Clinical Pharmacology & Therapeutics

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Pharmacokinetics

Definitions
- Pharmacokinetics: what the body does to the drug
- Pharmacodynamics: what the drug does to the body

Key Concepts

Clearance
- Volume of plasma cleared of a drug per unit time

Half-life
- Time taken for drug concentration to decline to half its original value.
- Depends on volume of distribution and clearance

Volume of Distribution
- Volume into which a drug appears to distribute.
- High for lipid-soluble drugs
- Low for water soluble drugs

First Order Kinetics
- Clearance of drug is always proportional to plasma concentration.
- Most drugs are in this category

Zero Order Kinetics
- Clearance of drug not always proportional to plasma concentration.
- Saturation of metabolism → constant rate of elimination regardless of plasma levels.
- E.g. phenytoin, salicylates, ethanol

Bioavailability
- Percentage of the dose of a drug which reaches the systemic circulation.
- 100% for IV administration

Multiple Dosing
- If a drug given at intervals the concentration will reach a steady state in ~ 5 half-lives.
- Loading dose: ↓ time needed to reach a steady state.
  - Useful if long or short t½
  - Phenytoin, digoxin, amiodarone, theophylline

Therapeutic Drug Monitoring

Indications
- Ix lack of drug efficacy or possibility of poor compliance
- Suspected toxicity
- Prevention of toxicity

Examples
- Aminoglycosides (essential)
- Vancomycin (essential)
- Li (essential)
- Phenytoin
- Carbamazepine
- Digoxin
- Ciclosporin
- Theophylline

NB. Warfarin is not monitored per se, it’s the biological effect which is monitored rather than the plasma drug level.

Drug Metabolism and Elimination

First Pass Metabolism
- Metabolism and inactivation of a drug before it reaches the systemic circulation.
- i.e. pre-systemic elimination
- Occurs in gut wall and liver
- E.g. propanolol, verapamil, morphine, nitrates

Pathways of Drug Metabolism and Elimination
- Excrete unchanged by the kidney (e.g. frusemide)
- Phase 1 metabolism then renal excretion
- Phase 2 metabolism then renal excretion

Phase 1 Metabolism
- Creation of reactive, polar functional groups
  - Oxidation: usually by CyP450 system
  - Reduction and hydrolysis

Phase 2 Metabolism
- Production of polar compounds for renal elimination
- Either the drug or its phase 1 metabolite
- Conjugation reactions
  - Glucuronidation, sulfonation, acetylation, methyl

Elimination: mainly renal (depends on GFR)

Cytochrome P450 System
- Most important system of phase 1 metabolism
- > 11 subtypes
- CyP3A4
  - Most important subtype
  - ≥ 30% of drugs: CCBs, β-B, statins, benzos
- CyP2D6
  - Second most important
  - ≥20% of drugs: antidepressants, some β-B, opiates

Pro-Drugs
- L-Dopa → dopamine
- Enalapril → enalaprilat
- Ezetimibe → ez-glucuronide
- MethylDopa → α-methylnorepinephrine
- Azathioprine → 6-mercaptopurine (by XO)
- Carbimazole → methimazole
- Cyclophosphamide

Pharmacogenomics
- Genetically determined variation in drug response

Acetylation
- Fast vs. slow acetylators (↑↑ fast in Japan vs. Europe)
- Affects: isoniazid, hydralazine and dapsone

Oxidation
- There are genetic polymorphisms for all known CyP450 enzymes except for CyP3A4

G6PD Deficiency
- Oxidative stress → haemolysis
- Quinolones, primaque, nitrofurantoin, dapsone

Acute Intermittent Porphyria
- AD, ↑ in White South Africans
- Large no. of drugs can → attacks: e.g. EtOH, NSAIDs…
Adverse Drug Reactions

Classification

Type A
- Common, predictable reactions
- Dose-related (but may occur @ therapeutic doses)
- Consequence of known pharmacology of the drug

Type B
- Rare, idiosyncratic reactions
- Usually not dose-related
- E.g. allergies and pharmacogenetic variations

Long-Term ADR
- Dependence, addiction
- Withdrawal phenomena
- Adaptive changes: e.g. tardive dyskinesia

Delayed ADR
- Cacinogenesis
- Teratogenesis

Determinants

Drug
- Pharmacodynamics
- Pharmacokinetics
- Dose
- Formulation
- Route of administration
- Rate of aminophylline

Patient
- Age
- Co-morbidities
  - Renal: digoxin, aminoglycosides
  - Hepatic: warfarin, opiates
- Organ dysfunction
- Genetic predisposition

Allergies

Type 1: anaphylaxis
- Penicillins, contrast media

Type 2: cytotoxic antibodies
- E.g. causing haemolysis
- Penicillins, cephalosporins, oral hypoglycaemics
- Methylpupa

Type 3: immune complexes
- Serum sickness-like reaction
- Penicillins, sulphonamides

Type 4: cell-mediated
- Contact dermatitis
- Topical abx
- Antihistamine cream

Pseudoallergies
- Pharmacological (not immune)

NSAIDs → bronchospasm
- Shift metabolism from prostaglandins → leukotrienes → bronchoconstriction
- May occur in non-asthmatic populations
  - Commoner if asthmatic

ACEi → cough and angioedema (anaphylactoid)
- ACEi inhibit bradykinin metabolism

Long-term ADRs

Withdrawal
- Opiates
- Benzos
- Corticosteroids

Rebound: Worse on withdrawing the drug then before starting
- Clonidine
- β-B
- Corticosteroids

“Adaptive”
- Neuroleptics: tardive dyskinesia

Delayed ADRs

Oestrogens
- Endometrial Ca
- Breast Ca

Cytotoxics
- Leukaemia
Important ADRs

Rashes

Urticaria:
- **Immune**: penicillins, cephalosporins
- **Non-immune**: contrast, opiates, NSAIDs

EM: sulfonamides NSAIDs, allopurinol, phenytoin, penicillin

EN: sulphonamides, OCP

Photosensitivity: amiodarone, thiazides, sulfonylureas

Fixed eruptions: erythromycin, sulphonamides

Lupus-like reactions: hydralazine, isoniazid, penicillamine

Hepatotoxicity

Cholestatic
- Clavulanic acid: may be delayed
- Fluclox: may be delayed
- Erythromycin
- Sulfonylureas (glibenclamide)
- OCP
- Tricyclics
- Chlorpromazine, prochlorperazine

Hepatocellular Damage
- Paracetamol
- Valproate, phenytoin, CBZ
- RMP, INH, PZA
- Halothane
- Methotrexate
- Statins

Chronic Hepatitis
- INH
- Methyldopa
- Methotrexate

Gallstones
- OCP

Bone Marrow Toxicity

Pancytopenia / aplastic anaemia
- Cytotoxics
- Phenytoin
- Chloramphenicol
- Penicillamine
- Phenothiazines
- Methyldopa

Neutropenia
- Carbamazapine
- Carbimazole
- Clozapine
- Sulfasalazine

Thrombocytopenia
- Valproate
- Salicylates
- Chloroquine

Peripheral Neuropathy
- INH
- Vincristine
- Amiodarone
- Nitrofurantoin
- Penicillamine

Pulmonary Fibrosis
- Bleomycin
- Busulfan
- Amiodarone
- Nitrofurantoin
- Sulfasalazine
- Methotrexate
- Methysergide

Gynaecomastia
- Spironolactone
- Digoxin
- Verapamil
- Cimetidine
- Metronidazole

SIADH
- Carbamezapine
- Cyclophosphamide
- Chlorpropamid
- SSRIs
- TCAs

Gingival Hypertrophy
- Nifedipine
- Phenytoin
- Ciclosporin

↑QTc
- Fluoroquinolones: cipro
- Venlafaxine
- Neuroleptics: phenothiazines, haldol
- Macrolides
- Anti-arrhythmics 1a/III: quinidine, amiodarone, sotalol
- TCAs
- Histamine antagonists

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### Side Effect Profiles

#### Cholinceptors

<table>
<thead>
<tr>
<th>Cholinergic</th>
<th>Anti-muscarinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Salivation</td>
<td>• Constipation</td>
</tr>
<tr>
<td>• Bronchoconstriction</td>
<td>• Urinary retention</td>
</tr>
<tr>
<td>• Lacrimation</td>
<td>• Mydriasis</td>
</tr>
<tr>
<td>• Urination</td>
<td>• Blurred vision</td>
</tr>
<tr>
<td>• Diarrhoea</td>
<td>• Bronchodilatation</td>
</tr>
<tr>
<td>• GI upset</td>
<td>• Drowsiness</td>
</tr>
<tr>
<td>• Emesis</td>
<td>• Dry eyes / skin</td>
</tr>
<tr>
<td>• Miosis</td>
<td></td>
</tr>
<tr>
<td>• Sweating</td>
<td></td>
</tr>
</tbody>
</table>

#### Causes
- Anti-cholinesterases
- Ipratropium
- Anti-histamines
- TCAs
- Antipsychotics
- Procyclidine
- Atropine

#### EPSEs

<table>
<thead>
<tr>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Typical antipsychotics</td>
</tr>
<tr>
<td>• Rarely: metoclopramide, prochlorperazine</td>
</tr>
<tr>
<td>▪ Esp. in young women</td>
</tr>
<tr>
<td>• Dyskinesias and dystonias are common c anti-parkinsonian drugs.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>• D2 block in the nigrostriatal pathway</td>
</tr>
<tr>
<td>• Excess AChM (hence effect of anti-AChM)</td>
</tr>
</tbody>
</table>

#### Parkinsonian
- Occurs w/i months
- Commoner in the elderly
- Bradykinesia, tremor, rigidity
- Rx: procyclidine (anti-AChM)

#### Dopamine

**Excess**
- Causes
  - L-dopa
  - Da agonists
- Features
  - Behaviour change
  - Confusion
  - Psychosis

**Deficit**
- Causes
  - Anti-psychotics
  - Anti-emetics: metoclopramide, prochlorperazine
- Features
  - EPSEs
  - ↑ PRL
  - Neuroleptic malignant syndrome

#### Cerebellum
- Dysdiadochokinesis, dysmetria, rebound
- Ataxia
- Nystagmus
- Intention tremor
- Slurred speech
- Hypotonia

**Causes**
- EtOH
- Phenytoin

#### Acute Dystonia
- Occurs w/i hrs-days of starting drugs
- Commoner in young males
- Involuntary sustained muscle spasm
- E.g. lock jaw, spasmodic torticollis, oculogyric crisis
- Rx: procyclidine

#### Akathisia
- Occurs w/i days-months
- Subjective feeling of inner restlessness
- Rx: propranolol (crosses BBB)

#### Tardive Dyskinesia
- Rhythmic involuntary movements of head, limbs and trunk.
- Chewing, grimacing
- Protruding, darting tongue
- Occur in 20% of those on long-term neuroleptics (yrs)
- Rx
  - Switch → atypical neuroleptic
  - Clozapine may help
  - (procyclidine worsens symptoms)

#### Neuroleptic Malignant Syndrome
- 4-10d after initiation or change of dose
- Mostly in young males
- **Features**
  - Motor: severe muscular rigidity
  - Mental: fluctuating consciousness
  - Autonomic: hyperthermia, ↑HR, sweating, ↑↓BP
  - Blood: ↑CK, leukocytosis
- **Rx**
  - Dantrolene: inhibits muscle Ca release
  - Bromocriptine / apomorphine: reverse Da block
  - Cool pt.
Drug Interactions

Pharmaceutical
- Take place outside the body
- Mainly IV drugs being mixed together
- E.g. calcium + sodium bicarbonate → precipitation

Pharmacokinetic

Altered Absorption
- Tetracyclines and quinolones c Ca, Fe, Al
  - Drugs chelate the metals and are not absorbed

Displacement from Plasma Proteins
- Warfarin + some NSAIDs
- Often clinically insignificant as clearance ↑s proportionally c displacement

Metabolism
- Enzyme Inhibitors
  - P450
    - XO: allopurinol
    - Dopa decarboxylase: carbidopa
    - Acetaldehyde dehydrogenase: disulfiram, metronidazole
  - Enzyme Inducers

Excretion
- Diuretics → ↓ Li clearance
- Loop diuretics: ↑ aminoglycoside ototoxicity

Indirect Interactions
- Diuretics and steroids → ↑ risk of digoxin toxicity
  - Via ↓ K+
- NSAIDs + warfarin → ↑ risk of GI bleed
- Abx + warfarin → ↑ bleeding risk
  - Abx kill GI microflora that make vit K

P450 Inducers
- Phenytoin
- Carbamazepine
- Barbiturates
- Rifampicin
- Alcohol (chronic)
- Griseofulvin
- St. John’s Wart

P450 Inhibitors
- Valproate
- INH
- Protease inhibitors
- Cipro, Cimetidine
- Erythromycin + clarithromycin
- Omeprazole
- Grapefruit juice
- Fluconazole / Fluoxetine

Important Drugs Metabolised by P450
- Ciclosporin
- OCP
- Warfarin
- Epileptic drugs: phenytoin, CBZ
- Statins
- Theophylline

Warfarin

<table>
<thead>
<tr>
<th>W+</th>
<th>W-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme inhibitors</td>
<td>Enzyme inducers</td>
</tr>
<tr>
<td>EtOH</td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
</tr>
<tr>
<td>Dipyridamole</td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td></td>
</tr>
</tbody>
</table>

Diuretics
- Potentiate: ACEi, Li, Digoxin
- Loop → ↑ risk of ototoxicity c aminoglycosides
- K-sparing → ↑ risk of hyperkalaemia c ACEi
Prescribing in the Young, the Old and the Pregnant

The Elderly

Pharmacokinetics

- **Distribution**
  - ↓ body water → ↑ [water soluble drugs]
  - ↑ body fat → ↓ [fat soluble drugs]
  - ↓ albumin → ↑ [protein-bound drugs]
  - ↓ wt.: ↓ standard dose → ↑ [drug]

- **Metabolism**
  - ↓ oxidation
  - ↓ first-pass metabolism (e.g. propranolol)
  - ↓ induction of liver enzymes
  - ↓ age → ↑ t½ of hepatically metabolised drugs
    - E.g. Warfarin

- **Elimination**
  - ↓ GFR
  - ↓ tubular secretion

**Bottom Line**

- ↑ age tends to → greater and longer drug effects

Altered Organ Sensitivity

- **ANS**
  - Defective compensatory mechanisms
  - ↓ β-receptor density
    - ↓ effectiveness of drugs targeting them

- **CNS**
  - ↑ sensitivity to anxiolytics and hypnotics

- **Cardiac Function**
  - ↓ perfusion of liver and kidneys → ↓ function → ↓ metabolism or elimination of drug

Compliance Problems

- Confusion ± changes in tablet morphology
- ↓ vision
- Arthritic hands
- Living alone
- Polypharmacy

Major Problem Drugs

- **Affecting the Cardiovascular System**
  - Anti-hypertensives
  - Digoxin
  - Diuretics

- **Affecting the CNS**
  - Anti-depressants
  - Ant-parkinsonian
  - Hypnotics

Neonates

Pharmacokinetics

- **Absorption**: ↓ gastric motility

- **Distribution**
  - Immature BBB
  - ↑ body water → ↓ [water soluble drugs]
  - ↓ body fat → ↑ [fat soluble drugs]
  - ↓ albumin → ↑ [protein-bound drugs]

- **Metabolism**
  - ↓ P450 activity
  - ↓ conjugation

- **Excretion**
  - ↓ GFR and ↓ tubular secretion

**Bottom Line**

- ↑ age tends to → greater and longer drug effects

Teratogens

- **Mechanisms**
  - Orally active = crosses placenta
  - Implantation (5-17d) → abortion
  - Embryonic (17-57d) → structural defects
  - Fetogenic (maturation) → relatively less dangerous

Common Drugs

- ACEI: affect kidney growth
- AEDs: NTDs
- Li: Ebstein’s anomaly
- Anti-folate: e.g. trimethoprim → NTDs
- Tetracyclines: stain teeth
- Warfarin: cardiac defects, ↓IQ, saddle nose, blindness
- Statins

Drugs to Avoid in Late Pregnancy

- Aspirin: haemorrhage, kernicterus
- Aminoglycosides: CN8 damage
- Anti-thyroid: goitre, hypothyroidism
- Benzos: floppy baby syndrome
- Chloramphenicol: grey baby syndrome
- Warfarin: haemorrhage
- Sulphonylureas: kernicterus

Mx in Pregnancy

- **Hypertension**
  - NB. Don’t prescribe ACEi to fertile young women.
  - Labetalol
  - Methyldopa
  - Nifedipine
  - Hydralazine

- **DM**
  - Poor glucose control → ↑ congenital abnormalities
  - Use insulin and/or metformin

- **Epilepsy**
  - Folic acid pre-conception
  - Drug levels tend to fall in pregnancy
  - ↑ risk of malformations (6% vs. 2%)
  - ↑ risk of haemorrhagic disease of the newborn (↓K)
  - Avoid valproate
  - Use lamotrigine (or CBZ)

Anticoagulation

- 1st trimester: LMWH
- 2nd trimester – 36wks: LMWH or warfarin
- 36wks – term: LMWH
- Term onwards: warfarin

Drugs and Breast-Feeding

- Sedatives (benzos, EtOH) → drowsiness
- Anti-thyroid → goitre
- Tolbutamide → hypoglycaemia in infant
**Important Drugs Affected by Renal Impairment**

**Digoxin**
- $T_1/2$: 36 → 90hrs
- Low therapeutic index: should be monitored
- **Toxicity**
  - Nausea, xanthopsia, gynaecomastia
  - A / V tachyarrhythmias, heart block
- Toxicity
  - Nausea, xanthopsia, gynaecomastia
  - A / V tachyarrhythmias, heart block

**Gentamicin**
- $T_1/2$: 2.5 → >50hrs
- **Must** be monitored
- **Toxicity**
  - Ototoxic: hearing + vestibular
  - Nephrotoxic tubules
  - ↑ risk of toxicity if ↓ Na (e.g. diuretics) or dehydration

**Atenolol**
- $T_1/2$: 6 → 100hrs
- **Toxicity**
  - Bradycardia, hypotension
  - Worsening of PVD and heart failure
  - Confusion
  - **CI**
  - Asthma / bronchospasm
  - Severe heart failure
  - PVD

**Amoxicillin**
- $T_1/2$: 2 → 14hrs
- **Toxicity**
  - Seizures (in meningitis: impaired BBB)
  - Rashes

**Captopril**
- $T_1/2$: 2 → 14hrs
- **Toxicity**
  - Hypotension
  - Taste disturbance
  - Cough
  - ↓ GFR
  - Angioedema

**Vitamin D**

**Forms**
- **Colecalciferol / D$_3$:** formed in skin and found in food
- **Ergocalciferol / D$_2$:** produced by UV light in fungi from ergosterol
- **Calcifediol:** 25 OH-Vit D$_3$ produced by the liver
- **Calcitriol:** 1, 25, (OH)$_2$ Vit D$_3$, produced by the kidney
- **Alfacalcidol:** 1 OH-Vit D$_3$

**Pathophysiology**
- 25 OH-Vit D$_3$ undergoes renal 1α-hydroxylation to the active form: 1, 25, (OH)$_2$ Vit D$_3$
- Impaired 1α-hydroxylase function in renal disease

**In Renal Impairment**
- Use **alfacalcidol** (1α-hydroxylated)
- Calcitriol rarely used

---

**Nephrotoxicity**

**Gentamicin**
- Renal tubular damage
  - → Accumulation → ↑ nephro-/oto-toxicity
- **Must** monitor drug levels

**Li**
- Inhibits Mg-dependant enzymes
  - e.g. adenylate cyclase
  - ADH requires adenylate cyclase ↓: Li → nephrogenic DI
- Also causes direct tubular damage
- **Must** monitor drug levels

**Ciclosporin**
- ↓ GFR: reversible
- Damages renal tubules: irreversible
- P450 substrate
- Consider monitoring

**ACEi / ARB**
- ↓ GFR: inhibit efferent arteriolar vasoconstriction
  - May be profound in RAS or CoA

**NSAIDs**
- ↓ GFR: prevent afferent arteriolar vasodilatation
- Papillary necrosis
Prescribing in Liver Disease

Cautions in Hepatic Impairment

**Hypoalbuminaemia**
- ↑ proportion of free drug
- Phenytoin, CBZ
- Prednisolone
- Diazepam
- Tolbutamide

**↓ Synthesis of Clotting Factors**
- Warfarin
- Abx (kill GI microflora)

**↓ First Pass Metabolism**
- Opiates
- Phenothiazines
- Imipramine

**α1-acidic Glycoprotein**
- Binds basic drugs
  - e.g. chlorpromazine, quinidine, imipramine

**Encephalopathy**
- Sedatives / Opiates: may → coma
  - Caution CI drugs that may → constipation
- Anxiolytics: temazepam safest (short t½)
  - Avoid chlormethiazole
- Anti-depressants: TCAs safest (but ↓ dose)
  - Avoid MOAIs

**Hepatorenal Syndrome**
- Withdraw nephrotoxic drugs
- Modify doses of renally-excreted drugs

Hepatotoxicity

**Cholestatic**
- Clavulanic acid: may be delayed
- Fluclox: may be delayed
- Erythromycin
- Sulfonylureas (glibenclamide)
- OCP
- Tricyclics
- Chlorpromazine, prochlorperazine

