<ul style="list-style-type: none"> Short term relief of gastric reflux-like symptoms in ≥ 18yo: In tablets or capsules containing ≤ 20mg with a maximum daily dose of 20mg Original pack of not more than 28 dose units
Podophyllotoxin [POM] [Rx]	Antimitotic	<ul style="list-style-type: none"> Treatment of warts (not in anogenital area): in medicines containing 0.5-1%, except in medicines containing ≤ 1mg/L or kg
Prochlorperazine [POM]	Antiemetic	<ul style="list-style-type: none"> Treatment of nausea associated with migraines In packs containing not more than 10 tablets/capsules
Prochlorperazine [Rx with exemption]		<ul style="list-style-type: none"> Treatment of nausea associated with emergency contraception by pharmacists/nurses with accreditation to sell levonorgestrel
Promethazine [POM]	Antihistamine (antiemetic)	<ul style="list-style-type: none"> Oral use, >2yo (unless for insomnia) Insomnia: original pack containing not more than 10 dosage units <p>Pharmacy Only: For >6yo when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p> <p>Treatment/prevention of motion sickness in >2yo: In original pack of not more than 10 tablets/capsules</p>
Rizatriptan [POM] [Rx]	Migraine treatment	<ul style="list-style-type: none"> Oral use: In medicines for acute relief of migraine attacks with or without aura in patients who have a stable, well established pattern of symptoms In a pack containing not more than 2 wafers (≤ 5mg)
Salicylic Acid [POM]	Keratolytic	<p>General sale: In medicines for dermal use containing $\leq 40\%$</p>

Selected Oral Contraceptives [Rx with exemption]	Estrogen (& progesterone)	<ul style="list-style-type: none"> Clinical and eligibility criteria Original pack containing not more than 6 months' supply OC Accreditation
Sildenafil and its structural analogues [Rx with exemption]	Phosphodiesterase 5 Inhibitor	<ul style="list-style-type: none"> Checklist, heart & diabetes check Erectile dysfunction in males aged 35-70yo In medicines for oral use containing \leq100mg per dose unit In original pack containing not more than 12 dosage units Sildenafil Accreditation
Sodium phosphate [POM]	Saline laxative	<ul style="list-style-type: none"> In oral preparations for bowel cleansing prior to diagnostic, medical, or surgical procedures
Sodium Picosulfate [POM]	Contact stimulant laxative	<ul style="list-style-type: none"> In oral preparations for bowel cleansing prior to diagnostic, medical, or surgical procedures <p>Pharmacy Only: in preparations for oral use as a liquid concentrate for laxatives</p>
Staphylococcus Aureus Vaccine [POM] (?)		<ul style="list-style-type: none"> In oral vaccines for the prophylaxis of bacterial complications of colds
Streptococcus Beta-Haemolyticus Vaccine [POM] (?)		<ul style="list-style-type: none"> In oral vaccines for the prophylaxis of bacterial complications of colds
Sulfacetamide [POM] [Rx]		<ul style="list-style-type: none"> For ophthalmic use in medicines containing \leq10%
Sumatriptan [POM] <i>SUMAGRAN Checklist</i>	Migraine treatment	<ul style="list-style-type: none"> Acute relief of migraine attacks without or with aura in patients who have a stable, well established pattern of symptoms Original pack containing not more than 2 tablets (\leq50mg) that has received consent of the Minister or Director-General
Theophylline [POM]	Phosphodiesterase 5 Inhibitor	<ul style="list-style-type: none"> Liquid form or oral use: in medicines containing \leq2%
Triamcinolone [POM]	Glucocorticoid	<ul style="list-style-type: none"> Buccal use: In medicines containing \leq0.1% in packs containing no more than 5g
Trimeprazine [POM] (?)	Antihistamine (antiemetic)	<ul style="list-style-type: none"> Oral use: $>$2yo Insomnia (oral use): original pack, containing not more than 10 dosage units <p>Pharmacy Only: For $>$6yo when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p>
Trimethoprim [Rx with exemption] <i>TRIMETHOPRIM algorithm</i>	Antibiotic	<ul style="list-style-type: none"> Uncomplicated UTI Oral use: containing \leq300mg per dose unit when sold in a pack of 3 solid dosage units to women aged 16-65yo Trimethoprim Accreditation
Triprolidine [POM]	Sedating Antihistamine	<ul style="list-style-type: none"> Oral use, $>$2yo <p>Pharmacy Only: For $>$6yo when used in combination (as a bedtime dose, or containing a sympathomimetic decongestant)</p>
Varicella Vaccine [Rx with exemption] - Zostavax		<ul style="list-style-type: none"> \geq50yo Authorised vaccinator
Zolmitriptan [POM]	Migraine treatment	<ul style="list-style-type: none"> Acute relief of migraine attacks without without aura in patients who have a stable, well established pattern of symptoms Pre-filled nasal spray device delivering not more than 5mg, when sold in original pack of not more than 2 devices

DISPENSING MEDICATIONS

Product Expiry Dates

Compounding

Cream	4 weeks
Ointment	3 months
Paste	3 months
Suppositories	3 months
Oral mixtures (with preservatives)	4 weeks
Oral mixtures (without preservative, stored in fridge)	7 days

Other

Eyedrops (Chloramphenicol)	28 days
Nasal spray (fluticasone, budesonide)	90 days
Flucloxacillin	15 days
Polytears	6 months

Toniq Sigs

Beginner's Guide To Toniq

Dnu @30	Do not use after (30 days calculated)
af	after food
pc	after food
aft	afternoon
agw	and a glass of water
appl	applicator
ap	apply
aps	apply sparingly to the affected area
asaa	Apply sparingly to the affected area
asaas	Apply sparingly to the affected area(s)
ataa	Apply thinly to the affected area
aaa	Apply to the affected area
mdu	as directed
prn	as required
hss	at bedtime
n	at night
nocte	at night
sta	at once
/11	Avoid grapefruit and its juice
/5	Avoid some food & medicines - see card
/5a	Avoid some medicines - ask pharmacist
bt*	bedtime
ac	before food
bf	before food
c	capsule
cs	capsules
CNT	CAUTION: NOT TO BE TAKEN
d	daily
dy	daily
/7a	Discard days after opening. Date opened .../.../...
d10	Discard 10 days after opening

d14	Discard 14 days after opening
d7	Discard 7 days after opening
d30	Discard contents 30 days after opening.
d90	Discard contents 90 days after opening.
da	discard contents after
disco	discard unused contents after
diw	dissolved in water
/2	Do not drink alcohol
max4	Do not exceed 4 doses in 24 hours
max8	Do not exceed 8 tablets in 24 hours.
/9	Do not stop taking this medicine
max5	DO NOT take more than FIVE tablets in 24 hours
max6	DO NOT take more than SIX tablets in 24 hours
max3	DO NOT take more than THREE tablets in 24 hours
dnu	Do not use after
/7	Do not use after/..../....
/4	Don't take with antacids,iron or calcium
en	each nostril
8	EIGHT
ed	every day
q8h	every EIGHT hours
q4h	every FOUR hours
qqh	every FOUR hours
q46h	every FOUR to SIX hours
q6h	every SIX hours
15ml	FIFTEEN ml
5	FIVE
5ml	FIVE ml
ext	FOR EXTERNAL USE ONLY
ff	for fever
fp	for pain
fpaf	for pain and fever
fpf	for pain and fever

fpor	for pain or fever
pf	for pain or fever
pfi	for pain, fever or inflammation
aspre	for prevention of asthma. Rinse mouth after use
fru	FOR RECTAL USE ONLY
asma	for relief of asthma symptoms
4	FOUR
qid	FOUR times daily
g	give
sos	if necessary
stat	immediately
statt	immediately, then
m	in the morning
mane	in the morning
i	Inhale
i1p	Inhale ONE puff
i1-2p	Inhale ONE to TWO puffs
i12p	Inhale ONE to TWO puffs
i2p	Inhale TWO puffs
inj	Inject
ins	Insert
i1s	Insert ONE suppository
pr	into the rectum
pv	into the vagina
/6	Keep in fridge - do not freeze
m8	Maximum of EIGHT tablets in 24 hours
Const	May cause constipation
/1	May cause sleepiness: limit alcohol
botfed	Mix each sachet with 120mL of formula and give
bfed	Mix each sachet with FIFTEEN mL cooled boiled water and give after feeds
mn	morning and night
ns	nights

9	NINE
ntb	NOT TO BE TAKEN
ntbt	Not to be taken
od	ONCE daily
1	ONE
pref	preferably
prefbt	preferably at bedtime
prefn	preferably at night
/8	Protect yourself from too much sunlight
p	puff
ps	puffs
prer	regularly to prevent asthma. Rinse mouth after use
rm*	Rinse mouth after use to prevent oral thrush/hoarseness.
rm	Rinse mouth after use.
reliev	Separate each puff by ONE or TWO minutes.
preven	Separate each puff by ONE or TWO minutes. Rinse your mouth after use.
7	SEVEN
sai	Shake and inhale
p12	Shake and inhale ONE or TWO puffs
p2	Shake and inhale TWO puffs
sbu	shake before use
sha	Shake the bottle
stb	SHAKE THE BOTTLE
shag	Shake well and give
shg	Shake well and give
swag	Shake well and give
swg	shake well and give
swi	shake well and inhale
shat	Shake well and take
swat	Shake well and take
swt	Shake well and take
6	SIX
soc	Suck or chew