**Hepatocellular Damage**
- Paracetamol
- Valproate, phenytoin, CBZ
- RMP, INH, PZA
- Halothane
- Methotrexate
- Statins

**Chronic Hepatitis**
- INH
- Metyldopa

**Gallstones**
- OCP
## Dyspepsia, GORD and PUD

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg Trisilicate</td>
<td>Ant-acid Neutralise gastric acid</td>
<td>Diarrhoea</td>
<td></td>
<td>Interfere ç drug absorption - take separately</td>
<td>Take when symptoms occur or are expected.</td>
</tr>
<tr>
<td>Al hydroxide</td>
<td>Ant-acid Neutralise gastric acid</td>
<td>Constipation</td>
<td></td>
<td>Interfere ç drug absorption - take separately</td>
<td>Take when symptoms occur or are expected.</td>
</tr>
<tr>
<td>Gaviscon</td>
<td>Alginate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ reflux</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ↑ viscosity of stomach contents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Form a raft on top of stomach contents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>PPIs</td>
<td>GI disturbance</td>
<td></td>
<td>P450 inhibitor</td>
<td></td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Activated in acidic pH</td>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Irreversibly inhibit H⁺/K⁺ ATPase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>More effective cf. H₂RAs</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cimetidine</td>
<td>H₂ receptor antagonist</td>
<td>Mainly ç cimetidine</td>
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<tr>
<td>Ranitidine</td>
<td>↓ gastric parietal cell H⁺ secretion</td>
<td>GI disturbance</td>
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</tr>
<tr>
<td>Misoprostol</td>
<td>Prostaglandin analogue</td>
<td>Diarrhoea is v. common</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acts on paraîtial cells to ↓H⁺ secretion</td>
<td></td>
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</tr>
</tbody>
</table>

**Caution**
- may mask symptoms of gastric Ca

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## Laxatives

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
</table>
| Bran Ispaghula                            | Bulk laxatives  
→ faecal mass → ↑ peristalsis | Bloating                    | Bowel obstruction |              |                                                                      |
| Docusate Glycerin (PR) Senna Picosulfate  | Stimulant laxative  
↑ intestinal motility | Bowel obstruction             | Co-danthrusate is a mild stimulant laxative used in Rx of opioid-induced constipation. |
| Lactulose Macrogol Phosphates (PR) Mg Salts | Osmotic laxative  
↑ stool water content | Bowel obstruction             | Lactulose is used in Rx of hepatic encephalopathy       |
| Liquid paraffin                           | Stool softener  
↓ absorption of ADEK vitamins Granulomatous reactions | Bowel obstruction |              |                                                                      |

## Miscellaneous Gastrointestinal Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
</table>
| Hyoscine butylbromide - Buscopan          | Antimuscarinic  
- Antispasmodic | Anti-AChM SEs  
- Dry mouth  
- Palpitations | Myasthenia gravis |              |                                                                      |
| Mebeverine Peppermint oil                 | Antispasmodic |                              |                   |              |                                                                      |
| Loperamide                                | Opioid receptor agonist  
Doesn’t cross BBB  
↓ no central effects. | Abdo cramps | Infective diarrhoea  
Colitis  
Caution in hepatic impairment | |                                                                      |
| Sulfasalazine Mesalazine                  | 5-Aminosalicylate  
Unknown MOA | Sulfasalazine has ↑ SEs  
- blood dyscrasias  
- hepatitis  
- rash, urticaria  
- oligospermia  
- pulmonary fibrosis | Caution in renal or hepatic impairment | Monitor FBC  
Topical in distal disease | |
| Budesonide                                | Steroid  
More potent cf. prednisolone  
High 1st pass metabolism  
↓ systemic effects. | | Used to induce remission in ileal Crohn's | |                                                                      |
| Infliximab: Remicade Etanercept: Enbrel Adalimumab: Humira | Chimeric anti-TNF mAb  
P75 TNFR-Fc fusion protein  
Human anti-TNF mAb | Severe infections  
TB  
Allergic reactions  
CCF  
CNS demyelination | TB | Screen for TB before use  
Parenteral admin  
Give ↓ hydrocortisone to ↓ allergic SEs | |
GORD

Conservative
- Lose wt.
- Raise head of bed
- Small regular meals ≥ 3h before bed
- Stop smoking and ↓ EtOH
- Avoid hot drinks and spicy food
- Avoid tight clothes
- Stop drugs: NSAIDs, steroids, CCBs, nitrates

Medical
- OTC antacids: Gaviscon, Mg trisilicate
  1: Full-dose PPI for 1-2mo
    ▪ Lansoprazole 30mg OD
  2: No response → double dose PPI BD
  3: No response: add an H2RA
    ▪ Ranitidine 300mg nocte
- Control: low-dose acid suppression PRN

Surgical: Nissen Fundoplication
- Indications: all 3 of:
  ▪ Severe symptoms
  ▪ Refractory to medical therapy
  ▪ Confirmed reflux (pH monitoring)

PUD

Conservative
- Lose wt.
- Stop smoking and ↓ EtOH
- Avoid hot drinks and spicy food
- Stop drugs: NSAIDs, steroids

Medical
- OTC antacids: Gaviscon, Mg trisilicate
- H. pylori eradication: PAC500 or PMC250
- Full-dose acid suppression for 1-2mo
  ▪ PPIs: lansoprazole 30mg mane
  ▪ H2RAs: ranitidine 300mg nocte
- Low-dose acid suppression PRN

Surgical
- Rarely performed
- Selective vagotomy
- Antrectomy + vagotomy
- Subtotal gastrectomy + Roux-en-Y

H. pylori Eradication Therapy
- 7 days Rx
- NB. PPIs and cimetidine → false –ve C\(^{13}\) breath tests and antigen tests \(\implies\) stop >2wks before.

PAC 500
- PPI: lansoprazole 30mg BD
- Amoxicillin 1g BD
- Clarithromycin 500mg BD

PMC 250
- PPI: lansoprazole 30mg BD
- Metronidazole 400mg BD
- Clarithromycin 250mg BD

Failure
- 95% success
- Mostly due to poor compliance
- Add bismuth
  ▪ Stools become tarry black
Ulcerative Colitis

Acute Severe UC
- **Resus:** Admit, IV hydration, NBM
- **Hydrocortisone:** IV 100mg QDS + PR
- Transfuse if required
- **Thromboprophylaxis:** LMWH
- **Monitoring**
  - Bloods: FBC, ESR, CRP, U+E
  - Vitals + stool chart
  - Twice daily examination
  - ± AXR

Improvement → oral therapy
- Switch to oral pred + 5-ASA
- Taper pred after full remission

No Improvement → rescue therapy
- Discussion between pt, physician and surgeon
  - **Medical:** ciclosporin, infliximab or visilizumab
  - **Surgical**

Inducing Remission in Mild to Moderate Disease
- **OPD treatment**

Oral Therapy
- **1st line:** 5-ASAs
- **2nd line:** prednisolone
- **3rd line:** ciclosporin or infliximab

Topical Therapy: mainly left-sided disease
- Proctitis: suppositories
- More proximal disease: enemas or foams
- 5-ASAs ± steroids (prednisolone or budesonide)

Additional Therapy: steroid sparing
- Azathioprine
- Infliximab: steroid-dependent pts

Maintaining Remission
- **1st line:** 5-ASAs PO – sulfasalazine or mesalazine
  - Topical Rx may be used in proctitis
- **2nd line:** azathioprine or 6-mercaptopurine
  - Relapsed on ASA or are steroid-dependent
  - Use 6-mercaptopurine if azathioprine intolerant
- **3rd line:** infliximab / adalimumab

Elective Surgery

Indications
- Chronic symptoms despite medical therapy
- Carcinoma or high-grade dysplasia

Procedures
- Proctocolectomy c ¯ end ileostomy or IPAA
- Total colectomy c (IRA)

Crohn’s Disease

Acute Severe Crohn’s

Assessment
- ↑temp, ↑HR, ↑ESR, ↑CRP, ↑WCC, ↓albumin

Management
- **Resus:** Admit, NBM, IV hydration
- **Hydrocortisone:** IV + PR if rectal disease
- **Abx:** metronidazole PO or IV
- **Thromboprophylaxis:** LMWH
- Dietician Review
  - Elemental diet
  - Consider parenteral nutrition
- **Monitoring**
  - Vitals + stool chart
  - Daily examination

Improvement → oral therapy
- Switch to oral pred (40mg/d)

No Improvement → rescue therapy
- Discussion between pt, physician and surgeon
  - **Medical:** methotrexate ± infliximab
  - **Surgical**

Inducing Remission in Mild to Moderate Disease
- **OPD treatment**

Supportive
- High fibre diet
- Vitamin supplements

Oral Therapy
- **1st line**
  - Ileocaecal: budesonide
  - Colitis: sulfasalazine
- **2nd line:** prednisolone (tapering)
- **3rd line:** methotrexate
- **4th line:** infliximab or adalimumab

Perianal Disease
- Occurs in ~50%
- **Ix:** MRI + EUA
- **Rx**
  - Oral Abx: metronidazole
  - Immunosuppression ± infliximab
  - Local surgery ± seton insertion

Maintaining Remission
- **1st line:** azathioprine or mercaptopurine
- **2nd line:** methotrexate
- **3rd line:** Infliximab / adalimumab

Elective Surgery

Indications
- Abscess or fistula
- Perianal disease
- Chronic ill health
- Carcinoma

Procedures
- Limited resection: e.g. ileocaecal
- Strictureplasty
- Defunction distal disease c temporary loop ileostomy

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C. diff Diarrhoea

High Risk Abx
- Cephalosporins
- Clindamycin

General
- Stop causative Abx
- Avoid antidiarrhoeals and opiates
- Enteric precautions

Specific

1st line: Metronidazole 400mg TDS PO x 10-14d

Metronidazole Failure
- Vanc 125mg QDS PO x 10-14d

Severe: Vanc 125mg QDS PO 1st line (may add metro IV)
- ↑ to 250mg QDS if no response (max 500mg)
- Urgent colectomy may be needed if
  - Toxic megacolon
  - ↑ LDH
  - Deteriorating condition

Recurrence (15-30%)
- Reinfection or residual spores
- Repeat course of metro x 10-14d
- Vanc if further relapse (25%)
Cardiovascular

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## Diuretics

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<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frusemide Bumetanide</td>
<td>Loop diuretics</td>
<td>↓ Na</td>
<td>Refractory hypokalaemia Anuric renal failure</td>
<td>↑ toxicity of digoxin (due to ↓K) NSAIDs Gentamicin Li</td>
<td>Monitor U+Es May add K+-sparing diuretic to ↓K loss.</td>
</tr>
<tr>
<td></td>
<td>Inhibit Na / K / Cl triple transporter in ascending loop of henle - ↑ NaCl excretion</td>
<td>↓ K ↓ Ca ↓ Mg ↑ urate Postural hypotension Tinnitus / deafness (rare)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bendrofluazide Metolazone Chlortalidone</td>
<td>Thiazide diuretics</td>
<td>↓Na ↓K ↑Ca ↑urate Postural hypotension ↑glucose and DM</td>
<td>Refractory hypokalaemia Gout Severe renal failure</td>
<td>↑ toxicity of digoxin Li</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhibit NaCl transporter in DCT - ↑ NaCl excretion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone Eplerenone</td>
<td>Aldosterone receptor antagonists</td>
<td>↑ K Gynaecomastia (spiro)</td>
<td>↑ toxicity of digoxin Li</td>
<td>Spiro doses - 25mg OD for HF - 100-400mg OD for diuresis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ↑ Na excretion - ↑ K and H excretion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiloride Triamterine</td>
<td>Block Na channels in collecting tubules - ↑ Na excretion - ↑ K and H excretion</td>
<td>↑K GI upset</td>
<td></td>
<td></td>
<td>Typically used in combo c K+-wasting diuretics.</td>
</tr>
<tr>
<td>Acetazolamide</td>
<td>Carbonic anhydride inhibitor - ↑ HCO₃ excretion</td>
<td>Rash: EM → SJS Peripheral tingling</td>
<td>Sulfonamide hypersensitivity</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A sulphonamide Use - open- / closed-angle glaucoma</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Osmotic diuretic</td>
<td></td>
<td></td>
<td></td>
<td>Use - ↓ IOP - ↓ ICP</td>
</tr>
</tbody>
</table>

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## The Renin-Angiotensin System

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td>ACEi</td>
<td>Hypotension</td>
<td>Suspected or confirmed bilat RAS</td>
<td>↑ risk of RF c NSAIDs</td>
<td>Monitor U+E&lt;br&gt;- ↑ Cr &gt;30% → MRA&lt;br&gt;Titrating dose&lt;br&gt;Avoid in&lt;br&gt;young women who&lt;br&gt;might become&lt;br&gt;pregnant&lt;br&gt;- consider β-B&lt;br&gt;↓ dose in RF</td>
</tr>
<tr>
<td>Captopril</td>
<td></td>
<td></td>
<td>Angioedema/hypersensitivity to ACEi</td>
<td>Diuretics, TCAs and antipsychotics → risk of ↓↓BP</td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td></td>
<td></td>
<td>Salt substitutes (contain K⁺)</td>
<td>Caution c drugs that ↑ K⁺&lt;br&gt;- e.g. spiro</td>
<td></td>
</tr>
<tr>
<td>Perindopril</td>
<td></td>
<td></td>
<td>P/B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>Ang II receptor (AT₁) antagonists</td>
<td>As for ACEI but no cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Losartan</td>
<td></td>
<td></td>
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<tr>
<td>Irbesartan</td>
<td></td>
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</tr>
</tbody>
</table>

### Physiology
- Angiotensinogen is an α2-globulin released by the liver.
- Renin from the JGA converts angiotensinogen → ang 1
- ACE is produced by pulmonary epithelial cells and converts ang 1 → ang 2.
- Ang 2 acts via AT₁ receptor
  - Vasoconstriction
  - Sympathetic activation
  - Aldosterone release from adrenal cortex
  - ↑ renal Na reabsorption
  - ADH release
- Ang 2 is degraded by angiotensinases in RBCs

### Principal Indications
- Heart failure
- HTN
- Post-MI
- Angina
- Diabetic Nephropathy

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## Beta Blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioselective - Bisoprolol - Atenolol - Metoprolol - Esmolol - Nebivolol</td>
<td>Block $\beta$ receptors&lt;br&gt;&lt;br&gt;<strong>Actions via $\beta_1 \rightarrow \downarrow CO</strong>&lt;br&gt;- $\downarrow$ heart rate&lt;br&gt;- $\downarrow$ contractility&lt;br&gt;- small $\downarrow$ BP: central effect + $\downarrow$ renin</td>
<td><strong>Bronchospasm</strong>&lt;br&gt;- inc. cardioselective&lt;br&gt;<strong>$\downarrow$ HR and $\downarrow$ BP</strong>&lt;br&gt;&lt;br&gt;Peripheral vasoconstriction&lt;br&gt;- $\downarrow$ cold extremities&lt;br&gt;- worsened Raynaud’s/PVD&lt;br&gt;&lt;br&gt;Lethargy / fatigue&lt;br&gt;Nightmares&lt;br&gt;&lt;br&gt;Metabolic&lt;br&gt;- $\downarrow$ HDL&lt;br&gt;- $\uparrow$ TGs&lt;br&gt;- $\uparrow$ risk of new onset DM (esp. $\uparrow$ thiazides)</td>
<td><strong>Asthma / bronchospasm</strong>&lt;br&gt;- PVD&lt;br&gt;- Severe bradycardia&lt;br&gt;- Severe heart failure&lt;br&gt;- $\downarrow$ $2^{nd}$-$3^{rd}$ degree AV block</td>
<td><strong>Verapamil and diltiazem $\rightarrow$ risk of AV block and $\downarrow$ HR</strong>&lt;br&gt;Enhanced $\downarrow$ BP effects $\uparrow$ other anti-HTN drugs</td>
<td>Propranolol is v. lipid soluble and easily crosses the BBB $\rightarrow$ CNS effects (nightmares).&lt;br&gt;Atenolol is water soluble and doesn’t cross BBB.</td>
</tr>
<tr>
<td>Non-selective - Carvedilol - Propranolol - Sotalol - Labetalol</td>
<td><strong>Effects</strong>&lt;br&gt;- $\uparrow$ diastolic perfusion&lt;br&gt;- $\downarrow$ $O_2$ demand&lt;br&gt;- $\downarrow$ afterload</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISA - Acebutolol - Pindolol - Oxprenolol</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Vasodilating - Carvedilol - Labetalol - Nebivolol</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Physiology

**$\beta_1$ receptors:**
- Heart: $\uparrow$ rate and contractility
- Kidney: $\uparrow$ renin release from JGA

**$\beta_2$ receptors:**
- Bronchi, GIT: SM relaxation
- Skeletal muscle: arteriolar dilatation
- Liver + skeletal muscle: glycogenolysis and gluconeogenesis

**$\beta_3$ receptors:**
- Adipose tissue: lipolysis

### Pharmacology

**Some $\beta$-B have arteriolar dilating effects which $\downarrow$ TPR**
- Block $\alpha_1$ receptors
- Carvedilol, labetalol, nebivolol

**Cardioselective agents have $\downarrow$ $\beta_2$ effects.**

**ISA: partial agonist activity at adrenoceptors**
- $\downarrow$ bradycardia
- $\downarrow$ cold extremities

**Lipophilic compounds more likely to $\rightarrow$ CNS effects**
- Propranolol, metoprolol

**Hydrophilic compounds may accumulate in renal failure**
- Atenolol, sotalol

**Esmolol is v. short acting:** use IV

### Principal Indications
- Angina
- Heart failure
- Acute MI
- Arrhythmias
- HTN
- Long QT syndrome
- Prophylaxis vs. variceal haemorrhage
- Migraine prophylaxis
- Thyrotoxicosis
- Glaucoma
- Anxiety
<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Selective</strong>&lt;br&gt;- Phenoxybenzamine&lt;br&gt;- Phentolamine</td>
<td>α-blockers</td>
<td>Postural Hypotension&lt;br&gt;Dizziness&lt;br&gt;Headache&lt;br&gt;Urinary incontinence&lt;br&gt;- esp. women&lt;br&gt;Blurred vision</td>
<td>B</td>
<td>↑s hypotensive effects of&lt;br&gt;- diuretics&lt;br&gt;- β-B&lt;br&gt;- CCBs</td>
<td>Phentolamine is short-acting and can be used to control BP in phaeo. Phenoxybenzamine is long-acting and is used to maintain α blockade once BP controlled. Doxazosin and tamsulosin are used in Rx of BPH</td>
</tr>
<tr>
<td><strong>Alpha 1</strong>&lt;br&gt;- Doxazosin&lt;br&gt;- Prazosin</td>
<td>α1- systemic vasodilatation&lt;br&gt;- relaxation of internal urethral sphincter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clonidine</strong></td>
<td>Centrally-acting α2 agonist&lt;br&gt;- ↓ CO&lt;br&gt;- ↓ PVR</td>
<td>Rebound HTN on withdrawal&lt;br&gt;Postural hypotension&lt;br&gt;Constipation&lt;br&gt;Nausea&lt;br&gt;Dry mouth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methyldopa</strong></td>
<td>Centrally-acting α2 agonist&lt;br&gt;Pro-drug&lt;br&gt; - → α-methyl NA</td>
<td>Blood dyscrasias&lt;br&gt;Hepatotoxic&lt;br&gt;Drug-induced lupus&lt;br&gt;Drowsiness</td>
<td>L&lt;br&gt;Depression</td>
<td>Avoid w/i 2wks of MAOI</td>
<td>Mainly used in P</td>
</tr>
<tr>
<td><strong>Hydralazine</strong></td>
<td>Vasodilator&lt;br&gt;- arteries &gt; veins</td>
<td>Drug-induced lupus&lt;br&gt;↑HR&lt;br&gt;GI upset&lt;br&gt;Headache</td>
<td>SLE&lt;br&gt;↓ dose in hepatic or renal impairment</td>
<td></td>
<td>Mainly used in P</td>
</tr>
<tr>
<td><strong>Nitroprusside</strong></td>
<td>Vasodilator&lt;br&gt;- arteries &gt; veins</td>
<td></td>
<td></td>
<td>Hypertensive crisis</td>
<td></td>
</tr>
<tr>
<td><strong>Minoxidil</strong></td>
<td>Vasodilator</td>
<td>Hypertrichosis</td>
<td></td>
<td></td>
<td>Used to promote hair growth</td>
</tr>
</tbody>
</table>
# Calcium Channel Blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dihydropyridines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Nifedipine</td>
<td>Mainly Arterial SM Activity</td>
<td>Flushing</td>
<td>Cardiogenic shock</td>
<td>Risk of ↓↓ BP  c α/β-B</td>
<td></td>
</tr>
<tr>
<td>- Amlodipine</td>
<td>- vasodilatation (inc. coronary)</td>
<td>Headache</td>
<td>Unstable angina</td>
<td>Fx ↑d by grapefruit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- particularly pre-capillary arterioles</td>
<td>Ankle oedema</td>
<td>Significant AS</td>
<td>Fx ↓d by:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dizziness</td>
<td>w/ 1mo of MI</td>
<td>- Rifampicin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ TPR  →  ↑ sympathetic tone  →  ↑ HR</td>
<td>↑ BP</td>
<td></td>
<td>- CBZ + phenytoin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gingival hypertrophy</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>esp. nifedipine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Non-dihydropyridines</strong></td>
<td>Mainly Cardiac Activity</td>
<td>Headache</td>
<td>HF</td>
<td>Risk of AV block, HF and asystole  c β-blockers.</td>
<td></td>
</tr>
<tr>
<td>- Diltiazem</td>
<td>- -ve inotropic effect (esp. verapamil)</td>
<td>Flushing</td>
<td>2nd/3rd degree AV block</td>
<td>↑ s fx of digoxin</td>
<td></td>
</tr>
<tr>
<td>- Verapamil</td>
<td>- verapamil also slows conduction @ SA and AV nodes</td>
<td>AV block</td>
<td></td>
<td>Fx of verapamil ↑d by:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Some activity @ arterial SM (&lt;DHPs)</td>
<td>HF</td>
<td></td>
<td>- Grapefruit juice</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ BP</td>
<td></td>
<td>- Macrolides</td>
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<td></td>
<td></td>
<td>Ankle oedema</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Constipation</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>Gynaecomastia (verap)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Pharmacology