/a	swallow whole, do not crush or chew
sw	swallowed whole (do not crush or chew)
t	tablet
ts	tablets
ta	take
/3	Take each dose on an empty stomach
4t	Take FOUR tablets
1c	Take ONE capsule
1c1	Take ONE capsule daily
1c3	Take ONE capsule THREE times daily
1c2	Take ONE capsule TWICE daily
12c	Take ONE or TWO capsules
12t	Take ONE or TWO tablets
1t	Take ONE tablet
1t1	Take ONE tablet ONCE daily
1t3	Take ONE tablet THREE times daily
1t2	Take ONE tablet TWICE daily
t1-2	Take ONE to TWO
3t	Take THREE tablets
2c	Take TWO capsules
2t	Take TWO tablets
2t1	Take TWO tablets daily
2t3	Take TWO tablets THREE times daily
2t2	Take TWO tablets TWICE daily
/10	Take with a large glass of water
/10.	Take with a large glass of water.
10	TEN
10ml	TEN ml
3	THREE
tds	THREE times daily
tid	THREE times daily
20ml	TWENTY ml
bd	TWICE daily

bid	twice daily
bd*	twice daily (preferably 12 hours apart)
2	TWO
u	unit
/d	until finished
uf	until finished
ut	up to
uaas	Use as a shampoo
uaass	Use as a soap substitute
dp	vortex
pro tu	when the cough is troublesome
wagow	with a glass of water
walgow	with a large glass of water
/b	with food
cc	with food
wf	with food
faw	with food and a large glass of water
wfw	with food and a large glass of water
ex aq	with water
ww	with water

Cautionary & Advisory Labels (CALs)

Introduction

We are planning to insert here a table of medications with the required CALs with them - thank you for your patience while we work on this.

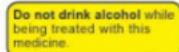
Below are the labels officially recognised as part of the Cautionary and Advisory Label scheme:

CAL 1



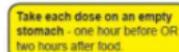
The intent of this label is NOT that people should stop taking the medicine if they intend to drive or operate machinery, but that they should determine whether or not drowsiness is a problem. For some medicines it is important to advise that the medicine should always be taken in order to continue being able to drive, but to be aware of the possibility of drowsiness. This label applies to all medicines with effects that include sedation or products that contain an ingredient having sedative properties. A label of this nature is already required by law in the sale of some over the counter medicines. The term limit is included on the label to indicate that alcohol consumption is not prohibited, but should be moderated. This is to reduce the probability of patients stopping their medicines so as not to interact with their alcohol intake, while reinforcing that excess alcohol is not recommended.

CAL 2



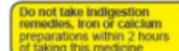
This label applies to medicines where alcohol is not recommended either through additive risk of sedating effects, alcohol altering the metabolism of the medicine, or the medicine may alter the metabolism of alcohol causing adverse effects.

CAL 3



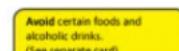
This label applies to medicines with actions that are decreased in the presence of food.

CAL 4



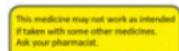
This label applies to those medicines with actions that are significantly altered by antacids, iron or calcium.

CAL 5



This label is not used on many medicines, but applies to those where certain foods or drinks may significantly affect the use of the medicine, such as monoamine oxidase inhibitors (MAOIs) and tyramine containing foods.

CAL 5a



This label is included on those medicines whose metabolism or actions are commonly altered by the concurrent use of other medicines e.g. warfarin, ciclosporin, oral contraceptives etc. It is intended to be a prompt to seek professional advice whenever another medicine is prescribed or before purchasing over the counter.

CAL 6



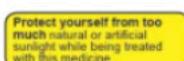
The storage conditions for many medicines are critical. This label will apply to those preparations where storage at temperatures between 2° and 8°C is necessary. Products should not be frozen since this may also result in a loss of activity or destabilisation.

CAL 7 and 7a



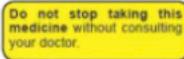
Certain products have a short shelf-life due to chemical instability or to the possibility of bacterial contamination. Dilution or admixing of medicines affects strengths of preservatives, stabilising agents, suspending agents etc. and the stability of the preparation cannot be guaranteed after a certain time. Ophthalmic preparations in particular carry the risk of contamination once the container is opened. Breakdown or loss of the preservative can occur, and coupled with the risk of bacterial contamination, the use of these products after their "use by" or "expiry" may be harmful.

CAL 8



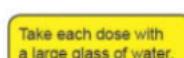
Some medicines cause serious photosensitivity reactions when people taking them are exposed to sunlight. Since it is not possible to predict an individual's response to a photosensitising medicine, it is considered desirable for a warning label to be attached to medicines which have been shown to cause photosensitising reactions.

CAL 9



This label is specifically applied to medicines that cause a reaction upon abrupt withdrawal which is greater, or different, from that which would be expected to occur if the condition had been left untreated. These may occur through development of new symptoms or a rebound effect of the condition being treated. This label is also recommended for medicines where a break in treatment is extremely undesirable, such as in tuberculosis and HIV which may lead to resistant strains.

CAL10



This label applies to medicines that have been implicated as a cause of oesophagitis or oesophageal ulceration. Studies have demonstrated that tablets and capsules may be retained in the oesophagus for considerable periods of time. Damage occurs when an irritant medicine is retained in the oesophagus. The incidence can be reduced if patients are advised to take the medicine with water.

CAL 11

Grapefruit or grapefruit juice
may interact with this medicine.
Discuss with your pharmacist.

This label applies to those medicines whose absorption or metabolism are considerably altered by grapefruit or grapefruit juice, and there is a risk of significant clinical effects. Clinicians should refer to drug interaction information for more detailed advice on significance and management.

CAL 13

CAUTION:
NOT TO BE TAKEN

This label is applied to medicines that are strictly for external use only.

CAL 14

SHAKE THE BOTTLE

An instruction to shake the bottle before measuring the required dose in order to ensure the medicine is evenly dispersed. Often used for suspensions.

CAL 17

Regular cervical smear tests
can prevent cancer of the
cervix. If you are aged between
20 & 70 have a test every
three years.

This label is used optionally and usually applied to dispensed oral contraceptives.

Dispensing label references:

The following instructions are added to dispensing labels as appropriate:

Ref A: swallow whole, do not crush or chew

Ref B: with food

Ref D: until the medicine is finished

CLINICAL CONSULTATIONS

SOAP Notes

Subjective (Symtoms)

Information reported by the patient or caregiver. Includes chief complaint (CC), history of present illness (HPI), allergies, past medical history (PMH), level of pain, etc.

Objective (Signs)

Information you observe (see, hear, touch, smell) or measure. Includes physical findings (e.g. bruising on left arm, blood pressure), measurable data (e.g. lab values, drug levels), and medicines (that you have verified — seen vials or computer record).

Assessment

What you think the problem is. Includes diagnosis, medicine therapy problem.

Plan

What you're doing about the problem you have identified. Includes interventions or actions taken, monitoring plan, and patient education.

Care Plan

Problem Identification and Prioritisation 20%

- Identifies the major problem.
- Provides a well-considered and appropriate rationale that includes patient's perspective and risk to the patient.

Consider:

- Who is the patient (living situation, lifestyle, mental, recreational)
- Medical conditions
- Medicines: what are they for, doses
- CrCl adjustments 5 year - CVD risk
- Patient Goals
- Complications

Concurrent problems 15%

- Identifies all the concurrent problems.

Consider

- Risk factors (cause of problem)
- Signs/symptoms
- Family hx
- Any immediate risks to the patient (need Tx asap)
- Or self resolving?

Goals of Therapy 10%

- Accurately states patient's goals.
- Pharmacist's goals are patient specific, SMART†, and complete

Consider

- Be specific to the patient's living situation + goals
- Pharmacological + non pharmacological Tx (e.g without promoting antibiotic resistance)
- Review risk factors
- Prevent complications and mortality
- Education
- Maintain/restore quality of life

Recommendation 25%

- Provides best option to address the problem.
- Option is described in sufficient detail such that it could be readily implemented.

- Provides a well-considered and appropriate rationale that considers key patient and evidence factors.

Consider

- Your final decision + reasoning should include:
- Medical Therapy Options and why you chose what you chose
- Mechanism of action for meds
- Risk benefit balance to the patient - discuss specific to the patient (e.g. allergy age, Crcl, pregnancy & breastfeeding, triple whammy)
- Medicine review - stop meds?
- Counselling points
- Education on condition (how to take meds)
- Non pharmacological Tx: referrals to dietician, Quitline, prevention, green prescription

Monitoring/Follow-up 10%

- Monitoring for all stated goals.=
- Is patient-specific, SMART†, and includes key safety and efficacy parameters.

Consider

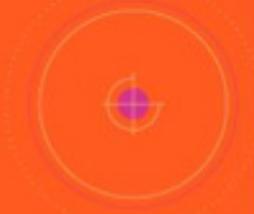
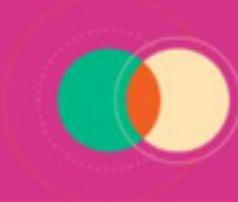
- Efficacy: improvement of S/S, targets to reach, adherence (lifestyle changes, complication prevention)
- Safety: ADRs of medicines, Interactions, Organ Function Tests, Complications

Evidence Base Practice 10%

- Provides key, relevant up-to-date evidence to rationalise the overall plan.