**MOA**
- Bind α1 subunit of L-type Ca channel at distinct sites
- Prevent channel opening and inhibit Ca entry

**Effects**
- All CCBs are vasodilators: ↓ afterload
- Also dilate coronary arteries
- Pre-capillary vasodilatation → transudative oedema
- Dihydropyridines act only @ arterial SM and can → reflex tachycardia
- Avoid short acting preparations
- Verapamil is highly negatively inotropic
  - CI in HF and  c β-B
- Verapamil is also negatively chronotropic
- Diltiazem is less negatively inotropic and chronotropic than verapamil

## Indications

### Verapamil and Diltiazem
- HTN
- Angina
- AF

### Nifedipine MR and Amlodipine
- HTN (long-acting)
- Angina: esp. good for Prinzmetal’s
- Raynaud’s
## Nitrates

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTN</td>
<td>NO donor c° rapid onset and short duration (30min)</td>
<td>↓BP (inc. postural)</td>
<td>AS and MS</td>
<td>Sildenafil, tadakafil and vardenafil are CI → ↓BP</td>
<td>SL spray or tabs (300ug)</td>
</tr>
<tr>
<td></td>
<td>High 1st pass metabolism</td>
<td>Headache</td>
<td>↓BP</td>
<td>↓s fx of heparins if given IV</td>
<td>Use for relief of pain in angina, ACS</td>
</tr>
<tr>
<td></td>
<td>Mainly venodilation → ↓ preload</td>
<td>Syncope</td>
<td>↓BP Constrictive pericarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Small ↑ coronary vasodilatation</td>
<td>Dizziness</td>
<td>Fascinates pericarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flushing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reflex tachycardia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISMN / ISDN</td>
<td>Long-acting nitrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISMN is active metabolite of ISDN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MN avoids unpredictable first-pass metabolism of DN</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Tolerance develops quickly: need 8h drug-free period (usually @ night)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Miscellaneous Anti-Anginals

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicorandil</td>
<td>K&lt;sub&gt;ATP&lt;/sub&gt; channel activator + nitrate component Arterial and venous dilator</td>
<td>Headache</td>
<td>Cardiogenic shock</td>
<td>Sildenafil → ↓BP</td>
<td>Indications - Uncontrolled angina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flushing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dizziness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GI ulcers (rare)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivabradine</td>
<td>Inhibits “funny” current in SA node → ↓ pacemaker activity → ↓ HR</td>
<td>Visual changes</td>
<td>↓BP or ↓HR and HB</td>
<td>Subject to hepatic induction / inhibition</td>
<td>Indication - Angina (useful if β-B CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓HR and HB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimetazidine</td>
<td>Inhibits fatty acid oxidation → ↑ myocardial glucose use</td>
<td></td>
<td>↓BP or ↓HR and HB</td>
<td></td>
<td>Indication - Angina</td>
</tr>
<tr>
<td>Ranolazine</td>
<td>Inhibits late Na current</td>
<td></td>
<td>↓BP or ↓HR and HB</td>
<td></td>
<td>Indication - Angina</td>
</tr>
</tbody>
</table>

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Vaughan-Williams Classification

Class I
- Na⁺ channel blockers (local anaesthetics).
- All slow conduction
  - Subclasses have additional effects on action potential
- Use-dependent: preferentially block open or refractory Na⁺ channels

1a: quinidine, procainamide, disopyramide
- Sites of action: A, SAN, AVN, V
- Repolarisation: Prolonged → ↑ AP duration
- Indications: V arrhythmias
- SEs: anti-AChM, negative inotropes

1b: lignocaine, mexiletine
- Sites of action: V only
- Repolarisation: Shortened → normal or ↓ AP duration
- Indications: V arrhythmia following MI

1c: flecainide
- Sites of action: A, SAN, AVN, V
- Repolarisation: Little effect
- Indications: Pre-excited AF (WPW), Acute AF

Class II
- β-Blockers: metoprolol, propranolol, esmolol, atenolol
- Sites of action: A, SAN, AVN, V
- MOA
  - ↑ refractory period of AVN → slow AVN conduction
  - Prevent arrhythmias due to sympathetic discharge (e.g. following MI)
- Indications: post-MI, AF (rate control), SVT
- Caution: negative inotropes

Class III
- Amiodarone and sotalol
- Sites of action: A, SAN, AVN, V
- MOA
  - K⁺ channel blockers
  - ↑↑ refractory period = ↑ QTc
- Indications: V and SV arrhythmias, pre-excited AF (WPW)
- Caution: can → arrhythmias (esp. TDP)

Class IV
- CCBs: verapamil and diltiazem (non-DHPs)
- Site of action: AVN
- MOA: Slow AVN conduction
- Indications: prevent recurrence of SVT, AF (rate control), acute SVT
- Caution: negative inotropes

Unclassified
Digoxin
- Cardiac glycoside
- MOA
- Positive inotrope: inhibits myocyte Na⁺/K⁺ ATPase → ↑ Na⁺ & ↑ Ca²⁺
- Negative chronotrope
  - Slows AV conduction → ↓ rate and ↑ AVN refractory period
  - Only slows resting rate, NOT exercise rate
- Indication: SVT and AF
- Caution
  - Toxicity can → arrhythmias
  - ↑ toxicity if ↓ K (reduced competition for binding site)

Adenosine
- MOA
  - Acts @ A1 receptors in cardiac tissue → myocyte hyperpolarization
  - Transient AV block
- Indication: SVTs

Clinical Classification
AVN
- Adenosine
- β-B
- Verapamil
- Digoxin
- Use: AF, SVT

Atria and Ventricles
- Class 1a, 1c and amiodarone

Ventricles only
- Class 1b
### Anti-Arrhythmic Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Indications</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disopyramide</td>
<td>Class Ia</td>
<td>Ventricular arrhythmias (esp. post-MI)</td>
<td>VT, VF, TdP Anti-muscarinic</td>
<td>Heart block (2/3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lignocaine</td>
<td>Class Ib</td>
<td>Ventricular arrhythmias (esp. post-MI)</td>
<td>Drowsiness，在Parasthesia，Dizziness，Bradycardia → cardiac arrest</td>
<td>Heart block</td>
<td>Cimetidine ↑ lidocaine levels</td>
<td>IV use only</td>
</tr>
<tr>
<td>Flecainide</td>
<td>Class Ic</td>
<td>Pre-excited AF (WPW) Cardioversion in AF Suppress V ectopics</td>
<td>Strong → ve inotrope - Oedema - Dyspnoea</td>
<td>Structural heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Class III</td>
<td>SVT AF / flutter Pre-excited AF V arrhythmias (inc. VF)</td>
<td>Eye – corneal microdeposits Thyroid – hyper / hypo Lung – pulmonary fibrosis GI/Liver – ↑ LFTs – N/V Neuro – peripheral neuropathy Skin – photosensitivity – blue-grey discoloration – phlebitis (give centrally)</td>
<td>β-B and CCB → ↑ risk of HB ↑ s levels of - digoxin (halve dig dose) - warfarin - phenytoin ↑ risk of V arrhythmias</td>
<td>Monitor: - TFTs, LFTs (base + 6-moly) - K⁺ (baseline) - CXR (baseline)</td>
<td>Requires loading dose Avoid sunlight</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Cardiac glycoside</td>
<td>AF / flutter SVT (HF)</td>
<td>Toxicity - Any arrhythmia - e.g. SVT ċ AV block - Nausea - Xanthopsia - Confusion - ↑ K⁺ Chronic - Gyneacomastia &quot;Reverse tick&quot; ECG - not a sign of toxicity</td>
<td>Complete heart block VF/VT HOCM SVTs 2⁰ to WPW</td>
<td>Dig fx/toxicity ↑d by: - CCB (esp. verapamil) - Amiodarone (halve dig dose) - Diuretics (loop/thiazide due to ↓ K⁺) ↓ digoxin intestinal absorption: - Antacids - Cholestyramine</td>
<td>Caution - Renal excretion.: caution in impairment - e.g. in the elderly Monitor - U+Es: Drug levels (6h post-dose) Load then maintenance</td>
</tr>
<tr>
<td>Adenosine</td>
<td>SVT: Dx and Rx</td>
<td>SVT: Dx and Rx</td>
<td>Bronchospasm Chest pain Flushing Nausea Light-headedness</td>
<td>Asthma Heart Block (2/3) Sick sinus syndrome</td>
<td>Fx prolonged by dipyridamole Fx ↓ by theophylline</td>
<td>t½ = 8-10secs</td>
</tr>
</tbody>
</table>

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## Anti-Platelet Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td>Irreversible, non-selective COX inhibitor → ↓ plat TxA2 → - ↓ plat activation - ↓ platelet adhesion, aggregation</td>
<td>Gastritis, Gastric ulceration, Bleeding Bronchospasm</td>
<td>&lt;16yrs (Reyes syn.) - except in Kawasaki’s Active PUD Bleeding disorders Gout R (if GFR &lt; 10ml/min) P, B Caution: - Asthma - Uncontrolled HTN</td>
<td>† risk of bleeding with other anti-coagulants and anti-platelets: W+ †s fx of - sulphonylureas - methotrexate</td>
<td>Stop 7d before surgery if sig. bleeding expected. Max dose: 4g/day</td>
</tr>
<tr>
<td><strong>Clopidogrel</strong> (Plavix)</td>
<td>Thienopyridine Irreversible adenosine R antagonist - inhibits ADP-induced fibrinogen binding to GPIIb/IIIa</td>
<td>Bleeding - esp. GI or intracranial GI upset Dyspepsia / PU TTP (rare) Blood dyscrasias (rare)</td>
<td>Severe LB</td>
<td>Avoid c warfarin.</td>
<td>Prodrug converted by hepatic CYP enzymes. Used following bare-metal or drug eluting stents. Stop 7d before surgery if sig. bleeding expected</td>
</tr>
<tr>
<td><strong>Abciximab</strong></td>
<td>MAb or synthetic inhibitors of GPIIb/IIIa</td>
<td>Bleeding Thrombocytopenia</td>
<td>Many, mainly concerned c bleeding.</td>
<td>Only abciximab can be given PO Given to high-risk pts. c NSTEMI</td>
<td></td>
</tr>
<tr>
<td><strong>Dipyridamole</strong></td>
<td>Phosphodiesterase inhibitor - ↑cAMP inhibits plat aggregation TxA2 synthetase inhibitor</td>
<td>Headache</td>
<td>Myasthenia gravis</td>
<td>Enhances effects of adenosine May be used c aspirin in 2(^{0}) prevention of stroke</td>
<td></td>
</tr>
</tbody>
</table>

### Indications for Anti-Platelet Therapy
- ACS
- Secondary prevention
  - IHD
  - Stroke
  - TIA
  - PVD
- Primary prevention
  - 10yr CVD risk >20% + controlled BP
- Tissue heart valve replacements

### Recommendations
- Clopidogrel is preferred over aspirin + DP-MR for 2\(^{0}\) prevention after stroke
- Aspirin + DP-MR is preferred over clopi following a TIA.
- Clopidogrel + aspirin is given in the emergent Mx of STEMI and NSTEMI
  - Continue clopi for 12mo in NSTEMI or 1mo in STEMI
- Clopi + aspirin not beneficial following stroke

### Aspirin OD
- Mixed met acidosis and resp alkalosis
- Pres: vomiting, dehydration, tinnitus, hyperventilation
- Lx
  - Salicylate and paracetamol level
  - U+E, ABG, glucose, LFTs, INR.
- Rx
  - Gastric lavage if <1h since OD
  - Correct dehydration and acidosis (c HCO\(_3\)^-).
  - Alkalinate urine: NaHCO\(_3\) + KCl
  - Haemodialysis: levels >700mg/L, cardiac/renal failure, seizures

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## Lipid Lowering Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosuvastatin</td>
<td>Statins HMG-CoA Reductase Inhibitors — block rate-limiting step in cholesterol synthesis → ↓ hepatocyte cholesterol → ↑ hepatic LDL receptors → ↓ LDL cholesterol ↑ HDL ↓ TGs (mild)</td>
<td>Myositis - stop if CK 5x ULN - can → rhabdo + ATN Deranged LFTs GI upset</td>
<td>L P (contraception needed during use and for 1mo after)</td>
<td>↑ risk of myositis ç : - Fibrates - Macrolides - Azoles - Grapefruit juice (ALS) - Protease Inhibitors - Ciclosporin - Nicotinic Acid</td>
<td>Monitor - LFTs ± CK Take statins nocte ↑ cholesterol synth overnight</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td></td>
<td></td>
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<tr>
<td>Simvastatin</td>
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<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td></td>
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</tr>
<tr>
<td>Pravastatin</td>
<td>(↓ing potency)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bezafibrate</td>
<td>Fibrates Stimulate lipoprotein lipase → ↓ TG: 36% ↓ LDL: 8% ↑ HDL: 10%</td>
<td>GI upset ↓ appetite Myositis Blood dyscrasias</td>
<td>Gallbladder disease PBC ↓ albumin (esp. nephrotic syndrome) R L P B</td>
<td>↑ risk of myositis ç statins ↑sx fx of anti-diabetics</td>
<td>W+ Use ↑ absorption of other drugs: e.g. digoxin Don’t take w/i ~3h of other drugs.</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Anion Exchange Resin Binds bile acids and prevents enterohepatic recycling ↓ liver must synthesise more bile acids from cholesterol → ↑ LDL receptors…</td>
<td>GI upset - bloating - constipation - N/V Can ↑ TGs Impair absorption of fat sol drugs / vits (ADEK)</td>
<td>Complete biliary obstruction</td>
<td>↓s absorption of other drugs: e.g. digoxin</td>
<td></td>
</tr>
<tr>
<td>Cholestipol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotinic Acid</td>
<td>Inhibits cholesterol and TG synthesis ↑ HDL</td>
<td><strong>Flushing</strong> n/v</td>
<td>Peptic ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>Inhibits intestinal cholesterol absorption Pro-drug</td>
<td>GI upset Myalgia</td>
<td>↑ risk of myositis ç statins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omega-3 FAs</td>
<td>↓ TGs</td>
<td>GI upset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orlistat</td>
<td>Pancreatic lipase inhibitor → impaired absorption of dietary fat</td>
<td>GI upset - steatorrhoea - abdo distension ↓ absorption of fat-sol drugs and vitamins</td>
<td>Cholestasis</td>
<td>Warfarin - Difficulty controlling INR</td>
<td>Use - adjunct in obesity Mx</td>
</tr>
</tbody>
</table>

### Statin Indications
- Any known CVD
- DM (age >40)
- 10yr CVD risk ≥20%
- Aim: TC ≤4mM

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Warfarin

MOA
- Inhibits Vit K epoxide reductase
- Prevents recycling of Vit K → functional Vit K deficiency
- Inhibits synthesis of factors 2, 7, 9, 10, C and S
- Initially procoagulant: protein S is depleted first.

Indications
Treatment | Prophylaxis
--- | ---
VTE | VTE
AF | AF
Mechanical heart valves | Mechanical heart valves
Large anterior MI (for 3mo) | Large anterior MI (for 3mo)
Dilated cardiomyopathy / LV aneurysm | Dilated cardiomyopathy / LV aneurysm

NB. Pts. Ca-assoc. VTE should initially be treated for 6mo with therapeutic dose of LMWH rather than warfarin.

Pharmacokinetics
- Long t½: 40hrs
- Takes 16hrs to affect INR
- Peak INR effect of a dose seen @ 2-3d
- Effect of a given dose lasts 4-5d
- Highly albumin-bound
- CyP metabolism

Side Effects
- Haemorrhage, bruising
- Skin necrosis (due to protein S deficiency)
- Purple toe syndrome (cholesterol embolism)
- Osteoporosis
- Hepatic dysfunction

Caution
- Hepatic impairment: avoid if severe
- Renal impairment: avoid if severe
- Alcoholics

Contraindications
- Pregnancy
  - Teratogenic in 1st trimester
  - Foetal haemorrhage in 3rd trimester
- PUD
- Severe HTN
- Caution if R/L, recent surgery, risk of falls

Interactions
<table>
<thead>
<tr>
<th>W+</th>
<th>W-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme inhibitors</td>
<td>CBZ</td>
</tr>
<tr>
<td>ETOH</td>
<td>Rifampicin</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>OCP</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>St. John’s Wart</td>
</tr>
<tr>
<td>Abx (may also ↓)</td>
<td>Cranberry juice</td>
</tr>
</tbody>
</table>

INR Target and Duration

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT prophylaxis</td>
<td>2-2.5</td>
<td></td>
</tr>
<tr>
<td>Calf DVT</td>
<td>2.5</td>
<td>Cause known: 6wks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No cause: 3mo</td>
</tr>
<tr>
<td>Above knee DVT</td>
<td>2.5</td>
<td>Cause known: 3mo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No cause: 6mo</td>
</tr>
<tr>
<td>PE</td>
<td>2.5</td>
<td>Cause known: 3mo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No cause: 6mo</td>
</tr>
<tr>
<td>Recurrent DVT/PE</td>
<td>2.5</td>
<td>Indefinite</td>
</tr>
<tr>
<td></td>
<td>3.5 if on W</td>
<td></td>
</tr>
<tr>
<td>AF</td>
<td>2.5</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Mitral valve disease</td>
<td>2.5</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Anti-phospholipid syn.</td>
<td>3.5</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Metal valves</td>
<td>3.5</td>
<td>Indefinite</td>
</tr>
</tbody>
</table>

Dosing: Tait Model
- Day 1-4: warfarin 5mg OD @ 6pm
- Day 5: check INR and adjust dose according to table
- Day 8: check INR and adjust dose according to table
- >Day 8: check INR and adjust dose according to table
- OPD: warfarinisation over 3-4wks is safe and effective

Raised INR

Major bleeding
- Stop warfarin
- Vit K IV
- Prothrombin complex concentrate
  - FFP 15ml/kg if unavailable

>8 (no bleed or minor bleeding)
- Stop warfarin and restart when INR <5
- Vit K IV/PO if risk factors for bleeding
  - E.g. head injury, stroke, epistaxis, prev Hx

6 – 8 (no bleed or minor bleeding)
- Stop warfarin and restart when INR <5

4.5 – 6
- ↓ or omit warfarin and restart when INR <5

Vitamin K
- Onset of action = 6h
- Oral is as efficacious as IV
- Oral Vit K can → prolonged anticoagulant resistance
  - If continuing anticoagulation, avoid if possible
  - Continuing warfarin: 0.5mg slow IV
  - Discontinuing warfarin: 2.5-5mg IV

PCC
- Factors 2, 7, 9 and 10
- Immediate reversal of anticoagulation
- Temporary effect: give Ca Vit K
- Risk of VTE and v. expensive

VTE Prophylaxis on Long-Haul Flights
- Low risk: avoid dehydration, regularly flex ankles
- Mod risk: as above + compression travel socks
  - Previous VTE, GA w/i last 1-2mo
- High risk: as above + consider LMWH before flight
  - Surgery under GA w/i last 1mo
Heparin

MOA
- Co-factor for ATIII: inhibits factors 2, 10, 11 and 12.
- LMWH and fondaparinux only inhibit factor 10.

LMWH or UH
- LMWH has longer t½ and response is more predictable → no monitoring needed
- UH has rapid onset and short t½
  - Useful when rapid control over effects needed (e.g. risk of bleeding)
  - Less risk of HIT and osteoporosis for LMWH

Indications

Treatment
- VTE
- ACS
- Acute arterial obstruction

LMWH or UH
- VTE
- Coagulation in extra-corporeal circuits

Side effects

- Thrombocytopenia
  - Immune-mediated
  - Develops ~6d after initiation (2-3% of people with UH)
  - → thrombosis
- Osteoporosis (long-term use)
- Hyperkalaemia: heparin inhibits aldosterone

Contraindications

- Bleeding disorders
- Plats <60
- Previous HIT
- PU

Dosing
- LMWH: e.g. enoxaparin
  - Prophylaxis: 20-40mg pre- and post-surgery
  - Treatment: 1.5mg/kg/24h
- UH
  - 5000iu bolus IV over 30min
  - Infuse UF @ 18iu/kg/h
  - Check APTT @ 6h (aim for 1.5-2.5x control)

Thrombolytics

MOA
- Convert plasminogen → plasmin
- Plasmin breaks down fibrin

Indications
- STEMI
- Stroke
- Life-threatening PE
- Acute limb ischaemia

Streptokinase (derived from streptococci)

Side Effects
- Bleeding
- Allergic reactions
  - Rash
  - Anaphylaxis
- Reperfusion dysrhythmias after MI
- Hypotension
- Development of Abs: only use streptokinase once

Admin: infusion over 1h

Rh-TPA

Side Effects
- Bleeding, hypotension, reperfusion dysrhythmias

Admin
- Tenectaplace, reteplase: bolus
- Alteplase: infusion
- Give with UH heparin IV for 24-48 to avoid rebound hypercoaguable state.