Communication 10%

- Writing can be easily understood consistently.
- Writing is organised, concise.
- Information is complete and clear.

S	Specific	Make your goals specific and narrow for more effective planning.	
M	Measureable	Define what evidence will prove you're making progress and reevaluate when necessary.	
A	Attainable	Make sure you can reasonably accomplish your goal within a certain timeframe.	
R	Relevant	Your goals should align with your values and long-term objectives.	
T	Time-based	Set a realistic, ambitious end-date for task prioritization and motivation.	

S	Specific	Make your goals specific and narrow for more effective planning.	
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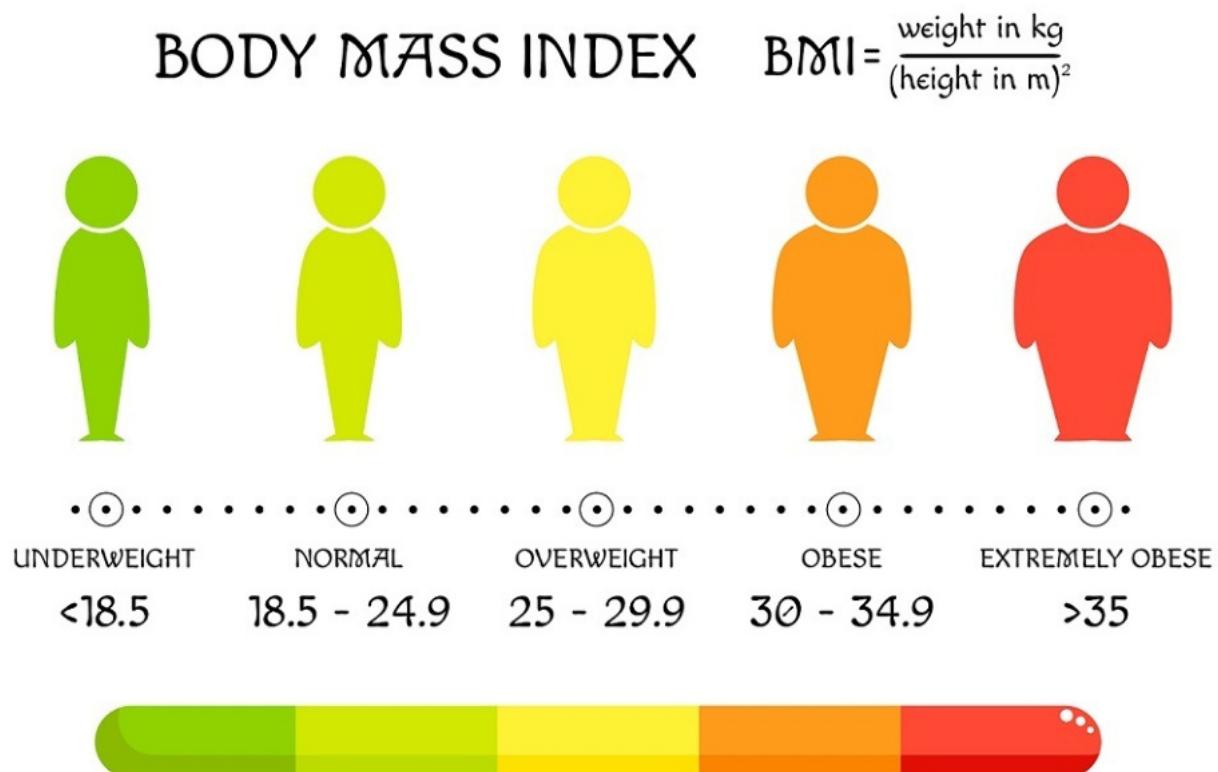
PHARMACEUTICAL CALCULATIONS

Introduction

Here we will walk you through how to do various calculations you may need to do on a daily basis (or not). Please note that if you want to double check your work [MDCalc](#) is a great resource!

Body Mass Index (BMI)

BMI = kg/m²



Cockcroft-Gault Equations

Creatinine Clearance (CrCl)

Remember that CrCl overestimates the GFR in obese patients and underestimates it in those that are underweight - this can be resolved by choosing the lower of the two: Actual Body Weight (ABW) or Ideal Body Weight (IBW)

$$CrCl(ml/min) = \frac{140 - age * Wt * K}{SCr}$$

Age = years

Wt = weight (kg)

SCr = serum creatinine units (umol/L)

K = 1.23 for males and 1.04 for females

Ideal Body Weight (IBW)

Remember:

- If ABW<IBW, use actual body weight
- If IBW<ABW, use ideal body weight

$$\text{IBW} = 45\text{kg} (+5\text{kg if male}) + [(height - 150\text{cm}) \times 0.9]$$

MDRD/CKD-EPI Equations

Body Surface Area (BSA)

Remember that the CKD-EPI equation and the Cockcroft Gault equation give you both an estimation of the GFR by giving you the eGFR and eCrCl respectively. But they are not interchangeable!