Contraindications

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhagic stroke at any time</td>
<td>TIA in last 6mo</td>
</tr>
<tr>
<td>Ischaemic stroke in last 6mo</td>
<td>Warfarin</td>
</tr>
<tr>
<td>CNS trauma or neoplasms</td>
<td>Pregnancy or w/1 wk post-partum</td>
</tr>
<tr>
<td>Major trauma/surgery in last 3wks</td>
<td>Refractory resuscitation</td>
</tr>
<tr>
<td>Gl bleed w/ last 1mo</td>
<td>Refractory HTN (&gt;180/110)</td>
</tr>
<tr>
<td>Known bleeding disorders</td>
<td>Advanced liver disease</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Infective endocarditis</td>
</tr>
<tr>
<td>Non-compressible puncture (e.g. LP)</td>
<td>Acute peptic ulcer</td>
</tr>
</tbody>
</table>
Atrial Fibrillation

Acute (<48h)
- Unstable → emergency cardioversion
- Control ventricular rate: β-B or CCB
- Start LMWH
- Cardiovert: electrical or flecainide / amiodarone

Paroxysmal AF
- Self-limiting, <7d, recurs
- Anticoagulate: use CHADSVAS
- Rx “pill-in-pocket”: flecainide, propafenone
- Prevention: β-B, sotalol or amiodarone

Persistent AF
- >7d, may recur even after cardioversion

Try rhythm control first-line if
- Symptomatic or CCF
- Younger (<65)
- Presenting first time cl lone AF
- Secondary to treated precipitant

Rhythm Control
- TTE first: structural abnormalities
- Anticoagulate cl warfarin for ≥3wks
  - or use TOE to exclude intracardiac thrombus.
- Pre-Rx ≥4wks cl sotalol or amiodarone if ↑ risk of failure
- Electrical or pharmacological cardioversion
- ≥4 wks anticoagulation afterwards (target INR 2.5)

Maintenance antiarrhythmic
- Not needed if successfully treated precipitant
- 1st: β-B (e.g. bisoprolol, metoprolol).
- 2nd: amiodarone

Rate control (target <90bpm at rest):
- 1st line: β-B or rate-limiting CCB (NOT both!)
- 2nd line: add digoxin (don’t use as monotherapy)
- 3rd line: consider amiodarone

Mx of Permanent AF
- Failed cardioversion / unlikely to succeed
  - AF >1yr, valve disease, poor LV function
  - Pt. doesn’t want cardioversion
  - → Rate control

CHA2-Ds2-VAS Score
- Determines necessity of anticoagulation in AF
- Warfarin CI in AF
  - Bleeding diathesis, ↓blasts, BP > 160/90, poor compliance
  - Dabigatran may be cost-effective alternative.

CHA2-Ds2: VAS
- CCF
- HTN
- Age ≥75 (2 points)
- DM
- Stroke or TIA (2 points)

Score
- 0: aspirin 300mg
- ≥1: Warfarin

Angina Pectoris

Lifestyle
- Stop smoking
- Wt. loss and ↑ exercise
- Healthy diet: oily fish, fruit, veg, ↓ sat fats, ↓ Na

Medical

2° Prevention: prevent cardiovascular events
- Aspirin 75mg OD
- ACEi (esp. if angina + DM)
- Statins: simvastatin 40mg
- Antihypertensives

Anti-anginals: prevents angina episodes
1. GTN (spray or SL) + either
  - 1st: β-B (e.g. Atenolol 50-100mg OD)
  - 2nd: CCB (e.g. Verapamil 80mg TDS)
2. If either β-B or CCB doesn’t control symptoms, try the other option.
3. Can try β-B + dihydropyridine CCB
  - e.g. amlodipine 10mg/24h
4. If symptoms still not controlled
  - ISMN 20-40mg BD (8h washout @ PM) or slow-release nitrate (lmdur 60mg OD)
  - Ivabradine (esp. if can’t take β-B)
  - Nicorandil 10-30mg BD
  - Ranolazine

Interventional: PCI

Indications
- Poor response to medical Rx
- Refractory angina but not suitable for CABG

Complications
- Restenosis (20-30% @6mo)
- Emergency CABG (<2%)
- MI (<2%)
- Death (<0.5%)

Clopidogrel ↓s risk of restenosis
- Bare metal stent: 1mo
- Drug-eluting (e.g. sirolimus) stent: 1yr

Surgical
- CABG

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Chronic Heart Failure

General Mx

1\textsuperscript{O}/2\textsuperscript{O} Cardiovascular Risk
- Stop smoking
- ↓ salt intake
- Optimise wt.: ↑ or ↓ - dietician
- Supervised group exercised based rehab programme
- Aspirin
- Statin

Rx Precipitants / Causes
- Underlying cause
  - Valve disease
  - Arrhythmias
  - Ischaemia
- Exacerbating factors
  - Anaemia
  - Infection
  - ↑BP

Specific Mx
- ACEi, β-B and spiro → ↓ mortality

1\textsuperscript{st} line: ACEi/ARB + β-B + loop diuretic
- ACEi/ARB: e.g. lisinopril or candesartan
  - Hydralazine + ISDN if not tolerated
- β-B: e.g. carvedilol or bisoprolol (licensed)
  - Start low, go slow
  - E.g. carvedilol 3.125mg/12h → 25-50mg/24h
  - Wait ≥2wks between increments
  - Switch stable pts taking a β-B for a comorbidity to a β-B licensed for heart failure
  - β-B therapy may be particularly good in COPD
- Loop diuretic: frusemide or bumetanide

2\textsuperscript{nd} line: get specialist advice
- Spironolactone / eplerenone
  - Watch K carefully (on ACEi too…)
- ACEi + ARB
- Vasodilators: hydralazine + ISDN
  - Additional Rx in Blacks

3\textsuperscript{rd} line
- Digoxin
- Cardiac resynchronisation therapy ± ICD

Other Considerations
- Monitoring
  - BP: may be v. low
  - Renal function
  - Plasma K
  - Daily wt.
- Use amlodipine for comorbid HTN or angina
- Avoid verapamil, diltiazem and nifedipine (short acting)

Hypertension

Do ABPM to confirm Dx before Rx (unless severe HTN)

Lifestyle interventions
- ↑ exercise
- ↓ smoking, ↓ EtOH, ↓ salt, ↓ caffeine

Indications for Pharmacological Rx
- <80yrs, stage 1 HTN (>140/90) and one of:
  - Target organ damage (e.g. LVH, retinopathy)
  - 10yr CV risk ≥20%
  - Established CVD
  - DM
  - Renal disease
- Anyone with stage 2 HTN (>160/100)
- Severe / malignant HTN (specialist referral)
- Consider specialist opinion if <40yrs with stage 1 HTN and no end organ damage.

BP Targets
- Under 80yrs: <140/90 (<130/80 in DM)
- Over 80yrs: <150/90

CV Risk Mx
- Statins for 1\textsuperscript{st} prevention if 10yr CVD risk ≥20%
- Aspirin may be indicated: evaluate risk of bleeding

<table>
<thead>
<tr>
<th>Antihypertensive Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 55</td>
</tr>
<tr>
<td>&gt; 55 / Black</td>
</tr>
<tr>
<td>1:</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>C (or D)</td>
</tr>
<tr>
<td>2:</td>
</tr>
<tr>
<td>A + C (I/D)</td>
</tr>
<tr>
<td>3:</td>
</tr>
<tr>
<td>A + C + D</td>
</tr>
<tr>
<td>4:</td>
</tr>
<tr>
<td>Resistant HTN</td>
</tr>
<tr>
<td>A+ C + D + consider further diuretic (e.g. spiro) or α-blocker or β-B.</td>
</tr>
<tr>
<td>Seek expert opinion</td>
</tr>
</tbody>
</table>

A: ACEi or ARB
- e.g. lisinopril 10mg OD (↑ to 30-40mg)
- e.g. candesartan 8mg OD (max 32mg OD)
C: CCB: e.g. nifedipine MR 30-60mg OD
D: Thiazide-like diuretic: e.g. chlortalidone 25-50mg OD

In step 2, use ARB over ACEi in blacks.
Avoid thiazides + β-B if possible: ↑ risk of DM
Only consider β-B if young and ACEi/ARB not tolerated.

Malignant HTN
- BP > 180/110 + papilloedema and/or retinal haemorrhage
- Controlled ↓ in BP over days to avoid stroke
- Atenolol or long-acting CCB PO
- Encephalopathy / CCF: fruse + labetalol / nitroprusside IV
  - Aim for 110 diastolic over ~4h
## Bronchodilators

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-agonists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting, Fast Onset</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-agonists</td>
<td>Act @ bronchial β2 receptors</td>
<td>Tachycardia</td>
<td></td>
<td>↓ K in high doses c</td>
<td>Salbutamol may be given IVI in acute severe asthma.</td>
</tr>
<tr>
<td>Salbutamol: Ventolin</td>
<td>- SM relaxation</td>
<td>Tremor</td>
<td></td>
<td>- Corticosteroids</td>
<td></td>
</tr>
<tr>
<td>Terbutaline: Bricanyl</td>
<td>- ↓ mucus secretion</td>
<td></td>
<td></td>
<td>- Loop / thiazide diuretics</td>
<td></td>
</tr>
<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td>- Theophylline</td>
<td></td>
</tr>
<tr>
<td>Salmeterol: Serevent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol: (Fast onset)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Muscarinic Antagonists</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium: Atrovent</td>
<td>Bronchodilatation</td>
<td>Dry mouth</td>
<td>Caution</td>
<td>- Closed Angle Glaucoma</td>
<td></td>
</tr>
<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td>- Prostatic hypertrophy</td>
<td></td>
</tr>
<tr>
<td>Tiotropium: Spiriva</td>
<td>↓ mucus secretion</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

## Inhaled Corticosteroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beclometasone</strong>: Becotide</td>
<td>Act over wks → ↓ inflammation</td>
<td>Oral candidiasis</td>
<td></td>
<td>↓ risk of complications</td>
<td></td>
</tr>
<tr>
<td><strong>Budesonide</strong>: Pulmicort</td>
<td>- ↓ cytokine production</td>
<td></td>
<td></td>
<td>- use a spacer</td>
<td></td>
</tr>
<tr>
<td><strong>Fluticasone</strong>: Flixotide</td>
<td>- ↓ prostaglandin / leukotriene synthesis</td>
<td></td>
<td></td>
<td>- rinse mouth after use</td>
<td></td>
</tr>
<tr>
<td><strong>Seretide</strong></td>
<td>- ↓ IgE secretion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Budesonide + formoterol</td>
<td>- ↓ leukocyte recruitment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Symbicort</strong></td>
<td>Prevent long-term ↓ in lung function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Fluticasone + salmeterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Seretide</strong></td>
<td>- Fluticasone + salmeterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seretide</td>
<td>Preven long-term ↓ in lung function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Budesonide</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Budesonide + formoterol</td>
<td></td>
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<td></td>
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<tr>
<td><strong>Symbicort</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- Fluticasone + salmeterol</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Symbicort</strong></td>
<td></td>
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</tr>
</tbody>
</table>
# Miscellaneous Respiratory Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Theophylline MR</strong></td>
<td>Methylxanthines</td>
<td>Nausea</td>
<td></td>
<td>↓d levels</td>
<td>Aminophylline is IV form</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>PDE inhibitors</td>
<td>Arrhythmias</td>
<td></td>
<td>- smoking</td>
<td>- give IV slowly</td>
</tr>
<tr>
<td></td>
<td>- ↑cAMP → bronchodilatation</td>
<td>Seizures</td>
<td></td>
<td>- EtOH</td>
<td>- Too fast → VT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ K</td>
<td></td>
<td>- CyP inducers</td>
<td>- monitor c¯ ECG and check plasma levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↑d levels</td>
<td>CyP metabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- CCBs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- CyP inhibitors</td>
<td></td>
</tr>
<tr>
<td><strong>Montelukast:</strong></td>
<td>Leukotriene receptor antagonist</td>
<td></td>
<td></td>
<td></td>
<td>Particularly useful for NSAID-</td>
</tr>
<tr>
<td><strong>Singulair</strong></td>
<td>Block cysteinyl leukotrienes</td>
<td></td>
<td></td>
<td></td>
<td>and exercise-induced asthma</td>
</tr>
<tr>
<td><strong>Zafirlukast</strong></td>
<td></td>
<td>? Churg-Strauss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Roflumilast</strong></td>
<td>PDE-4 inhibitor</td>
<td>GI</td>
<td>Sev immunological disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Omalizumab</strong></td>
<td>Humanised anti-IgE mAb</td>
<td></td>
<td></td>
<td></td>
<td>SC injection every 2-4wks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Used for severe asthma</td>
</tr>
<tr>
<td><strong>Carbocysteine</strong></td>
<td>Mucolytic</td>
<td>GI bleed (rare)</td>
<td>Active peptic ulceration</td>
<td></td>
<td>Use: COPD</td>
</tr>
<tr>
<td><strong>Dornase ALFA (DNase)</strong></td>
<td>Mucolytic</td>
<td></td>
<td></td>
<td></td>
<td>Use: CF</td>
</tr>
<tr>
<td><strong>Non-sedating</strong></td>
<td>Selective H₁ R inverse agonists</td>
<td>Hypotension</td>
<td>CI: sev hepatic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Certirizine</td>
<td>aka H₁ antagonists</td>
<td>Arrhythmia: ↑ QT</td>
<td>Caution</td>
<td>- Long QT</td>
<td></td>
</tr>
<tr>
<td>- Des-/Loratidine:</td>
<td></td>
<td>Older agents</td>
<td></td>
<td>- BPH</td>
<td></td>
</tr>
<tr>
<td>Clarityn</td>
<td></td>
<td>- Drowsiness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Fexofenadine</td>
<td></td>
<td>- Anti-AChM</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Sedating</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- Chlorphenamine:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piriton</td>
<td></td>
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</tbody>
</table>
Chronic Asthma

General Measures: TAME
- Technique for inhaler use
- Avoidance: allergens, smoke (ing), dust
- Monitor: Peak flow diary (2x/d)
  - Written instruction based on peak flow
- Educate
  - Liaise with specialist nurse
  - Need for Rx compliance
  - Emergency action plan

Drug Ladder

1 SABA PRN
   - If use >1/d or nocte symptoms → step 2

2 Low-dose inhaled steroid: beclometasone 100-400ug bd
   - 200ug bd is good starting dose for most

3 LABA: salmeterol 50ug bd
   - Good response: continue
   - Benefit but control still poor: ↑ steroid to 400ug bd
   - No benefit: discontinue + ↑ steroid to 400ug bd

If control is still poor consider trial of:
- Leukotriene receptor antagonist (e.g. montelukast)
  - Esp. if exercise- or NSAID-induced asthma
- MR Theophylline

4 Trials of
   - ↑ inhaled steroid to up to 1000ug bd
- Leukotriene receptor antagonist
- MR Theophylline
- MR β agonist PO

5 Oral steroids: e.g. prednisolone 5-10mg od
   - Use lowest dose necessary for symptom control
   - Maintain high-dose inhaled steroid
   - Refer to asthma clinic

Chronic COPD

Assess Severity
- Mild: FEV1 >80% (but FEV/FVC <0.7 and symptomatic)
- Mod: FEV1 50-79%
- Severe: FEV1 30-49%
- Very Severe: FEV1 < 30%

General Measures
- Stop smoking
  - Specialist nurse
  - Nicotine replacement therapy
  - Bupropion, varenicline (partial nicotinic agonist)
  - Support programme
- Pulmonary rehabilitation / exercise
- Rx poor nutrition and obesity
- Screen and Mx comorbidities
  - e.g. cardiovasc, lung Ca, osteoporosis
  - Depression
- Influenza and pneumococcal vaccine
- Review 1-2x/yr
- Air travel risky if FEV1<50%

Mucolytics
- Consider if chronic productive cough
- E.g. Carbocisteine (CI in PUD)

Breathlessness and/or exercise limitation
- SABA and/or SAMA (ipratropium) PRN
- SABA PRN may continue at all stages

Exacerbations or persistent breathlessness
- FEV1 ≥50%: LABA or LAMA (tiotropium) (stop SAMA)
- FEV1 <50%: LABA+ICS combo or LAMA

Persistent exacerbations or breathlessness
- LABA+LAMA+ICS
  - 500ug fluticasone BD
  - 1000ug beclometasone BD
- Roflumilast / theophylline (PDIs) may be considered
- Consider home nebs

LTOT
- Aim: PaO2 ≥8 for ≥15h / day (↑ survival by 50%)
- Clinically stable non-smokers & PaO2 <7.3 (stable on two occasions >3wks apart)
- PaO2 7.3 – 8 + PHT / cor pulmonale / polycythaemia / nocturnal hypoxaemia
- Terminally ill pts.

Surgery
- Recurrent pneumothoraces
- Isolated bullous disease
- Lung volume reduction
Central Nervous System

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## Anti-Parkinsonian Drugs

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<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Levodopa</strong></td>
<td>Dopamine Pro-drug</td>
<td>Dyskinesia</td>
<td>Glaucoma (closed) MAOIs</td>
<td>fx ↓d by antipsychotics</td>
<td>Always give c peripheral dopa-decarboxylase inhibitor</td>
</tr>
<tr>
<td></td>
<td>Crosses BBB and converted to Da by dopa-decarboxylase</td>
<td>On-Off phenomena</td>
<td>MAOIs</td>
<td>HTN crisis c non-selective MAOIs</td>
<td>- Carbidopa (Co-careldopa)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Psychosis</td>
<td>Melanoma</td>
<td>Anti-HTNs enhance ↓BP fx</td>
<td>- Benserazide (Co-beneldopa)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ABP↓</td>
<td></td>
<td>Food (protein) affects absorption</td>
<td>Loss of response w/i 2-5yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mouth dryness</td>
<td></td>
<td></td>
<td>Give domperidone for n/v</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insomnia</td>
<td></td>
<td></td>
<td>Short t½ ↓ at least TDS dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N/V</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>EDS</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Apomorphine</strong></td>
<td>Non-selective Da agonist</td>
<td>V. emetogenic</td>
<td></td>
<td></td>
<td>Only give SC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- give domperidone for 2 days before starting Rx Injection site reactions</td>
<td></td>
<td></td>
<td>Rescue pen for “off” freezing</td>
</tr>
<tr>
<td><strong>Bromocriptine</strong></td>
<td>Ergot-derived Da agonists</td>
<td>Fibrosis</td>
<td></td>
<td>Cardiovascular disease</td>
<td>Not often used in parkinsonism due to SEs</td>
</tr>
<tr>
<td>Cabergoline</td>
<td></td>
<td>Vasospasm: cardiac, digital</td>
<td>Porphyria</td>
<td>Levels ↑d by:</td>
<td></td>
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<tr>
<td>Pergolide</td>
<td></td>
<td>GI upset</td>
<td>Psychosis</td>
<td>- octreotide</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Postural hypotension</td>
<td></td>
<td>- macrolides</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Drowsiness</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Neuropsych syndromes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Ropinirole</strong></td>
<td>Synthetic Da agonists</td>
<td>GL upset</td>
<td></td>
<td>Used alone to delay need for L-dopa</td>
<td></td>
</tr>
<tr>
<td>Rotigotine</td>
<td></td>
<td>Drowsiness</td>
<td>Adjunct to L-dopa to ↓ end-of-dose effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pramipexole</td>
<td></td>
<td>Postural hypotension</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Neuropsych syndromes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Selegilene</strong></td>
<td>Selective MAO-B inhibitors</td>
<td>GL upset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rasagiline</td>
<td>Prevent intraneuronal degradation of Da</td>
<td>Insomnia (selegiline)</td>
<td>Adjunct to L-dopa to ↓ end-of-dose effects</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Buccal preps → better bioavailability</td>
<td>Postural hypotension (no cheese reaction)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Entacapone</strong></td>
<td>COMT inhibitors</td>
<td>Reddish-brown urine</td>
<td></td>
<td>Interact c sympathomimetics</td>
<td>↓ “off” period of L-DOPA</td>
</tr>
<tr>
<td>Tolcapone</td>
<td>Inhibit peripheral Da degradation</td>
<td>GI disturbance</td>
<td></td>
<td></td>
<td>Tolcapone has better efficacy but requires LFT monitoring.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dyskinesias</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Tolcapone → hepatotoxic</td>
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<tr>
<td><strong>Amantadine</strong></td>
<td>→ Da release</td>
<td>GL upset</td>
<td></td>
<td></td>
<td>May be used in PD for late-onset dyskinesia</td>
</tr>
<tr>
<td></td>
<td>Weak anti-cholinergic</td>
<td>Sleep disturbance</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Livedo reticularis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Neuropsych syndromes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Procyclidine</strong></td>
<td>Muscarinic antagonists</td>
<td>Anti-AChM</td>
<td></td>
<td></td>
<td>Usefull in drug-induced parkinsonism and mild PD in young pts: esp. tremor</td>
</tr>
<tr>
<td>Benzhexol</td>
<td>Reduce tremor</td>
<td>Memory impairment</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Confusion</td>
<td></td>
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</tr>
</tbody>
</table>