Also remember that answers to the CKD-EPI Equation are standardised to a BSA of 1.73m² thus you will need to adjust the answer to your patient's respective BSA.

$$BSA = \sqrt{\frac{Height(cm) * Weight(kg)}{3600}}$$

Example

- The eGFR reported by the lab = 55mL/min/1.73m² but your patient has a BSA of 1.50m²
- Then your patients true eGFR = **(1.5/1.73) x 55 = 47mL/min**

Eye Drops

Prescriptions for eye drops will often tell you how many drops the patient needs to administer e.g. 1 drop b.e qid for 10 days. Your challenge is to convert that to how many packs you need to supply:

12 drops = 1 mL

60 drops = 5mL

You can look up on NZF the respective product you need to supply to see in what pack sizes they come.

Inhalers

This one is very straightforward. Prescriptions will tell you how many inhalations/puffs the patient needs, simply check the number of actuations of each product and supply accordingly (NZF will tell you this)

Insulin

Calculating how many cartridges of insulin to supply can be tricky as prescriptions often list how many units patient need to administer and pharmacists need to work out how many cartridges to give. We will show you two ways on how to do this: the long way and the short way. Let's look at an example question - assume that the type of insulin is not relevant.

Patient needs to administer 10 units tds (with meals) and prime with 2 units each time. How many insulin cartridges will you give?

The Long Way

1. Find out how many units the person needs for 3 months
 - $(10 \text{ units} + 2 \text{ units for priming}) \times 3 \text{ times a day} \times 90 \text{ days} = 3240 \text{ units}$ per month
2. Convert units to mls
 - NZF tells you that each ml contains 100 units.
 - Thus: $3240 \text{ units} / 100 \text{ units} = 32.4 \text{ mls}$
2. Convert mls to cartridges
 - NZF also tells you that insulin comes in 3ml cartridges, this means that $32.4 \text{ mls} / 3 = 10.8 \text{ cartridges}$
 - Remember to always round up to ensure you give the patient enough since we cannot give a portion of a cartridge - we thus need to give the patient **11 cartridges**
3. Find out monthly allotment
 - The next step is to allocate those cartridges in monthly allotments - this allows you give insulin according to the funding criteria as well as ensure patients do not administer expired insulin to themselves (insulin lasts 28-42 days depending on what kind it is).
 - To avoid misjudging how many cartridges to allocate per month - find out how much insulin they need per month and then distribute accordingly.
 - $11 \text{ cartridges} / 3 = 3.6 \text{ cartridges}$ (needed minimum per month)
 - The patient thus needs at least 4 cartridges a month, hence we divide as such: **4 + 4 + 3**

The Short Way

The shortcut we are going to use is:

Total Daily Units x 0.3 = 90 days cartridge supply or

Total Daily Units x 0.1 = 30 days cartridge supply

1. Fill Equation
 - $\text{Total Daily Units} \times 0.3 = 90 \text{ days cartridge supply}$
 - $(10 \text{ units} + 2 \text{ units for priming}) \times 3 \text{ times a day} = 36 \text{ total daily units}$
 - $36 \text{ units} \times 0.3 = 10.8 \text{ cartridges}$ (3 month supply)
2. Calculate monthly allotment
 - $10.8 / 3 = \text{minimum } 3.6 \text{ cartridges a month}$
 - Patient needs at least 4 cartridges a month, so allocate 11 cartridges as **4 + 4 + 3**

Smoking (Pack Year History)

No. of packs smoked per day (20 per pack) x No. of smoking years

Dose Conversions

Prescription Example:

Child Weight = 50kg

Child Age = 13

Paracetamol 250mg/5ml Orange Flavour

Mitte 15ml every 4-6 hours prn for 1 month

Solving

1. Check if Dose Clinically Appropriate

According to NZF - dose is 15mg/kg every 4-6 hours. Dose is clinically appropriate.