### L-DOPA Motor Fluctuations
- **Peak dose dyskinesias**
- **End-of-dose dyskinesia / akinesia**: deterioration as dose wears off c progressively shorter benefit.
- **On-Off effect**: unpredictable fluctuations in motor performance unrelated to timing of dose.
## Anti-Epileptic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valproate</td>
<td>Na⁺ channel blockers</td>
<td>GI upset, Hepatotoxicity</td>
<td>Acute porphyria</td>
<td>fx ↓d by:</td>
<td>1st line for 1st generalised seizures</td>
</tr>
<tr>
<td></td>
<td>Use-dependent</td>
<td>Appetite ↑ → ↑wt.</td>
<td>Personal/fam hx of</td>
<td>- antimalarials</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhibit action potential generation</td>
<td>Liver failure</td>
<td>severe liver dysfunction</td>
<td>- antidepressants</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pancreatitis</td>
<td>L/P</td>
<td>- antipsychotics</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reversible hair loss</td>
<td></td>
<td>- some anti-epileptics</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Oedema</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Ataxia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Teratogenicity, Tremor,</td>
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<td></td>
<td></td>
<td>Thrombocytopenia</td>
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<td></td>
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<td>Encephalopathy: due to ↑ ammonia</td>
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<tr>
<td>Carbamazepine</td>
<td>- Tegretol</td>
<td>Skin reactions (e.g. SJS)</td>
<td>Unpaced AV conduction</td>
<td>↓s fx of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood dyscrasias (↓WCC)</td>
<td>defects</td>
<td>- COCP</td>
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<tr>
<td></td>
<td></td>
<td>Foetal NTDs</td>
<td></td>
<td>- Doxy</td>
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<tr>
<td></td>
<td></td>
<td>GI upset</td>
<td></td>
<td>- corticosteroids</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Dose-related</td>
<td></td>
<td>- anti-epileptics (inc. CBZ)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- Dizziness/vertigo</td>
<td></td>
<td>- nifedipine</td>
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<tr>
<td></td>
<td></td>
<td>- Ataxia</td>
<td></td>
<td>- Warfarin</td>
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<td></td>
<td></td>
<td>- Diplopia</td>
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<tr>
<td>Phenytoin</td>
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<tr>
<td>Lamotrigine</td>
<td>Inhibits glutamate release</td>
<td>Rashes (SJS, TEN, lupus)</td>
<td>L</td>
<td>fx ↓d by:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Cerebellar fx</td>
<td></td>
<td>- OCP</td>
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<tr>
<td></td>
<td></td>
<td>Blood dyscrasias</td>
<td></td>
<td>- phenytoin, CBZ</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Hepatotoxic</td>
<td></td>
<td>- TCAs and SSRIs</td>
<td></td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>Ca²⁺ channel blocker</td>
<td>GI upset</td>
<td>?makes tonic-clonics worse</td>
<td>levels ↑d by valproate</td>
<td></td>
</tr>
<tr>
<td>Vigabatrin</td>
<td></td>
<td>Visual field defects</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rizatriptan</td>
<td>5HT&lt;sub&gt;1B/1D&lt;/sub&gt; receptor agonist</td>
<td>Sensations of tingling/heat/tightness/pressure</td>
<td>IHD</td>
<td>↑ risk of CNS toxicity c SSRIṣ</td>
<td>Used for Rx of acute attacks</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>Reverses dilatation of cerebral vessels</td>
<td>Dizziness</td>
<td>Coronary vasospasm</td>
<td></td>
<td>Don’t use &gt;2-3x / wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PVD</td>
<td></td>
<td>- → chronic migraine</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>Partial 5HT&lt;sub&gt;1&lt;/sub&gt; receptor agonist</td>
<td>GI upset</td>
<td>IHD</td>
<td></td>
<td>Use limited by SEs</td>
</tr>
<tr>
<td>Pizotifen</td>
<td>5HT&lt;sub&gt;2&lt;/sub&gt; receptor antagonist and antihistamine</td>
<td>Drowsiness ↑ appetite and ↑ wt.</td>
<td>Coronary vasospasm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PVD</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>HTN (mod/sev)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>5HT and NA reuptake inhibitor</td>
<td>Anti-cholinergic</td>
<td>Recent MI (w/i 3mo)</td>
<td>MAOIs → HTN and CNS excitation</td>
<td>Hepatic metabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-adrenergic</td>
<td>Heart block</td>
<td>Levels ↑d by</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-histamine</td>
<td>L</td>
<td>- SSRIṣ</td>
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<td></td>
<td></td>
<td></td>
<td>- Cimetidine</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>↑ risk of arrhythmias c amiodarone.</td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
</table>
| Methylpred   | Inhibits PLA₂ → ↓ PG and ↓ PAF  
↑ PMN extravasation → ↑ PMN in blood  
Lymphopaenia  
↓ Phagocytosis  
↓ Ab production  
↓ cytokine and proteolytic enzyme | Cushing’s  
- DM  
- Central obesity  
- Dyslipidaemia  
- PUD  
- Osteoporosis  
- Hirsutism, acne |                  |              | High dose (up to 1g/day) for acute flares.  
Short course (3-5d ays) |
| Interferon-β1| Inhibits PLA₂ → ↓ PG and ↓ PAF  
↑ PMN extravasation → ↑ PMN in blood  
Lymphopaenia  
↓ Phagocytosis  
↓ Ab production  
↓ cytokine and proteolytic enzyme | Flu-like symptoms  
Injection site reaction | Decompensated L  
Severe depression |              | Relapsing remitting or secondary progressive MS  
Monitor for hepatotoxicity |
| Glatiramer   | Random polymer of amino acids found in myelin basic protein  
? acts as decoy | Flu-like symptoms  
Injection site reaction |                  |              | Relapsing remitting MS |
| Natalizumab  | anti-α₄ integrin  
? acts as decoy | Flu-like symptoms  
Injection site reaction |                  |              |                                                                     |
| Alemtuzumab  | anti-CD52  
? acts as decoy | Flu-like symptoms  
Injection site reaction | | | | |
| Baclofen     | GABA₅ agonist  
Skeletal muscle relaxant | Sedation  
↓ tone  
Nausea  
Urinary disturbance | PUD | fx ↑d by TCAs | Rx painful muscle spasms  
Don’t withdraw abruptly  
- hyperthermia  
- ↑ spasticity |
| Dantrolene   | Prevents Ca²⁺ release from sarcoplasmic reticulum  
Skeletal muscle relaxant | Hepatotoxicity  
GI upset | L |          | | |
| Oxybutynin   | Antimuscarinic  
Skeletal muscle relaxant | Dry mouth  
GI upset  
Blurred vision | Myasthenia  
Gl/bladder obstruction |          | Used for detrusor instability |
## Anti-Emetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>D₂-receptor antagonist</td>
<td>EPSEs - Dystonias - Oculogyric crisis</td>
<td>&lt;20yrs</td>
<td>↑ risk of EPSEs Æ antipsychotics, TCAs and SSRIs.</td>
<td>Indications: - GI causes – esp. GORD - Chemo, morning-after-pill, opiates - PD - Migraine - Vestibular (prochlorperazine)</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Prokinetic action in GIT → ↑ absorption of other drugs</td>
<td>Drowsiness Rash, allergy ↑ prolactin</td>
<td>GI obstruction L Prolactinoma</td>
<td></td>
<td>Domperidone doesn't cross BBB ↓ less EPSEs cf. others</td>
</tr>
<tr>
<td>Domperidone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>5HT₃-receptor antagonist</td>
<td>Constipation Headache</td>
<td>Avoid if ↑QTc</td>
<td>Levels ↓ by: - Rifampicin - CBZ, phenytoin AVOID Æ drugs that ↑ QTc</td>
<td>Indications: - Post-op - Chemo CYP metabolism</td>
</tr>
<tr>
<td>Granisetron</td>
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<tr>
<td>Cyclizine</td>
<td>H₁-receptor antagonist</td>
<td>Anti-ACHM</td>
<td>Severe HF MOAs</td>
<td>MOAs can → ↑ antimuscarinic fx</td>
<td>Indications: - Opioids (but not ACS) - Vestibular</td>
</tr>
<tr>
<td>Cinnarizine</td>
<td></td>
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<tr>
<td>Hyoscine</td>
<td>Anti-muscarinic</td>
<td>Anti-muscarinic</td>
<td>Glaucoma (closed-angle) BPH</td>
<td>↓s fx of SL GTN</td>
<td>Indications: - Prophylaxis vs. motion sickness - Hypersalivation</td>
</tr>
<tr>
<td>hydrobromide</td>
<td></td>
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<tr>
<td>Dexamethasone</td>
<td>Steroid – unknown anti-emetic effect</td>
<td></td>
<td></td>
<td></td>
<td>Indications: - Chemo (adjunct) - Surgery</td>
</tr>
<tr>
<td>Aprepitant</td>
<td>Neurokinin receptor blocker</td>
<td></td>
<td></td>
<td></td>
<td>Indications: - Chemo (adjunct)</td>
</tr>
</tbody>
</table>

### Causes of N/V
- Drugs
  - Abx: e.g. erythromycin
  - Anti-parkinsonian: e.g. L-DOPA
  - Cytotoxic agents
  - Opioids
  - Digoxin
  - GI: GORD, gastro, pancreatitis, obstruction
  - Neoplasia: oesophageal, gastric, duodenal
  - Vestibular: e.g. labyrinthitis, sea-sickness
  - Neuro: e.g. migraine, ↑ICP
  - Vagal: e.g. pancreatitis, MI, torsion
  - Pregnancy

### Physiology
Vomiting regulated by Vomiting Centre and CTZ, both located in the medulla.

#### CTZ
- Outside BBB ↓: accessible to drugs
- Also receives input from vestibular system re. motion
- Expresses: D₂ and 5-HT₃ receptors
- CTZ projects to Vomiting Centre

#### Emetogenic Receptors:
- H₁
- D₂
- 5HT₃
- mACh

#### Vomiting Centre
- Controls visceral and somatic functions involved in vomiting.
- Receives input from CTz
- Also receives muscarinic and histaminergic input (H₁)
### Anti-Depressants

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine</td>
<td>SSRI</td>
<td>N / V / diarrhoea</td>
<td>Active mania</td>
<td>P450 inhibitor → ↑ s levels of TCAs</td>
<td>Takes 4-6wks for full clinical effect</td>
</tr>
<tr>
<td>Citalopram</td>
<td></td>
<td>Insomnia</td>
<td>Children &lt;18yrs</td>
<td>- benzos</td>
<td>Don’t stop suddenly</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td></td>
<td>Headache</td>
<td>- except fluoxetine</td>
<td>- clozapine, haldol</td>
<td>Avoid w/i 2wks of MAOI</td>
</tr>
<tr>
<td>Sertraline</td>
<td></td>
<td>Sexual dysfunction</td>
<td></td>
<td>SSRI + MAOI → serotonin syndrome</td>
<td>Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIADH</td>
<td></td>
<td>↑ risk of bleeding ∆ aspirin</td>
<td>- Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Withdrawal effects</td>
<td></td>
<td></td>
<td>- OCD</td>
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<td></td>
<td></td>
<td></td>
<td>- Eating disorders</td>
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<td>- Anxiety disorders</td>
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<tr>
<td>Venlafaxine</td>
<td>SNRI</td>
<td>HTN</td>
<td>HF (3/4)</td>
<td>SSRI + MAOI → serotonin syndrome</td>
<td>2nd line anti-depressant</td>
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<tr>
<td></td>
<td></td>
<td>GI upset</td>
<td>Uncontrolled HTN</td>
<td>↑ risk of bleeding ∆ aspirin</td>
<td>Stop drug if signs of rash</td>
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<td></td>
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<td>↑QTc</td>
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<td>Amitriptyline</td>
<td>TCA</td>
<td>α1</td>
<td>Recent MI</td>
<td>MAOIs → HTN and CNS excitation</td>
<td>Avoid w/i 2wks of MAOI</td>
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<tr>
<td>Lofepramine</td>
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<td>- postural hypotension</td>
<td>Arrhythmias</td>
<td>Levels ↑d by SSRIs</td>
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<td>Clomipramine</td>
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<td>- sedation</td>
<td>Severe L Mania</td>
<td>↑ risk of arrhythmias ∆ amiodarone</td>
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<tr>
<td>Imipramine</td>
<td></td>
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<td>Caution</td>
<td>TCAs lower the seizure threshold</td>
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<td>Doxepin</td>
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<td>- Glaucoma</td>
<td>- ↓ effects of AEDs</td>
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<td>Nortriptyline</td>
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<td>- BPH</td>
<td>↑ fx of antipsychotics</td>
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<tr>
<td>Phenelzine</td>
<td>MAOI</td>
<td>Sedation</td>
<td>Hypertensive Crisis</td>
<td>Moclobemide is reversible and is selective for MAOI-A ∴ less chance of interactions.</td>
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<tr>
<td>Isoxcarboxacid</td>
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<td>Hypotension</td>
<td>- tyramine containing foods</td>
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<tr>
<td>Moclobemide (A)</td>
<td></td>
<td>Anti-AChM</td>
<td>- opioids: esp. pethidine</td>
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<td>Selegiline (B)</td>
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<td>SSRIs and TCAs → serotonin syn.</td>
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</tbody>
</table>

### Serotonin Syndrome
- **Cognitive:** headache, agitation, confusion, coma
- **Autonomic:** sweating, ↑HR, palpitations, HTN, hyperthermia
- **Somatic:** myoclonus, clonus, hypertonia, tremor

### Monoamine Oxidase
- Metabolises monoamines
- **MAO-A:** adrenaline, norad, serotonin, tyramine, dopamine
- **MAO-B:** dopamine

### TCA Toxicity
- Metabolic acidosis
- **Anti-AChM:** dilated pupils
- **CNS:** hypertonia, hyperreflexia, extensor plantars, seizures
- **Cardiac:** ↑HR, ↑QTc → TDP
- **Pulmonary:** hypoventilation
- **Rx:** NaHCO₃
<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
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<tr>
<td>Paracetamol</td>
<td>Antipyretic Analgesic</td>
<td>Hepatic failure in OD</td>
<td>Severe L</td>
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<td>Strong opioids</td>
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<td>- hepatic impairment</td>
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<td>Nortriptyline</td>
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# Other Psychiatric Drugs

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<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li</td>
<td>Mood stabiliser</td>
<td>Polyuria and polydipsia, Nephrotoxic, GI upset, Fine tremor, Hypothyroidism</td>
<td>Hypothyroidism P/R/H</td>
<td>Toxicity ↑d by: - NSAIDs - Diuretics (esp. thiazides) - ACEi / ARB</td>
<td>Monitor - drug levels - U+Es - TTFs</td>
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<tr>
<td></td>
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<td>Use - Acute mania - Prophylaxis of BAD - Resistant depression</td>
<td>↑ toxicity when ↓ Na or dehydrated - ↑ Li reabsorption in renal PCT</td>
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<tr>
<td>Chlorpromazine</td>
<td>Typical antipsychotics</td>
<td>Sedation Anti-AChM EPSEs Neuroleptic malignant syn. ↑QTc, postural hypotension ↑ PRL Sexual dysfunction ↑ wt.</td>
<td>fx ↑d by: - Li - TCAs</td>
<td>Monitor FBC, U+E, LFTs</td>
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<tr>
<td>Sulpiride</td>
<td>Atypical antipsychotics Da antagonists</td>
<td>Sedation Respiratory depression Withdrawal</td>
<td>Resp depression levels / fx ↑d by: - antipsychotics - azoles - macrolides</td>
<td>Rx overdose with flumazenil Hepatic metabolism IV diazepam is given as an emulsion to ↓ risk of thrombophlebitis</td>
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<td>Zuclopenthixol</td>
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<td>Clozapine</td>
<td>Atypical antipsychotics Da antagonists</td>
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<td>Can still → EPSEs @ high doses - apart from clozapine</td>
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<td>Olanzapine</td>
<td>Atypical antipsychotics Da antagonists</td>
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<td>Clozapine - Rx of refractory schizophrenia - better @ Rx of negative symp</td>
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<tr>
<td>Quetiapine</td>
<td>Atypical antipsychotics Da antagonists</td>
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<td>Risperidone</td>
<td>Atypical antipsychotics Da antagonists</td>
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<tr>
<td>Benzodiazepines</td>
<td>Promote GABA binding to GABA_A receptors</td>
<td>Sedation Respiratory depression Withdrawal</td>
<td>Resp depression levels / fx ↑d by: - antipsychotics - azoles - macrolides</td>
<td>Rx overdose with flumazenil Hepatic metabolism IV diazepam is given as an emulsion to ↓ risk of thrombophlebitis</td>
<td></td>
</tr>
<tr>
<td>Phenobarbitol</td>
<td>Potentiate GABA_A receptors</td>
<td>Sedation Respiratory depression</td>
<td></td>
<td>See CBZ, phenytoin. CYP inducer Primidone is phenobarbital prodrug</td>
<td></td>
</tr>
</tbody>
</table>

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Migraine

Acute episode
- 1\(^{st}\): Paracetamol + metoclopramide / domperidone
- 2\(^{nd}\): NSAID (e.g. ketoprofen) + M/D
- 3\(^{rd}\): Rizatriptan (5-HT\(_{1B/1D}\) agonist)
  ▪ CI: IHD, uncontrolled HTN, SSRIs
- 4\(^{th}\): ergotamine

Prophylaxis
- Avoid triggers
- 1\(^{st}\): Propanolol, amitriptyline, topiramate
- 2\(^{nd}\): Valproate, pizotifen (\(\uparrow\) wt.), gabapentin

Epilepsy

Seizure Type | 1\(^{st}\) line | 2\(^{nd}\) line
--- | --- | ---
Generalised - tonic-clonic | Valproate | Levitiracetam
- absence | Lamotrigine | 
- myoclonic | 
Focal onset | Lamotrigine | Levitiracetam
Carbamazepine | 

In Women / Pregnancy
- Avoid valproate: take lamotrigine (or CBZ)
- 5mg folic acid daily if child-bearing age
- CBZ and Phenytoin are enzyme inducers
  ▪ \(\downarrow\) effectiveness of the OCP
- Oral vit K in last month

Driving Advice
- Must not drive w/i 12mo of seizures
- Pts. who only have seizures while sleeping for \(\geq\)3yrs can drive.
- Person must comply \(\overline{\text{}}\) Rx
Parkinson's Disease

General
- MDT: neurologist, PD nurse, physio, OT, social worker, GP and carers
- Assess disability
  - e.g. UPDRS: Unified Parkinson’s Disease Rating Scale
- Physiotherapy: postural exercises
- Depression screening

Medical

Young onset ± biologically fit
1. Da agonists: ropinirole, pramipexole
2. MOA-B inhibitors: rasagiline, selegiline
3. L-DOPA: co-careldopa or co-beneldopa

Biologically frail ± comorbidities
1. L-DOPA
2. MOA-B inhibitors

Response Fluctuations
- MOA-B inhibitors
  - ↓ end-of-dose effects
- COMT inhibitor: tolcapone, entacapone
  - Lessen "off" time @ end-of-dose
- Apomorphine: potent Da agonist
  - SC rescue pen for sudden “off” freezing
- Amantidine: weak Da agonist
  - Rx of drug-induced dyskinesias

Adjunctive Therapies
- Domperidone
  - Rx of drug-induced nausea
- Atypical antipsychotics: e.g. quetiapine, clozapine
  - Disease-induced psychosis
- SSRIs: citalopram, sertraline
  - Depression

Surgical
- Interrupt basal ganglia
- Deep brain stimulation
- Stem cell Transplant

Drug-induced Movement Disorders

Causes
- Neuroleptics
- Anti-emetics: metoclopramide, prochlorperazine
- L-DOPA → acute dystonias

Mx

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Rx</th>
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<tbody>
<tr>
<td>Acute Dystonia</td>
<td>Procyclidine</td>
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<tr>
<td>Parkinsonism</td>
<td>Procyclidine, Da agonists</td>
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<tr>
<td>Akathisia</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>Switch to atypical anti-</td>
</tr>
<tr>
<td></td>
<td>psychotic</td>
</tr>
<tr>
<td>Neuroleptic malignant syn.</td>
<td>Dantrolene, Da agonists: e</td>
</tr>
</tbody>
</table>

Other Movement Disorders
- Restless legs: ropinerole
- Benign essential tremor: propranolol
- Focal dystonias: botulinum toxin, benzos
  - Blepharospasm
  - Spasmodic torticolis
  - Writer’s cramp
Pain Control

Principles
- Oral where possible
- Fixed interval to give continuous relief
- Stepwise approach

WHO Analgesia Ladder

1. Non-opioid ± adjuvants
   - Paracetamol
   - NSAIDs
     - Ibuprofen: 400mg/8h PO
     - Diclofenac: 50mg PO / 75mg IM

2. Weak opioid + non-opioid ± adjuvants
   - Codeine
   - Dihydrocodeine
   - Tramadol

3. Strong opioid + non-opioid ± adjuvants
   - Morphine: 5-10mg/2h max
   - Oxycodone
   - Fentanyl

NSAIDs
- → gastric and duodenal ulceration
- Na and H₂O retention
  - Worsen heart failure
  - Interfere with ACEi / ARB
- May worsen / precipitate asthma
- COX-2 selectives ↑ CV risk

Potent Opioids
- Establish dose with intermediate release preparations then give maintenance with modified release
  - Start with oramorph 4-10mg/4h PO = breakthrough dose PRN
  - Switch to modified release (MST) BD: BD dose = total 24h dose / 2.
  - Give 1/6 total daily dose as oramorph for breakthrough pain
- Consider PCA

Mx of SEs
- Constipation: codanthusrate (stimulant laxative)
- Nausea: metoclopramide
- Drowsiness: tolerance develops

Other Options
- Nerve blocks: visceral pain
- Direct local anaesthetic injections: facet joint pain

Adjuvants
- Anything not specifically mentioned on the ladder
  - Surgery
  - Chemo

Neuropathic Pain

Common Causes
- DM
- EtOH
- Ca
- Trigeminal neuralgia
- Post-herpetic neuralgia
- HIV

Main Options
- 1st: pregabalin / gabapentin
- 2nd: TCAs
- 3rd: opioids
- 4th: CBZ, valproate, lamotrigine

Topical: lidocaine patches, capsaicin

NB. HIV-assoc. sensory neuropathy responds better to gabapentin than amitriptyline.
Multiple Sclerosis

MDT: neurologist, radiologist, physio, OT, specialist nurses, GP, family

Acute Attack
- **Methylpred** 1g IV/PO /24h for 3d
  - Doesn’t influence long-term outcome
  - ↓ duration and severity of attacks

Preventing Relapse

DMARDs
- **IFN-β**: ↓ relapses by 30% in relapsing remitting MS
- **Glatiramer**: similar efficacy to IFN-β

Biologics
- **Natalizumab**: anti-VLA-4 Ab
  - ↓ Relapses by 2/3 in RRMS
- **Alemtuzumab**: anti-CD52
  - 2nd line in RRMS

Symptomatic
- **Fatigue**: modafinil
- **Depression**: SSRI (citalopram)
- **Pain**: amitriptylline, gabapentin
- **Spasticity**: physio, baclofen, dantrolene, botulinum
- **Urgency / frequency**: oxybutynin, tolterodine
- **ED**: sildenafil
- **Tremor**: clonazepam

Myasthenia Gravis

**Diagnosis: Tensilon Test**
- Edrophonium bolus IV
- Positive = improvement of power w/i 1min

**Mx**

**Symptom Control**
- Anticholinesterase: e.g. pyridostigmine.
  - Cholinergic SEs

**Immunosuppression**
- Rx relapses c ¯ pred
- Steroids ± sparing-agents
  - Azathioprine, methotrexate, cyclosporin
- Can → total remission

**Thymectomy**
- Consider if young onset and disease not control by anticholinesterases
- Always remove a thymoma if present
  - May be malignant
- Remission in 25%, benefit in further 50%.

**Myasthenic Crisis**
- Plasmapheresis
- IVlg
Psychiatry

Antidepressants

SSRIs: selective serotonin reuptake inhibitors
- Citalopram, sertraline, fluoxetine

SNRIs: serotonin noradrenaline reuptake inhibitors
- Venlafaxine

NaSSA: Norad and specific serotonergic antidepressant
- Mirtazapine

NRI: Norad reuptake inhibitor
- Reboxetine

TCAs: tricyclic antidepressants
- Amitriptyline
- Imipramine
- Clomipramine

MAOIs: monoamine oxidase inhibitors
- Meclobemide (RIMA)
- Phenelzine

Bipolar Affective Disorder
- Lithium (TDM essential)
- AEDs: valproate, CBZ
- Neuroleptics: olanzapine

Antipsychotics

Typical
- Haldol
- Chlorpromazine

Atypical
- Clozapine
- Olanzapine
- Risperidone
- Quetiapine
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<th>Interactions</th>
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<td><strong>Bactericidal</strong></td>
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<td>- Inhibit bacterial transpeptidase enzyme</td>
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<td></td>
<td>- Required for cell wall construction</td>
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<td>Pen V</td>
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<td>- Required for cell wall construction</td>
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<td>Gen V. broad spectrum</td>
<td>All Gm+ except MRSA</td>
<td>GI upset</td>
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<td></td>
<td>- Gm-, Gm+ and anaerobes</td>
<td>Most Gm-yes</td>
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<td>- Pseudomonas</td>
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<td>Imipenam</td>
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Inhibitors of Protein Synthesis

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<tr>
<th>Drug</th>
<th>MOA</th>
<th>Use</th>
<th>Side Effects</th>
<th>CIs</th>
<th>Interactions</th>
<th>Other</th>
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<tbody>
<tr>
<td>Chloramphenicol</td>
<td>Bacteriostatic - 50s subunit</td>
<td>Conjunctivitis</td>
<td>Irreversible aplastic anaemia</td>
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<td>Aminoglycosides</td>
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<td>Myasthenia gravis</td>
<td>↓ absorption of c-</td>
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<td>Tobramycin Neomycin</td>
<td>Bactericidal Amino-acyl site of 30s subunit</td>
<td>Neutropenic sepsis</td>
<td>Ototoxic</td>
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<td>Caution in R</td>
<td>milk, antacids</td>
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<td>Tetracycline Doxycycline</td>
<td>Tetracyclines Bacteriostatic 30s subunit</td>
<td>COPD exacerbation</td>
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<td>MRSA and VRE</td>
<td>Blood dyscrasias</td>
<td>Caution in R and L</td>
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<td>Linezolid is a non-selective MAOI</td>
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<td>Erythromycin Clarithromycin Azithromycin</td>
<td>Macrolides Bacteriostatic 23s component of 50s subunit</td>
<td>Pen allergy Atypical pneumonia</td>
<td>↑ QTc</td>
<td>Caution if ↑QTc</td>
<td>P450 inhibitor W+</td>
<td>Also have GI prokinetic action</td>
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<td>Chlamydia</td>
<td>Dry skin</td>
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<td>H. pylori</td>
<td>Cholestatic hepatitis</td>
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<td>Synercid</td>
<td>Streptogramins Bacteriostatic 50s subunit</td>
<td>VRE MRSA</td>
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<td>Only used when other agents failed.</td>
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<td>Clindamycin</td>
<td>Lincosamides Bacteriostatic 50s subunit</td>
<td>Active vs. Gm+ cocci and bacteroides</td>
<td>AAC Hepatotoxicity</td>
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<td>Stop drug if pt. develops diarrhoea</td>
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<td>Drug</td>
<td>MOA</td>
<td>Use</td>
<td>Side Effects</td>
<td>Cls</td>
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<td>Vancomycin</td>
<td>Glycopeptides Bactericidal</td>
<td>Aerobic and anaerobic Gm+ MRSA, HAN, Infective endocarditis AAC (PO)</td>
<td>Nephrotoxic Ototoxic - tinnitus - SNHL Hypersensitivity rash Neutropenia</td>
<td>↓ dose in renal impairment</td>
<td>Must monitor levels - pre-dose trough level</td>
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<tr>
<td>Teicoplanin</td>
<td>Glycopeptides Bactericidal</td>
<td>Inhibits cell wall synthesis Unable to penetrate Gm- outer cell wall Poor oral absorption</td>
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<td>Ciprofloxacin</td>
<td>Fluoroquinolones Bactericidal</td>
<td>Broad spectrum: esp. Gm- GI infections: campy, shig… Pseudomonas: esp. in CF Prostatitis, PID Anthrax</td>
<td>↑ QTc GI upset Tendonitis ± rupture ↓ seizure threshold Photosensitivity</td>
<td>P</td>
<td>P450 inhibitor Antacids → ↓ absorption</td>
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<td>Levofloxacin</td>
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<td>Ofloxacin</td>
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<td>Moxifloxacin</td>
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<td>Metronidazole</td>
<td>Nitroimidazole Bactericidal</td>
<td>Anaerobes GI sepsis Aspiration pneumonia AAC H. pylori PID Protozoa:Giardia</td>
<td>Metallic taste GI upset Metro: gynaecomastia</td>
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<td>Avoid EtOH - Disulfiram-like reaction Aldehyde dehydrogenase inhibitor</td>
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<td>Nitrofurantoin</td>
<td>Nitroimidazole Bactericidal</td>
<td>Inhibits DNA synthesis</td>
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<td>Tinidazole</td>
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<td>Rifampicin</td>
<td>Rifamycins Bactericidal</td>
<td>Mycobacteria Legionella Prophylaxis vs. meningits</td>
<td>Yellow secretions Hepatitis</td>
<td>Jaundice</td>
<td>P450 inducer - W- - ↓OCP - ↓AEDs Rifaximin has v. poor oral absorption and is ↓ used in hepatic encephalopathy. Stop immediately if rash or dyscrasias occurs.</td>
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<td>Rifaximin</td>
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<td>Rifabutin</td>
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<td>Trimethoprim</td>
<td>Bacteriostatic Folate antagonists</td>
<td>UTI PCP Toxoplasmosis</td>
<td>Blood dyscrasias EM → SJS EN Nephro- + hepato-toxicity</td>
<td>Severe R and L P</td>
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<td>Sulfamethoxazole</td>
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<td>Daptomycin</td>
<td>Cell membrane toxin</td>
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<td>Colistin</td>
<td>Cell membrane toxin</td>
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<td>Ethambutol</td>
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<td>Optic neuritis</td>
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<td>Pyrazinamide</td>
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<td>Anti-TB</td>
<td>Hepatitis Gout Caution in gout</td>
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<td>Monitor LFTs</td>
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<td>Isoniazid</td>
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<td>Anti-TB</td>
<td>Peripheral neuropathy Hepatitis</td>
<td>P450 inhibitor ↑ risk of SEs if slow acetylator</td>
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<td>Fusidate</td>
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<td>Active vs. staphs Impetigo (topical) Blepharitis (topical) Osteomyelitis (PO)</td>
<td>Hepatitis</td>
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<td>Needs 2nd Abx to prevent resistance</td>
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## Anti-Malarials

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<th>Drug</th>
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<th>Side Effects</th>
<th>CIs</th>
<th>Interactions</th>
<th>Other</th>
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<tbody>
<tr>
<td>Chloroquine</td>
<td>Benign malaria</td>
<td>Visual change: rarely retinopathy</td>
<td>Caution in G6PD deficiency</td>
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<td>Prophylaxis</td>
<td>Seizures</td>
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<td>EM → SJS</td>
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<td>Primaquine</td>
<td>Benign malaria</td>
<td>Haemolysis if G6PD deficient</td>
<td>Caution in G6PD deficiency</td>
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<td>- eliminate liver</td>
<td>Methaemoglobinaemia</td>
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<td>Malarone</td>
<td>Falciparum malaria</td>
<td>Abdo pain</td>
<td>Avoid in renal impairment if</td>
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<td>Prophylaxis</td>
<td>Gi upset</td>
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<td>Mefloquine</td>
<td>Prophylaxis</td>
<td>Nausea, dizziness, Neuropsychiatric signs</td>
<td>Hx of epilepsy or psychosis</td>
<td>Avoid if low risk of resistance</td>
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<td>Riamet - artemether +</td>
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## Anti-Virals

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<th>Side Effects</th>
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<tr>
<td>Aciclovir</td>
<td>Guanosine analogue</td>
<td>Genital herpes</td>
<td>GI upset</td>
<td>CMV Rx - retinitis</td>
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<td>Phosphorylated by viral thymidine</td>
<td>Herpes meningitis</td>
<td>ARF</td>
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<td>Caution in renal impairment</td>
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<td>Valaciclovir</td>
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<td>BM suppression</td>
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<td>Famciclovir</td>
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# Anti-Retrovirals

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<tr>
<td>NRTI</td>
<td>Emtricitabine</td>
<td>Nucleoside Reverse Transcriptase Inhibitors</td>
<td>Hepatitis</td>
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<td>Stavudine</td>
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<td>- stop if ↑ LFTs</td>
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<tr>
<td></td>
<td>Tenofovir</td>
<td>Except Tenofovir which is nucleotide reverse transcriptase inhibitor</td>
<td>Lactic Acidosis (type B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abacavir</td>
<td></td>
<td>Painful peripheral neuropathy</td>
<td></td>
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<tr>
<td></td>
<td>Didanosine</td>
<td></td>
<td>Rash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lamivudine</td>
<td></td>
<td>GI disturbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zidovudine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIs</td>
<td>Ritonavir</td>
<td>Inhibit viral protease required for virus assembly</td>
<td>Metabolic syndrome</td>
<td>P450 inhibitors</td>
</tr>
<tr>
<td></td>
<td>Indinavir</td>
<td>Ritonavir is used to boost levels of other PIs</td>
<td>Lipodystrophy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saquinavir</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Lopinavir / ritonavir “Kaletra”</td>
<td></td>
<td>Metabolic syndrome</td>
<td>P450 inhibitors</td>
</tr>
<tr>
<td>NNRTI</td>
<td>Efavirenz</td>
<td>Non-competitive inhibition of reverse transcriptase</td>
<td>Insomnia, vivid dreams, dizziness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nevirapine</td>
<td>NB. Nevirapine is used to prevent HIV transmission during pregnancy</td>
<td>EM → SJS</td>
<td></td>
</tr>
<tr>
<td>Integrase inhibitors</td>
<td>Raltegravir</td>
<td>Inhibit integration of transcribed viral DNA into host genome</td>
<td></td>
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<tr>
<td></td>
<td>Elvitegravir</td>
<td></td>
<td></td>
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<tr>
<td>CCR5 inhibitor</td>
<td>Maraviroc</td>
<td>Binds CCR5 preventing interaction with gp120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusion inhibitor</td>
<td>Enfuviritide</td>
<td>Binds gp41 and inhibits fusion</td>
<td>Hypersensitivity at injection site</td>
<td></td>
</tr>
</tbody>
</table>

## Indications
- CD4 ≤350
- AIDS-defining illness
- Pregnancy
- HIVAN
- Co-infected c HBV when Rx is indicated for HBV

Use 2 NRTIs + 1 NNRTI or PI

## Lipodystrophy
- Fat redistribution
  - ↓ SC fat
  - ↑ abdo fat
  - Buffalo hump
- Insulin resistance
- Dyslipidaemia

## Immune Reconstitution Inflammatory Syndrome
- Improvement in immune function 2<sup>nd</sup> to ARV Rx
- Marked inflammatory reaction vs. residual opportunistic organisms
- Paradoxical worsening of symptoms on initiation of ARVs

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# Anti-Fungals

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Mechanism</th>
<th>Indication</th>
<th>SEs</th>
<th>Misc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyenes</td>
<td>Amphotericin B</td>
<td>Interacts with ergosterol → pore formation</td>
<td>Severe systemic fungal infections (IV) - cryptococcal meningitis - pulm. Aspergillosis - systemic candidiasis</td>
<td>Nephrotoxic (IV) - IV reaction (after 1-3h) - fever - hypotension - nausea/vomiting</td>
<td>Monitor Cr - PO version is non-toxic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungicidal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nystatin</td>
<td></td>
<td>Candidiasis: cutaneous, vaginal, mucosal, oesophageal</td>
<td>Toxic if given IV</td>
<td>PO or topical</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Imidazoles</td>
<td>Ketoconazole</td>
<td>Blocks ergosterol synth by inhibiting 14α-demethylase → ↓ membrane fluidity</td>
<td>Chronic mucocutaneous candidiasis</td>
<td>Hepatotoxic</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>Miconazole</td>
<td>Inhibits replication</td>
<td>Dermatophyte infections</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Mucocutaneous candidiasis</td>
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<tr>
<td></td>
<td>Clotrimazole</td>
<td></td>
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</tr>
<tr>
<td>Triazoles</td>
<td>Fluconazole</td>
<td>Prevents hyphae formation</td>
<td>Oral/vag/oesophagus candida - Alternative to ampho B for systemic infections</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Itraconazole</td>
<td>Broad spectrum</td>
<td>Blasto/histo/coccidio - Sporotrichosis - Chromomycosis - Aspergillus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungistatic</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Voriconazole</td>
<td></td>
<td>Invasive candida or aspergillus in immunocomp - BMT transplant pt. prophylaxis</td>
<td>Photophobia - Rash - Hepatotoxic</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td></td>
<td>Invasive candida, mucor and aspergillus in immunocomps</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Allylamines</td>
<td>Terbinafine</td>
<td>Blocks ergosterol synth by inhibiting squalene epoxidase → membrane disruption</td>
<td>Dermatophyte Infections</td>
<td>GI effects - Hives - ↑LFTs - Reversible agranulocytosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungicidal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echinocandins</td>
<td>Caspofungin</td>
<td>Inhibit β-glucan synthesis</td>
<td>Invasive aspergillus or candidiasis</td>
<td>V. low toxicity - GI upset - Hypersensitivity</td>
<td>IV only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungicidal vs. yeasts</td>
<td>Empiric Rx for fungal infection in febrile neutropenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungistatic vs. moulds</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flucytosine</td>
<td>Inhibits DNA/RNA synthesis</td>
<td>Cryptococcal meningitis (in combo with amphotericin B)</td>
<td>Bone marrow suppression - Deranged LFTs</td>
<td></td>
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<tr>
<td></td>
<td>Griseofulvin</td>
<td>Disrupts spindle formation in mitosis</td>
<td>Dermatophyte infections of skin/hair/nails</td>
<td></td>
<td>Very slow acting</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>
Bacterial Infections

Pneumonias

CAP

Mild  amoxicillin 500mg TDS PO for 7d or clarithro 500mg BD PO for 7d

Mod  amoxicillin 500mg TDS and clarithro 500mg BD PO/IV for 7d (clarithro alone if pen allergy)

Sev  Co-amoxiclav 1.2g TDS IV / cefuroxime 1.5g TDS IV and clarithro 500mg BD IV for 7-10d

Add fluclox if staph suspected.

Atyp  Chlamydia: tetracycline
PCP: Co-trimoxazole
Legionella: Clarithro + rifampicin

HAP

- Mild / <5d: Co-amoxiclav 625mg PO TDS for 7d
- Severe / >5d: Tazocin for 7d
  - ± vanc for MRSA
  - ± gent for Pseudomonas

Aspiration Pneumonia

- Co-amoxiclav 625mg PO TDS for 7d

Exacerbation of COPD

- Rx if ↑ sputum purulence /↑ sputum volume or ↑ dyspnoea or consolidation on CXR
- Amoxicillin 500mg PO TDS for 7d
- Or, doxy 200mg STAT + 100mg BD for 7d

Legionella

- Levofloxacin or,
- Clarithromycin + rifampicin

PCP

- 1st: co-trimoxazole
- 2nd: pentamidine

TB

- 2mo: RHZE
- 4mo: RH
- Give pyridoxine 20mg OD throughout Rx
- Longer Rx if resistant organisms or extra-pulmonary TB

Infective Endocarditis

- Empiric
  - Acute severe: Fuclox + gent IV
  - Subacute: Benpen + gent IV
- Streps: benpen + gent IV
- Enterococci: amoxicillin + gent IV
- Staphs: fluclox ± rifampicin IV
- Fungi: flucytosine IV + fluconazole PO.
  - Ampicillin if flucytosine resistance or Aspergillus.

Meningitis

- Community: benpen 1.2g IV/IM
- <50: ceftriaxone 2g IV/IM BD
- >50: ceftriaxone + ampicillin 2g IV /4h
- Viral suspected: aciclovir
- Give Dex 0.15mg/kg/6h ☉ first dose of Abx unless in septic shock or meningococcal sepsis

Urinary Tract Infection

- Pyelonephritis: cefotaxime 1g IV BD for 10d
- Lower UTI: Rx for 7d
  - 1st: Trimethoprim 200mg BD
  - 1st: Nitrofurantoin 50mg QDS (avoid in ↓ eGFR)
  - 2nd: Cephalexin 500mg BD
  - 2nd: Amoxicillin 500mg TDS
- Prostatitis: Cipro 500 mg BD for 28d

Genital Tract

- Chlamydia / NSU: azithromycin 1g STAT
- Gonorrhoea
  - Azithromycin 1g STAT + ceftriaxone 500mg IM
- PID: ofloxacine + metronidazole

GIT

- GI sepsis: cefuroxime + metronidazole
- Campylobacter: ciprofloxacin
- Shigella: ciprofloxacin
- C. diff
  - 1st: metronidazole PO
  - 2nd: Vancomycin PO

Sepsis

- Tazocin
  - ± Vanc if MRI suspected
  - ± Gent for gram -ves
  - If anaerobe: cef and met

Skin

- Impetigo
  - Localised: topical fusidate
  - Widespread: flucox 250 QDS
- Erysipelas: Pen V 500mg QDS or ben pen
- Cellulitis
  - Empiric: flucox 500mg QDS
  - Known Strep: Pen V or Ben pen
Viral Infections

**Herpes Viruses**

- **HSV**
  - Aciclovir
  - Valaciclovir
  - Famciclovir

- **VZV**
  - Aciclovir

- **CMV**
  - Ganciclovir / valganciclovir
  - Foscarnet
  - Cidofovir

**Hepatitis**

- **HBV**
  - Combination or individual use of
    - Peg-interferon-α
    - Tenofovir
    - Entecavir

- **HCV**
  - Peg-interferon-α + ribavarin

**Influenza**

- Bed rest + paracetamol
- **If severe**
  - Mx in ITU
  - Cipro and ao-amoxiclav: prevent Staph and Strep
- **Oseltamivir**
  - Neuraminidase inhibitor active vs. flu A and B
  - May be indicated if >1yr of symptoms of <48hr
- **Zanamivir**
  - Inhaled NA inhibitor active vs. influenza A and B
  - >5yrs of symptoms <48h

**HIV**

**Indications**

- CD4 ≤350
- AIDS-defining illness
- Pregnancy
- HIVAN
- Co-infected with HBV when Rx is indicated for HBV

**Regimens**

- 1 NNRTI + 2 NRTIs
  - NNRTI = efavirenz
  - NRTI = emtricitabine + tenofovir (Truvada)
  - Atripla = efavirenz + emtricitabine + tenofovir
- PI + 2 NRTIs
  - PI = lopinavir (+ low dose ritonavir = Kaletra)

**Aim**

- Undetectable VL after 4mo
- If VL remains high despite good compliance
  - Change to a new drug combination
  - Request resistance studies
Protozoal Infections

Malaria

Prophylaxis
- **No resistance:** proguanil + chloroquine
- **Resistance:** mefloquine or malarone
  - **Malarone:** atovaquone + proguanil

Rx
- **Benign:** chloroquine then primaquine
- **Falciparum:** riamet or malarone
  - **Riamet:** artemether + lumefantrine
  - IV antimalarials if severe

Toxoplasmosis
- Pyrimethamine + sulfadiazine

Giardia
- Tinidazole

Entamaeoba histolytica
- Metronidazole

Fungal Infections

PCP
- High-dose co-trimoxazole IV
- Or, pentamidine IV
- Prednisolone if severe hypoxaemia

Cryptococcal Meningitis
- Amphotericin B + flucytosine for 2wks
- Then fluconazole for for 6mo / until CD4 >200

Candida
- **Oral:** nystatin drops
- **Thrush:** clotrimazole
- **Systemic:** amphotericin B or voriconazole