- 15mg x 50 kg = 750mg
- 750mg/250mg x 5ml = 15ml

2. Find Total Amount to Give

This step is necessary if the prescriber has not indicated a certain amount e.g. mitte 100ml

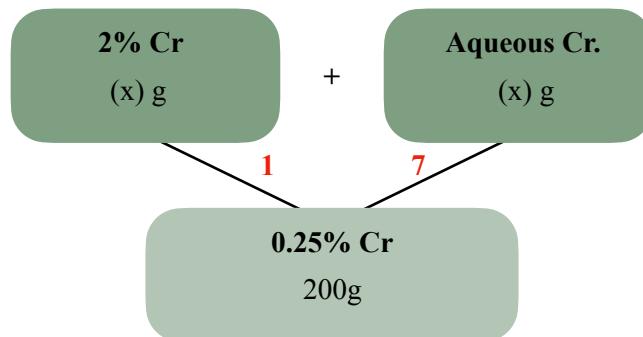
- 15ml x max of 4 daily doses x 30 days = 1350ml

Dilutions

This form of calculation becomes a bit more complex. We will start off with simpler questions:

2 Concentrations Dilution Questions

You are required to dispense 200g of 0.25% Betamethasone cream. You only have a 2% Cream. The diluent to use is Aqueous Cream. What quantity of each will be required?



1. Approach 1: Dilution Ratio Method

When 2 concentrations are involved, the dilution ratio is obtained by dividing starting conc / final conc

- $2\% / 0.25\% = 8$
- The dilution factor is 8 which can be rewritten as a ratio of 1 part 2% per 7 parts aqueous cream.

The value of 1 part is therefore the final volume / dilution factor

- $200g / 8 = 25g$

If one part is 25g then:

- $2\% | 1 \times 25 = 25g$
- *Aqueous Cream* | $7 \times 25 = 175g$

2. Approach 1: CV = CV Method

$CV = CV$ can be used as moles are preserved - they are just dispersed throughout a greater quantity. Taking this into account, we therefore equate the 'final' CV to the 'starting' CV and not the diluent.

- $(0.25\%)(200g) = (2\%)(xg)$
- $xg = 25g$

If 25g of the 2% is required and we have a total of 200g, then the Aqueous Cream must be:

- $200g - 25g = 175g$

3. Approach 3: Active Pharmaceutical Ingredient (API) Method

In this method, we try and find out we are trying to find out how many grams of the 2% is equal to 200g of the 0.25%?

0.25% simply means that there are 0.25g of the active ingredient dispersed in 100g. We can therefore find out how much there is in 200g, our final mass.

- If $100\text{g} = 0.25 \text{ g}$ then $200\text{g} = 0.5\text{g}$

There needs to be a total of 0.5g of active ingredient in our final mass. We can therefore find out how much of the 2% will provide us with this much active ingredient.

- If $100\text{g} = 2\text{g}$ then $x\text{g} = 5\text{g}$
- $x\text{g} = 25\text{g}$

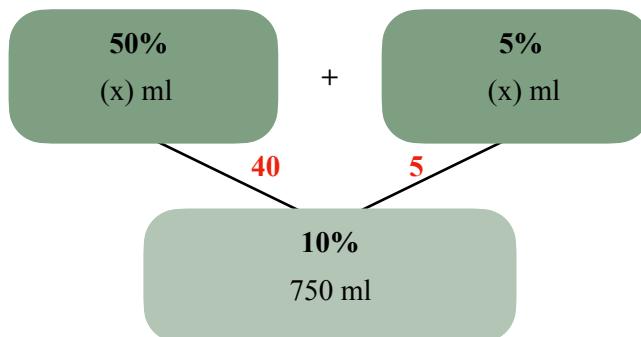
If there is a total of 200g and we obtain 25g from the 2%, then the aqueous cream must be:

- $200\text{g} - 25\text{g} = 175\text{g}$

3-Way Concentrations Dilution Questions

When 2+ concentrations are involved, we cannot use $\text{CV}=\text{CV}$ or the API method as these equations only allows for 2 factors at a time. The best method is the dilution ratio method — however with a variation this time.

You are on the ward in a difficult situation. A Patient requires 750mls of 10% Glucose to be administered immediately. The ward only has bags containing Glucose 50% and Glucose 5%. You are able to remove fluid and add fluid aseptically easily in these bags but cannot wait until a 10% solution is delivered. What quantities of each would you need to use to produce 750mls of 10% Glucose.



1. Calculate Relative Doses

When 2+ concentrations are involved, the dilution ratio is obtained using a relative dose method - subtract each individual starting concentration from the final desired one.