Tinea Infections
- **Skin:** terbinafine or topical ketoconazole / miconazole
- **Scalp:** griseofulvin or terbinafine
- **Nails:** terbinafine

Pityriasis versicolor
- Selenium or ketoconazole shampoo

Aspergillus
- Amphotericin B
- Itraconazole, voriconazole
Endocrine

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### Oral Hypoglycaemics

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<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metformin</strong></td>
<td>Biguanide</td>
<td>Lactic acidosis</td>
<td>Caution in renal or hepatic impairment</td>
<td>Renally excreted</td>
<td>- ↓ dose or avoid if ↓eGFR - Cannot cause hypos</td>
</tr>
<tr>
<td></td>
<td>Insulin sensitizer</td>
<td>Gl upset - anorexia → wt. loss</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>- ↓ gluconeogenesis</td>
<td></td>
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<tr>
<td></td>
<td>- ↑ peripheral glucose use</td>
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<td></td>
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<tr>
<td></td>
<td>- ↓ LDL and VLDL</td>
<td></td>
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</tr>
<tr>
<td><strong>Pioglitazone</strong></td>
<td>Thiazolidinedione</td>
<td>Wt. gain</td>
<td>H/L</td>
<td>Don’t use with insulin</td>
<td>V. protein bound - Hepatic metabolism</td>
</tr>
<tr>
<td></td>
<td>Peripheral insulin sensitizer</td>
<td>Fluid retention</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>PPAR gamma ligand (nuclear receptor involved in glucose and lipid homoeostasis)</td>
<td>Hepatotoxicity</td>
<td></td>
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<tr>
<td></td>
<td>Block hyperpolarising K⁺ channel on β cells</td>
<td>May exacerbate HF</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>→ depolarisation and insulin release</td>
<td></td>
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</tr>
<tr>
<td><strong>Gliclazide (s)</strong></td>
<td>Sulfonylureas</td>
<td>Hypoglycaemia - can be prolonged</td>
<td>Severe L/R</td>
<td>Renally excreted</td>
<td>V. albumin bound - Caution in elderly c↓ renal function</td>
</tr>
<tr>
<td><strong>Tolbutamide (s)</strong></td>
<td></td>
<td>Wt. gain (↑ appetite)</td>
<td></td>
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<tr>
<td><strong>Glipizide (s)</strong></td>
<td></td>
<td>Gl upset</td>
<td></td>
<td></td>
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<tr>
<td><strong>Glibenclamide (l)</strong></td>
<td></td>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(Chlorpropamide)</td>
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</tr>
<tr>
<td><strong>Nateglinide</strong></td>
<td>Meglitinides</td>
<td>Hypoglycaemia</td>
<td></td>
<td></td>
<td>V. short acting → ↓ risk of hypo Give before meal</td>
</tr>
<tr>
<td><strong>Repaglinide</strong></td>
<td></td>
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<tr>
<td><strong>Exenatide</strong></td>
<td>Insulin secretagogue</td>
<td>Hypoglycaemia</td>
<td></td>
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</tr>
<tr>
<td><strong>Liraglutide</strong></td>
<td>GLP-1 analogue</td>
<td>Gl upset</td>
<td></td>
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</tr>
<tr>
<td><strong>Sitagliptin</strong></td>
<td>Insulin secretagogues</td>
<td>Hypoglycaemia</td>
<td></td>
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</tr>
<tr>
<td><strong>Vildagliptin</strong></td>
<td>Dipeptidylpeptidase-4 inhibitor</td>
<td>Gl upset</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Acarbose</strong></td>
<td>Intestinal α-glucosidase inhibitor</td>
<td>Flatulence - Loose stools/diarrhoea - Abdo pain / bloating - Hepatotoxicity (rare)</td>
<td>IBD L</td>
<td>Monitor LFTs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delays carb absorption → ↓ post-prandial blood glucose</td>
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<tr>
<td></td>
<td>Little effect on fasting glucose</td>
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</tbody>
</table>
## Insulin

<table>
<thead>
<tr>
<th>Examples</th>
<th>Short-acting</th>
<th>Insulin Analogues</th>
<th>Intermediate- and long- acting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actrapid</td>
<td>Aspart: NovoRapid</td>
<td>Isophane Insulin</td>
</tr>
<tr>
<td></td>
<td>Humulin S</td>
<td>Lispro: Humalog</td>
<td>Insulatard</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Glargine: Lantus</td>
</tr>
<tr>
<td>Onset (sc)</td>
<td>30-60min</td>
<td>15min</td>
<td>1-3hrs</td>
</tr>
<tr>
<td>Peak (sc)</td>
<td>2-4hrs</td>
<td>1-3hrs</td>
<td>4-12hrs</td>
</tr>
<tr>
<td>Duration (sc)</td>
<td>6-8hrs</td>
<td>2-5hrs</td>
<td>12hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Glargine: 24hrs</td>
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<tr>
<td></td>
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<td></td>
<td>Detemir: 20hrs</td>
</tr>
<tr>
<td>Uses</td>
<td>Maintenance: 15-30min before meals</td>
<td>Sliding scales</td>
<td>Glargine is given OD (nocte) as basal therapy</td>
</tr>
</tbody>
</table>

### Effects of insulin

**Adipose tissue**
- ↑ lipoprotein lipase activity → ↓ TGs
- ↑ GLUT-4 activity → ↑ glucose storage as fat
- ↓ lipolysis → ↓ fatty acids release into circulation

**Liver**
- ↓ glycogenolysis
- ↓ gluconeogenesis
- ↑ glycogenesis
- Inhibition of ketogenesis

**Muscle**
- ↓ proteolysis
- ↑ GLUT-4 activity → ↑ glucose uptake

**NB.** Lipoprotein lipase allows triglyceride uptake from LDL by adipocytes.

### Side Effects

- **Hypoglycaemia**
  - At risk: EtOH binge, β-B (mask symptoms), elderly
  - Need to admit sulfonylurea-induced hypo

- **Lipohypertrophy**
  - Rotate injection site: abdomen, thighs

- **Wt. gain in T2DM**
  - ↓ wt. gain if insulin given c¯ metformin

### Problems c¯ Actrapid in the Basal-Bolus Regime

- Absorbed over 3-4hrs: not physiological
- Must give 15min before meal
- Can → late post prandial hypoglycaemia
- Immediate post-prandial hyperglycaemia may → ↑ risk of DM complications

### Short Acting Insulin Analogues

- Fast onset and shorter duration
- Can be given just before start of meal
- Less chance of post-prandial hypoglycaemia

### Factors Affecting Absorption

- Temperature
- Exercise
- Preparation: actrapid vs. glargine
- Dlvy method
  - IV: 1min peak conc
  - SC: 90min peak conc
  - Injection site and depth

### Administration

- s/c: typical route
- IVI
  - DKA
  - Control in critical illness
  - Control in peri-operative period

---

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## Thyroid Drugs

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Thyroxine</td>
<td></td>
<td>Precipitation of heart failure&lt;br&gt;Osteopaenia&lt;br&gt;AF&lt;br&gt;Over-Rx → hyperthyroidism</td>
<td></td>
<td>W+</td>
<td>Introduce T4 slowly in the elderly</td>
</tr>
<tr>
<td>Carbimazole Propythiouracil</td>
<td>Thionamides&lt;br&gt;- thyroperoxidase inhibitors&lt;br&gt;- prevent iodination of tyrosine&lt;br&gt;→ ↓ T4/T3 synthesis</td>
<td>Agranulocytosis&lt;br&gt;- often transient and benign&lt;br&gt;Hypersensitivity: rash, pruritis&lt;br&gt;Hepatitis</td>
<td>Pregnancy&lt;br&gt;Children&lt;br&gt;Tracheal compression&lt;br&gt;- do surgery</td>
<td></td>
<td>Prophytiouracil is reserved for those intolerant of carbimazole due to risk of hepatitis&lt;br&gt;Titrate to normal TSH or block and replace.</td>
</tr>
<tr>
<td>Radioiodine: I(^{131})</td>
<td>Radioiodine is localised to thyroid&lt;br&gt;→ destruction of gland</td>
<td>→ hypothyroidism&lt;br&gt;Can precipitate thyroid storm</td>
<td></td>
<td></td>
<td>Stop thionamide before use</td>
</tr>
</tbody>
</table>

## Pituitary Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromocriptine Cabergoline Pergolide</td>
<td>Ergot-derived DA agonists</td>
<td>Fibrosis&lt;br&gt;GI upset: esp. nausea&lt;br&gt;Postural hypotension&lt;br&gt;Drowsiness&lt;br&gt;Neuropsych syndromes</td>
<td>Cardiovascular disease&lt;br&gt;Porphyria&lt;br&gt;Psychosis</td>
<td>Levels ↑ by:&lt;br&gt;- octreotide&lt;br&gt;- macrolides</td>
<td>Use&lt;br&gt;- prolactinoma&lt;br&gt;- can be used in acromegaly&lt;br&gt;Monitor heart ĝ echo</td>
</tr>
<tr>
<td>Octreotide Lanreotide</td>
<td>Somatostatin analogues</td>
<td>Diarrhoea&lt;br&gt;Gallstones</td>
<td></td>
<td></td>
<td>Use&lt;br&gt;- acromegaly&lt;br&gt;- carcinoid syndrome</td>
</tr>
<tr>
<td>Pegvisomant</td>
<td>GH receptor antagonist</td>
<td></td>
<td></td>
<td></td>
<td>Use&lt;br&gt;- acromegaly</td>
</tr>
<tr>
<td>Metyrapone</td>
<td>11β-hydroxylase inhibitor&lt;br&gt;- inhibits adrenal cortisol production</td>
<td>Hypoadrenalism</td>
<td></td>
<td></td>
<td>Use&lt;br&gt;- can be used Cushing’s syn.&lt;br&gt;- particularly if resistant to surgery</td>
</tr>
</tbody>
</table>
# Calcium Metabolism

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinacalcet</td>
<td>Calcimimetic</td>
<td></td>
<td></td>
<td></td>
<td>Used for Rx of 2° HPT in ESRF</td>
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<tr>
<td></td>
<td>- $\rightarrow$ ↓ PTH secretion</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sevelamer</td>
<td>Phosphate binder</td>
<td>GI upset</td>
<td>GI obstruction</td>
<td></td>
<td>Used to ↓PO$_4$ in ESRF</td>
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<tr>
<td>Lanthanum</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Alendronate</td>
<td>Bisphosphonates</td>
<td>GI upset</td>
<td>Achalasia</td>
<td>Oesophageal stricture</td>
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<tr>
<td>Etidronate</td>
<td>↓ ostoclastic bone resorption</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Pamidronate</td>
<td></td>
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</tr>
<tr>
<td>Ibandronate</td>
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<tr>
<td>Risedronate</td>
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<tr>
<td>Zoledronate</td>
<td></td>
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</tr>
<tr>
<td>Strontium</td>
<td>↑ bone formation</td>
<td>DRESS syndrome</td>
<td></td>
<td></td>
<td>Use if bisphosphonates not tolerated</td>
</tr>
<tr>
<td></td>
<td>↓ bone resorption</td>
<td></td>
<td></td>
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<tr>
<td>Teriparetide</td>
<td>Recombinant PTH</td>
<td>GI upset</td>
<td>Skeletal malignancies</td>
<td>Paget's</td>
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<tr>
<td></td>
<td>- pulsatile admin $\rightarrow$ ↑ bone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>formation and ↓ resorption</td>
<td></td>
<td></td>
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<tr>
<td>Denosumab</td>
<td>Anti-RANK ligand</td>
<td></td>
<td></td>
<td></td>
<td>Used if bisphosphonates not tolerated</td>
</tr>
<tr>
<td></td>
<td>- ↓ osteoclast activation</td>
<td></td>
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<tr>
<td>Ergocalciferol</td>
<td>Vitamin D2</td>
<td></td>
<td></td>
<td></td>
<td>Commonly used for Vit D deficiency</td>
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<tr>
<td>Colecalciferol</td>
<td>Vitamin D3</td>
<td></td>
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<tr>
<td>Alfacalcidol</td>
<td>$1\alpha$ (OH) Vit D3</td>
<td></td>
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<td>Use in renal disease</td>
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<tr>
<td>Calcitriol</td>
<td>$1, 25,(OH)$ Vit D3</td>
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<td>Use in renal disease</td>
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## Sex Hormones

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<tr>
<th>Drug</th>
<th>Benefits</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
<td>COCP</td>
<td>Contraception</td>
<td>↑ risk of VTE</td>
<td>Personal Hx of VTE</td>
<td>P450 metabolism</td>
<td>Don’t need extra contraception when taking oral Abx that don’t induce liver enzymes, unless d/v</td>
</tr>
<tr>
<td></td>
<td>↓ dysmenorrhoea, ↓ menorrhagia</td>
<td>Small ↑ risk of breast Ca</td>
<td>Risk of VTE</td>
<td>enzyme inducers ↑ fx of steroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ PMT</td>
<td>Small ↑ risk of IHD</td>
<td>Risk of arterial disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ benign breast disease</td>
<td>Gallstones</td>
<td>Hx of breast Ca</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ ovarian and endometrial Ca</td>
<td>Cholestatic jaundice</td>
<td></td>
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<tr>
<td></td>
<td>↓ risk of PID</td>
<td>Breast tenderness</td>
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<td></td>
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<td>Hepatoma</td>
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<tr>
<td></td>
<td></td>
<td>↑ risk of VTE</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>↑ wt.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Breast tenderness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POP</td>
<td>n/v</td>
<td>Headache</td>
<td>Severe arterial disease</td>
<td>P450 metabolism</td>
<td></td>
</tr>
<tr>
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<td></td>
<td>↑ wt.</td>
<td>Hx of breast Ca</td>
<td>enzyme inducers</td>
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<tr>
<td></td>
<td></td>
<td>Breast tenderness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRT</td>
<td>↓ hot flushes, ↓ vaginal dryness, ↑ libido</td>
<td>↑ risk of Ca: breast, endometrial, ovarian</td>
<td>Oestrogen-dependent Ca</td>
<td></td>
<td>Excess Ca risk disappears w/i 5yrs of stopping</td>
</tr>
<tr>
<td></td>
<td>↓ urinary frequency / urgency</td>
<td>↑ risk of VTE</td>
<td>Hx of breast Ca</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ risk of bowel Ca</td>
<td>↑ risk of stroke and IHD</td>
<td>UnDx vaginal bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ risk of osteoporotic #s</td>
<td>Cholestatic jaundice</td>
<td>VTE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### COCP Cautions and Contraindications

**VTE Risk: caution if 1, avoid if ≥2**
- FHx of VTE
- BMI >30, avoid if >35
- Long-term immobilisation
- Hx of superficial thrombophlebitis
- >35yrs, avoid if >50yrs
- Smoking

**Arterial Risk: caution if 1, avoid if ≥2**
- FHx of arterial disease
- DM
- HTN
- Smoking, avoid if >40/d
- >35yrs, avoid if >50yrs
- Migraine w/o aura, avoid if migraine c aura
1. Lifestyle Modification: DELAYS
   - Diet
   - Exercise
   - Lipids (statins if >40 regardless of lipids)
   - Aspirin (consider if >50yrs or <50 yrs other RFs)
   - ABP ↓
   - Yearly / 6moly f/up
   - Smoking cessation

2. Start Metformin
   (if HBA1c >target after lifestyle changes)
   - SE: nausea, diarrhoea, abdo pain, lactic acidosis
   - CI: GFR<30, tissue hypoxia (sepsis, MI), morning before GA and iodinated contrast media
   - 500mg after evening meal, ↑ing to 2g max.

3. Metformin + Sulfonylurea
   (if HBA1c >target)
   - E.g. gliclazide MR 30mg c ¯ breakfast
   - SE: hypoglycaemia, wt. gain
   - CI: omit on morning of surgery

   Other Options
   - Consider adding a rapid-acting insulin secretagogue (e.g. nateglinide) to metformin instead of a sulfonylurea.
     - May be preferable if erratic lifestyle.
   - Consider adding pioglitazone to metformin instead of a sulfonylurea

4. Additional Therapy

   1st line
   - Add insulin → insulin + metformin + sulfonylurea

   2nd line
   - Add sitagliptin or pioglitazone if insulin unacceptable
     - Employment, social or recreational issues
     - Obesity
   - Metformin + sulfonylurea + sitagliptin / pio

   3rd line
   - Add exenatide (SC) if insulin unacceptable or BMI>35
   - Metformin + sulfonylurea + exenatide

   4th line
   - Consider acarbose if unable to use other glucose-lowering drugs

Targets
   - Capillary blood glucose
     - Fasting: 4.5-6.5mM
     - 2h post-prandial: 4.5-9mM
   - HbA1c
     - Reflects exposure over last 6-8wks
     - Aim <45 - 50mM (6 - 7%)
Thyroid Disorders

Hypothyroidism

Levothyroxine
- Titrate to normalize TSH
- Enzyme inducers ↑ thyroxine metabolism
- Clinical improvement takes ~2wks

Caution
- In elderly pts. c subclinical heart failure thyroxine can ppt. acute worsening: palpitations, angina, MI
  - Introduce thyroxine gradually
- Excessive thyroxine → osteopaenia and AF

Thyrotoxicosis

Confirm Aetiology
- Use Tc scan to determine if thyroxicosis is high or low uptake.
  - Low
    - Subacute de Quervain’s thyroiditis
    - Postpartum thyroiditis
    - Amiodarone
  - High
    - Graves: 40-60%
    - TMNG: 30-50%
    - Thyroid Adenoma: 5%
    - Functioning thyroid Ca

Mx
- Low Uptake
  - Symptomatic: propranolol, atenolol
  - NSAIDs for de Quervain’s
- High Uptake
  - β-B
  - Carbimazole
    - Titration to normal TSH
    - Or, block and replace
  - Radioiodine
  - Surgery

Adrenal Steroids

Glucocorticoid Replacement
- Need for 1O and 2O adrenal failure

Hydrocortisone
- Preferred due to gluco- and mineralo-corticoid activity.
- 20-30mg in divided doses
  - 10mg AM, 5mg lunch, 5mg evening

↑ dose at intercurrent illness / injury
- If eating
  - 3x normal dose for 3d
  - Then 2x normal dose for 3d
- Vomiting / can’t tolerate PO
  - 100mg IV TDS

Cushing’s
- Treat underlying cause: e.g. pituitary or adrenal tumour
- May use drugs temporarily or permanently if pt. can’t undergo surgery: e.g. lung Ca

Metyrapone
- Inhibits final step in cortisol synthesis
- 80% response in Cushing’s disease
  - Usually temporary
- Can be used as part of block and replace strategy

Other anti-glucocorticoid drugs
- Ketoconazole: inhibits steroid synthesis
- Mifepristone: progesterone and glucocorticoid receptor antagonist

Mineralocorticoid Replacement
- Need for 1O adrenal failure only

Fludrocortisone
- Balance between HTN and postural hypotension

Primary Hyperaldosteronism

Bilateral adrenal hyperplasia (70%)
- Spironolactone
- Eplerenone
- Amiloride

Conn’s adenoma (30%)
- Surgical excision or medical therapy

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Pituitary Disorders

Cranial DI
- Desmopressin
  - Nasal spray
  - IV
- Avoid dilutional hyponatraemia by daily polyuria episode

Acromegaly
- 1st line: trans-sphenoidal excision
- 2nd line: somatostatin analogues – octreotide
- 3rd line: GH antagonist – pegvisomant
- 4th line: radiotherapy

Somatostatin Analogues
- 90% respond
- IGF1 normalised in 60%

Prolactinoma
- 1st line: D₂ agonist
- 2nd line: Trans-sphenoidal excision
  - If visual or pressure symptoms don’t response to medical Rx

D₂ Agonists
- Bromocroptine, Cabergoline
- ↓ PRL secretion and ↓ tumour size

Hypopituitarism
- ACTH: hydrocortisone
- GH: rh-GH
- FSH / LH
  - Testosterone
  - OCP
- TSH: T4

Osteoporosis

Conservative
- Stop smoking, ↓ EtOH
- Wt. bearing or balancing exercise (e.g. Tai Chi)
- Ca and vit-D rich diet
- Home-based fall-prevention program with visual assessment.