- $50\% - 10\% = 40\%$
- $5\% - 10\% = 5\%$

2. Obtain Dilution Ratio

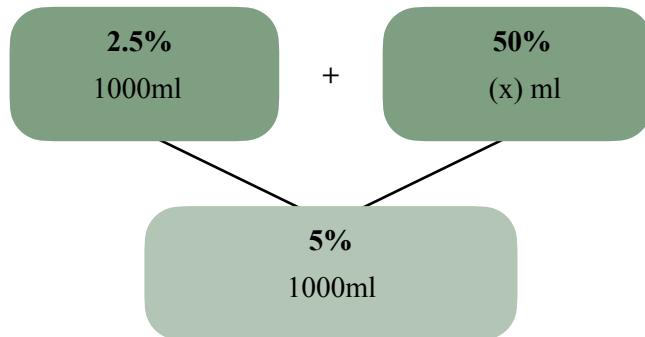
- Ratio of **40:5** can be simplified to **8:1** or written as dilution factor **9**
- This means for every **8** parts of 50% we need **1** part of 5% to obtain a resulting solution of 10%

3. Calculate mls of starting solutions

- The value of 1 part is $750\text{ml} / 9 = 83\text{ml}$, therefore:
- $50\% | 8 \times 83\text{ml} = 666\text{ml}$
- $5\% | 1 \times 83\text{ml} = 83\text{ml}$

Strengthening (Opposite Dilutions)

A nurse rings you to ask for a 1000ml bag containing 5% glucose and 4.5% sodium chloride. You only have a 1000ml bag of 2.5% glucose and 4.5% sodium chloride. You do however have 50% glucose vials. How much extra glucose do you need to tell the nurse to add to the 1000mL bag to increase the glucose concentration from 2.5% to 5%



This question slightly differs as in this scenario this is not a dilution but rather a strengthening concentration question, therefore not only the dilution method will not work but the CV method will not either as moles are not preserved. The best method to use here is the API method. Note that the required final volume has already been met (1000ml) - however the concentration has not.

1. Calculate Difference between Starting Amount and Final Amount

2.5% suggests there are 2.5g of active ingredient per 100ml therefore:

- If 100ml = 2.5g then 1000ml = **25g**

However the desired concentration is 5%, which is 50g:

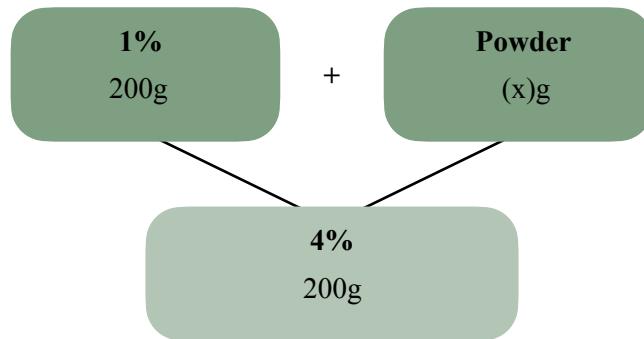
- If 100ml = 5g then 1000ml = **50g**

2. Obtain Difference

If we have 25g of glucose, but we desire a total 50g of it — we need extra 25g worth of glucose. We have the 50% concentration available to us to achieve this. What amount of the 50% concentration will provide us with 25g of active glucose ingredient?

- If 100ml = 50g then x ml = 25g
- x ml = **50ml**

An ointment contains 1% w/w calamine. How much calamine powder would it be appropriate to add to 200g of the ointment to produce a 4% w/w calamine ointment?



1. Calculate Difference between Starting Amount and Final Amount

We desire a 4% concentration by adding active ingredients to the 1% concentration

- 4% means that in 100g there are 4g of active ingredient, therefore in 200g there are **8g**
- 1% means that in 100g there are 1g of active ingredient, therefore in 200g there are **2g**

What we find is that there is a difference of 6g (8-2) in the active ingredient. However we cannot conclude that this is the amount of powder required because adding the calamine powder, our active ingredient, increases both the calamine quantity (API) and the total quantity (200g) of the ointment. **As the total mass also changes**, this needs to be taken into consideration.

If we contrast to the previous question, where the strengthening agent (the glucose vials) came with a given concentration of 50%, this was not necessary. This is because **volumes are not additive, masses are**.

Therefore:

- The 4% ointment = 1% ointment + calamine powder (x)
- $8/200g = (2g + x)(200g + x)$
- **X = 6.25g**

Measures of Risk & Benefit

Symbol	Definition	Equation
RR	Relative risk	(Incidence in unexposed group/incidence in exposed) x 100
AR or (AR _{AO})	Absolute risk	Incidence in unexposed group - incidence in exposed (ignore negative sign)
NNT	Number of patients needed to treat over a specified time period (study length) to achieve one beneficial outcome	1/AR (for primary efficacy outcome)
NNH	Number of patients needed to treat over a specified time period (study length) to cause one harmful outcome	1/AR _{AO} (for adverse outcome)

FULL INDEX | THE PHARMACY HANDBOOK

You have reached the end of the Pharmacy Handbook! Thank you for making this journey with us, we hope we have been helpful in your time at Pharmacy School and we wish you all the best as future pharmacists!

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