1st and 2nd prevention of osteoporotic #s
- Bisphosphonates: alendronate is 1st line
- Ca and Vit D supplements
  - e.g Calcium D₃ Forte
- Strontium ranelate: bisphosphonate alternative

Alternative for 2nd prevention of osteoporotic #s
- Teriparatide: PTH analogue → new bone formation
- Denosumab: anti-RANKL → ↓ osteoclast activation
- Raloxifene: SERM, ↓ breast Ca risk cf. HRT

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Malignancy and Immunosuppression

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# Anti-Proliferative Agents

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<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Use</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Alkylates DNA</td>
<td>BM suppression</td>
<td></td>
<td></td>
<td>Cancer</td>
<td>Give mesna to prevent haemorrhagic cystitis</td>
</tr>
<tr>
<td></td>
<td>Affects B cells &gt; T cells</td>
<td>Haemorrhagic cystitis</td>
<td></td>
<td></td>
<td>RA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alopecia</td>
<td></td>
<td></td>
<td>SLE</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sterility: esp. males</td>
<td></td>
<td></td>
<td>Systemic sclerosis</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Wegener's</td>
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<tr>
<td>Cisplatin</td>
<td>Alkylates DNA</td>
<td>BM suppression</td>
<td></td>
<td></td>
<td>Cancer</td>
<td>Carboxplatin is assoc. c less severe SEs</td>
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<tr>
<td></td>
<td></td>
<td>Severe n/v</td>
<td></td>
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<td>- Ovarian</td>
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<td></td>
<td></td>
<td>Nephrotoxic</td>
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<td>- Lung: SSLC</td>
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<td></td>
<td></td>
<td>Ototoxic</td>
<td></td>
<td></td>
<td>- Testicular</td>
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<tr>
<td></td>
<td></td>
<td>Peripheral neuropathy</td>
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<tr>
<td>Azathioprine</td>
<td>Blocks de novo purine synthesis</td>
<td>BM suppression</td>
<td></td>
<td></td>
<td>Allopurin → ↑ toxicity</td>
<td>Prevent Tx rejection</td>
</tr>
<tr>
<td></td>
<td>Active metabolite is 6-mercaptopurine</td>
<td>Hepatotoxicity n / v / d Arthralgia</td>
<td></td>
<td></td>
<td>Steroid-sparing agent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Affects T cells &gt; B cells</td>
<td>BM suppression</td>
<td></td>
<td></td>
<td>- IBD</td>
<td>Do TPMT (thiopurine methyltransferase) assay before use.</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>- SLE</td>
<td>50% of pts intolerant of azathioprine tolerate 6-MP</td>
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<td>- RA</td>
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<tr>
<td>Mycophenolate mofetil</td>
<td>Blocks de novo nucleotide synthesis</td>
<td>BM suppression</td>
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<td>Prevent Tx rejection</td>
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<td>Affects T cells &gt; B cells</td>
<td>Skin malignancy</td>
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<td>AI disease</td>
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<tr>
<td>Methotrexate</td>
<td>Dihydrofolate reductase inhibitor</td>
<td>BM suppression</td>
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<td>Pulmonary fibrosis</td>
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<td>Hepatotoxicity</td>
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<td>Mucositis</td>
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<td>Chlorambucil</td>
<td>Alkylates DNA</td>
<td>BM suppression</td>
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<td></td>
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<td>Cancer: e.g. CLL</td>
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<td>EM → SJS</td>
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## Inhibitors of Cell Signalling

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Use</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciclosporin</td>
<td>Calcineurin inhibitors - Blocks IL-2 production</td>
<td>Nephrotoxic</td>
<td></td>
<td></td>
<td>P450 metabolism</td>
<td>Prevent Tx rejection</td>
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<td></td>
<td>Hepatic dysfunction</td>
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<td>GvHD</td>
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<td>Tremor</td>
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<td>UC</td>
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<td>Hypertrichosis</td>
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<td>RA</td>
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<td>Gingival hypertrophy</td>
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<td>Psoriasis</td>
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<td>Encephalopathy</td>
<td></td>
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<td>Monitor LFTs</td>
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<tr>
<td>Tacrolimus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P450 metabolism</td>
<td>Prevent Tx rejection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nephrotoxic (&lt; cf. ciclosporin)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Diabetogenic</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Neurotoxic (&gt; cf. ciclosporin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sirolimus</td>
<td>Blocks mTOR pathway</td>
<td>Dyslipidaemia</td>
<td></td>
<td></td>
<td></td>
<td>Prevent Tx rejection</td>
</tr>
</tbody>
</table>

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**Chemotherapeutics**

**Important Cytotoxic Classes**

**Alkylating agents**
- Cyclophosphamide, chlorambucil, busulfan, cisplatin
  - **Mechanism**
    - DNA x-linking
    - Base mis-paring
    - Excision of alkylated DNA → strand breaks

**Antimetabolites**: methotrexate, 5-FU

**Cytotoxic Abx**
- Anthracyclines: doxorubicin, daunorubicin
- Bleomycin
  - **Mechanism**
    - Intercalate c̅ DNA
    - Free radical formation

**Microtubule Inhibitors**
- Vinca alkaloids: vincristine, vinblastine
- Taxanes: paclitaxel

**Topoisomerase Inhibitors**
- Etoposide

**Immune Modulators**: thalidomide, lenalidomide

**MAbs**
- Trastuzumab (anti-Her2): breast Ca
- Bevacizumab (anti-VEGF): RCC, CRC, lung
- Cetuximab (anti-EGFR): CRC
- Rituximab (anti-CD20): NHL

**Tyrosine Kinase Inhibitors**
- Erlotinib: lung Ca
- Imatinib: CML
- Sunitinib: RCC

**Endocrine Modulators**: tamoxifen, anastrazole

**Common Side Effects**
- n/v: prophylactic anti-emetics
- Alopecia
- Neutropenia: 10-14d after chemo
  - **Extravasation of chemo agent**
    - Pain, burring, bruising @ infusion site
    - Stop infusion, give steroids, apply cold pack
    - Liaise early c̅ plastics
- Hyperuricaemia
- Oral mucositis

**Specific Problems**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Haemorrhagic cystitis: give mesna</td>
</tr>
<tr>
<td></td>
<td>Hair loss</td>
</tr>
<tr>
<td></td>
<td>BM suppression</td>
</tr>
<tr>
<td>Doxorubicin + other</td>
<td>Cardiomyopathy</td>
</tr>
<tr>
<td>anthracyclines</td>
<td>Extravasation reactions</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Pulmonary fibrosis</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td></td>
<td>- don’t give IT</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Severe n/v</td>
</tr>
<tr>
<td></td>
<td>Nephrotoxic</td>
</tr>
<tr>
<td></td>
<td>Ototoxic</td>
</tr>
<tr>
<td></td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td></td>
<td>Hypersensitivity</td>
</tr>
<tr>
<td></td>
<td>- Pre-Rx c̅ antihistamines + steroids</td>
</tr>
<tr>
<td>5-FU</td>
<td>Palmar-plantar erythrodysthesia</td>
</tr>
<tr>
<td></td>
<td>Mucositis</td>
</tr>
</tbody>
</table>

**Mx Chemo-induce Emesis**

**Low risk of emesis**
- Domperidone / metoclopramide started pre-Rx

**High risk of emesis**
- Ondansetron / granisetron +
- Dexamthasone +
- Aprepitant

**Common Regimens**

**Breast Ca: FEC**
- 5-FU
- Epirubicin
- Cyclophosphamide

**Breast Ca: CMF**
- Cyclophosphamide
- Methotrexate
- 5-FU

**Testicular Teratoma: BEP**
- Bleomycin
- Etoposide
- CisPlatin

**Ovarian**
- Carboplatin
- Paclitaxel

**NHL: R-CHOP**
- Rituximab
- Cyclophosphamide
- Hydroxydaunomycin (doxorubicin)
- Oncovin
- Prednisolone

**HL: ABVD**
- Adriamycin (doxorubicin)
- Bleomycin
- Vinblastine
- Dacarbazine

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Immunosuppression

Prednisolone

MOA
- Inhibits PLA₂ → ↓ PG and ↓ PAF
- ↓ PMN extravasation → ↑ PMN in blood
- Lymphocyte sequestration in tissues → lymphopenia
- ↓ Phagocytosis
- Lymphocyte apoptosis
- ↓ Ab production
- ↓ cytokine and proteolytic enzyme release

Dose
- Use lowest possible dose: alternate days if possible
- Graded withdrawal if used >3wks

Advice
- Don’t stop steroids suddenly
- Consult doctor when unwell
- ↑ dose if illness or stress (e.g. pre-op)
- Carry a steroid card: dose and indication
- Avoid OTCs: e.g. NSAIDs
- Osteoporosis and PUD prophylaxis
  - Ca and vitamin D supplements: Calcichew-D3
  - Bisphosphonates: alendronate
  - PPI: lansoprazole

SEs (mostly long-term use >6wks)
- GI  
  - Candidiasis
  - PUD
  - Oesophageal ulceration
  - Pancreatitis
- Cardio  
  - HTN
  - CCF
- MSK  
  - Proximal myopathy
  - Osteoporosis
- Endo  
  - Growth suppression
  - HPA suppression
  - Cushing’s syndrome
- Metabolic  
  - Na and fluid retention
  - ▲ PMN
  - ▼ K
- CNS  
  - Depression, psychosis
- Eye  
  - Cataracts
  - Glaucoma
- Immune  
  - ▲ susceptibility to infection

Interactions
- Fx ↓ d by hepatic inducers
- Fx ↑ d by
  - Hepatic inhibitors
  - OCP

Transplant Regimens

Liver
- Tacrolimus
- Azathioprine
- Prednisolone ± withdrawal @ 3mo

Renal
- Pre-op induction
  - Alemtuzumab (Campath: anti-CD52)
- Post-op
  - Predniolone 7d
  - Tacrolimus long-term
Musculoskeletal

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# Rheumatic Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine Mesalazine</td>
<td>5-Aminosalicylate Unknown MOA</td>
<td>Sulfasalazine has ↑ SEs - blood dyscrasias - hepatitis - rash, urticaria - oligospermia - pulmonary fibrosis</td>
<td>Caution in renal or hepatic impairment</td>
<td></td>
<td>Monitor FBC Better for use in young women cf. methotrexate</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Dihydrofolate reductase inhibitor</td>
<td>BM suppression Pulmonary fibrosis Hepatotoxic</td>
<td>R L</td>
<td>↑ toxicity → - NSAIDs - ciclosporin - steroids</td>
<td>Cancer RA Psoriasis Crohn’s</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>↓ activation of dendritic cells</td>
<td>Visual change - rarely retinopathy Seizures BM suppression</td>
<td>Caution in G6PD deficiency</td>
<td></td>
<td>Monitor vision</td>
</tr>
<tr>
<td>Penicillamine</td>
<td></td>
<td>Nephrotic syndrome Drug-induced lupus Taste change</td>
<td>SLE</td>
<td></td>
<td>Chelates Cu and Pb Prevents stones in cystinuria</td>
</tr>
<tr>
<td>Infliximab - Remicade</td>
<td>Chimeric anti-TNF mAb</td>
<td>Severe infections TB Allergic reactions CCF CNS demyelination ↑ AI disease and C</td>
<td>TB</td>
<td></td>
<td>Screen for TB before use Parenteral admin Give → hydrocortisone ↓ allergic SEs</td>
</tr>
</tbody>
</table>

## Anti-Gout

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colchicine</td>
<td></td>
<td>Diarrhoea Renal impairment</td>
<td>Caution in renal impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allopurinol</td>
<td>XO inhibitor</td>
<td>Severe skin reactions - EM → SJS Gl upset Hepatotoxic</td>
<td>Caution in R and L - ↓ dose</td>
<td>↓ metabolism of azathioprine - AVOID</td>
<td>Initial Rx can → ↑ gout - initiate → NSAID / colchicine cover</td>
</tr>
<tr>
<td>Feboxustat</td>
<td>XO inhibitor</td>
<td>Headache Rash Abnormal LFTs</td>
<td>Caution in R and L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probenecid</td>
<td>Uricosuric</td>
<td>Gl upset</td>
<td>Caution in R and L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rasburicase</td>
<td>Recombinant uric oxidase</td>
<td></td>
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</tr>
</tbody>
</table>
### NSAIDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Least → Most Toxic</td>
<td>- Ibuprofen - Diclofenac - Aspirin - Naproxen - Indomethacin - Ketoprofen</td>
<td>Non-selective COX inhibitors</td>
<td>Gastritis and PUD</td>
<td>Renal or cardiac failure</td>
<td>± bleeding with warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analgesic</td>
<td>↓ GFR</td>
<td>PUD</td>
<td>± effects of ACEIs and ARBs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antipyretic</td>
<td>Interstitial nephritis</td>
<td>Severe hepatic impairment</td>
<td>± toxicity of methotrexate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-inflammatory</td>
<td>Papillary necrosis</td>
<td>Caution</td>
<td>Can be given with other agents for gastro protection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↑ K</td>
<td>- in the elderly</td>
<td>- PPI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peripheral oedema</td>
<td>- asthma</td>
<td>- H₂RAs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bronchospasm</td>
<td></td>
<td>- mioprostol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hypersensitivity</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Selective COX-2 inhibitor</td>
<td>↑ cardiovascular events</td>
<td>Renal SEs as above</td>
<td>IHD</td>
<td>± effects of ACEIs and ARBs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cerebrovascular disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>L/R failure</td>
<td>Assess CV risk before use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Only used for short periods in young pts. ± intolerance of other NSAIDs</td>
</tr>
</tbody>
</table>

### Eicosanoid Synthesis

[Diagram of Eicosanoid Synthesis]

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## Neuromuscular Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neostigmine</td>
<td>Anticholinesterases</td>
<td>Cholinergic</td>
<td>Asthma</td>
<td></td>
<td>Edrophonium preferred for the Dx of MG due to its v. short t½.</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>- ↑ ACh in the synaptic cleft</td>
<td></td>
<td>Intestinal / urinary obstruction</td>
<td></td>
<td>Pyridostigmine preferred for the Rx of MG due to long t½.</td>
</tr>
<tr>
<td>Edrophonium</td>
<td>- Enhance neuromuscular transmission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baclofen</td>
<td>GABA&lt;sub&gt;B&lt;/sub&gt; agonist</td>
<td>Sedation</td>
<td>PUD</td>
<td>fx ↑d by TCAs</td>
<td>Rx painful muscle spasms</td>
</tr>
<tr>
<td></td>
<td>Skeletal muscle relaxant</td>
<td>↓ tone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nausea</td>
<td></td>
<td></td>
<td>Don’t withdraw abruptly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urinary disturbance</td>
<td></td>
<td></td>
<td>- hyperthermia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ↑ spasticity</td>
</tr>
<tr>
<td>Dantrolene</td>
<td>Prevents Ca&lt;sup&gt;2+&lt;/sup&gt; release from sarcoplasmic reticulum</td>
<td>Hepatotoxicity</td>
<td>Hepatic impairment</td>
<td></td>
<td>Used to relieve chronic spasticity and in malignant hyperthermia</td>
</tr>
<tr>
<td></td>
<td>Skeletal muscle relaxant</td>
<td>GI upset</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Osteoarthritis

Conservative
- ↓ wt.
- Alter activities: ↑ rest, ↓ sport
- Physio: muscle strengthening
- Walking aids, supportive footwear, home mods

Medical
- Analgesia
  - Paracetamol
  - NSAIDs
    - 1st: Ibuprofen: 400mg TDS
    - 2nd: diclofenac
  - Tramol
- Joint injection: local anaesthetic and steroids

Surgical
- Arthroscopic washout: esp. knee.
  - Trim cartilage, remove foreign bodies.
- Arthroplasty: Replacement (or excision)
- Osteotomy: small area of bone cut out.
- Arthrodesis: last resort for pain management
- Novel Techniques
  - Microfracture: stem cell release → fibro-cartilage formation
  - Autologous chondrocyte implantation

Rheumatoid Arthritis

Conservative
- Refer to rheumatologist
- Regular exercise
- PT
- OT: aids, splints

Medical
- DAS28: monitor disease activity
- DMARDs and biologicals: use early
- Steroids: PO or intra-articular for exacerbations
- NSAIDs: good for symptom relief
  - e.g. arthrotec: but → diarrhoea
- Mx CV risk: RA accelerates atherosclerosis
  - Prevent osteoporosis and gastric ulcers

DMARDs
- 1st line for treating RA
- Early DMARD use assoc. ↓ better long-term outcome
- All DMARDs can → myelosuppression → pancytopenia

Main agents:
- Methotrexate: hepatotoxic, pulm. fibrosis, teratogenic
- Sulfasalazine: SJS, ↓ sperm count, pulmonary fibrosis
- Hydroxychloroquine: visual change, rash, seizures

Other Agents:
- Leflunomide: ↑ risk of infection and malignancy
- Gold: nephrotic syndrome
- Penicillamine: drug-induced lupus, taste change, nephrotic syn.

Biologics

Anti-TNF
- Severe RA not responding to DMARDs
  - DAS28 >5.1
  - Failed methotrexate + ≥1 other DMARD
- Screen and Rx TB first
- Infliximab: chimeric anti-TNF Ab
- Etanercept: TNF-receptor
- Adalimumab: human anti-TNF Ab
- SEs: ↑ infection (sepsis, TB), ↑ AI disease, ↑ Ca

Rituximab (anti-CD20 mAb)
- Severe RA not responding to anti-TNF therapy

Surgical
- Ulna stylectomy
- Joint prosthesis
Gout

Acute Rx
- NSAID: diclofenac or indomethacin
- Colchicine
  - NSAIDs CI: warfarin, ulcers, heart HF, CRF
  - SE: diarrhoea
- In renal impairment: NSAIDs and colchicine are CI
  - → Use steroids

Prevention
- Conservative
  - Lose wt.
  - Avoid prolonged fasts and EtOH excess
- Xanthine Oxidase Inhibitors: Allopurinol
  - Use if recurrent attacks, tophi or renal stones
  - Introduce c NSAID or colchicine cover for 3/12
  - SE: rash, fever, ↓WCC (c azathioprine)
  - Use febuxostat (XO inhibitor) if hypersensitivity
- Uricosuric drugs: e.g. probenecid, losartan
  - Rarely used
- Recombinant urate oxidase: rasburicase
  - May be used pre-cytotoxic therapy
Cardiovascular

ACS
- Oxygen
- **Analgesia**
  - Morphine 5-10mg IV
  - Metoclopramide 10mg IV
- **Anti-platelet**
  - Aspirin 300mg PO
  - Clopidogrel 300mg PO
- **Anti-ischaemia**
  - GTN: 2 puffs or 1 tab SL
  - IV if pain continues
  - Atenolol
  - STEMI: 5mg IV
  - NSTEMI: 50mg PO /24h
- **Anti-coagulate**
  - Enoxaparin

STEMI
- 1st: PCI
- 2nd: thrombolysis
  - Add tirofiban in high-risk pts.

NSTEMI
- Tirofiban
- Angiography ± PCI w/i 96hrs

Long-Term
- **ACEi**: e.g. lisinopril 2.5mg OD
- Aspirin 75mg OD
- β-B: e.g. bisoprolol 1.25mg OD
  - Verapamil if β-B not tolerated
- Clopidogrel 75mg OD
  - STEMI: 1mo
  - NSTEMI: 1yr
- Statin: e.g. atorvastatin 80mg OD

Acute Pulmonary Oedema

Initial Mx
- Oxygen
- Diamorphine 2.5-5mg + metoclopramide
- Frusemide 40-80mg IV
- GTN 2 puffs or 2 tabs SL
- ISMN 2-10mg/h IVI
  - Keep SBP >90mmHg

Rx underlying cause

If no improvement
- CPAP
- If SBP <90: dobutamine
  - 2-20ug/kg/min IVI
  - Via a central line

Anaphylaxis
- Oxygen
- Adrenaline 0.5mg IM: 0.5ml of 1:1000
  - Repeat every 5min as necessary, guided by cardiorespiratory function
- Chlorphenamine 10mg IV
- Hydrocortisone 200mg IV
- Nebs: salbutamol 5mg + ipratropium 0.5mg

Malignant HTN
- BP > 220 / 120 + either
  - Grade 3: haemorrhages, exudates
  - Grade 4: papilloedema

Mx
- Aim to ↓ DBP to 100-115mmHg over 4-6hrs
  - Nitroprusside or labetalol
  - Phentolamine if phaeo known or suspected

SVT

Unstable → DC cardioversion

Irregular Rhythm: Rx as AF

Regular Rhythm
- Adenosine 6mg IV bolus, then 12mg, then 12mg
- Choose from
  - Verapamil
  - Atenolol
  - Digoxin
  - Amiodarone

Irregular Rhythm
- Pre-excited AF: amiodarone or flecainide
- TDP: MgSO₄

Broad Complex Tachycardia

Unstable → DC cardioversion

Regular Rhythm
- Amiodarone or lignocaine

Irregular Rhythm
- Pre-excited AF: amiodarone or flecainide
- TDP: MgSO₄

Septic Shock

Initial Rx
- Oxygen
- Abx: cultures 1st then follow guidelines (e.g Tazocin)
- Fluids: 1L crystalloid or 500ml colloid over 30min
  - If BP still ↓ consider CVP and further fluids
  - Aim CVP ≥8mmHg and UO >0.5ml/kg/hr
- Inotropes if SBP <90mmHg after fluid resus
  - Norad 1-10ug/min: maintain MAP >65mmHg

Further Mx
- Insulin sliding scale: keep glucose <8.3mM
- DVT prophylaxis: enoxaparin 40mg OD SC
- Stress ulcer prophylaxis: PPI

Cardiac Arrest

Shockable
- Adrenaline 1mg + amiodarone 300mg after 3rd shock
  - Repeat adrenaline every other cycle

Non-Shockable
- Adrenaline 1mg as soon as IV access obtained
  - Repeat adrenaline every other cycle

Bradycardia <40bpm
- Atropine 0.6–1.2g (max 3g) IV
- Isoprenaline IVI
Neurological

Meningitis

Acute Mx
- Septicaemic
  - Ceftriaxone 2g IVI
  - + ampicillin 2g IVI /4h if >50yrs
- Meningitic
  - Ceftriaxone ± ampicillin post-LP
  - Dexamethasone 0.15mg/kg IVI QDS

Continuing Mx
- Ceftriaxone 2g IVI BD

Status Epilepticus

Reverse Potential Causes
- Thiamine 250mg IV if EtOH
- 100ml 20% glucose unless known to be normal

IV Bolus Phase
- Lorazepam 2-4mg IV over 30s
  - Repeat if no response w/i 2min
- Alternatives
  - Diazepam 10mg IV/PR (20mg max)
  - Midazolam 10mg buccal

IV Infusion Phase
- Phenytoin 18mg/kg IVI
  - 50mg/min max
- Or, diazepam IVI

Induction Phase
- Propofol or thiopentone

Respiratory

Acute Asthma

Initial Rx
- O₂ driven nebulisers
  - Salbutamol 5mg
  - Ipratropium 0.5mg
  - Repeat salbutamol every 15min until improvement
    - Monitor ECG
- Steroids
  - 100mg hydrocortisone
  - Or, 50mg prednisolone

No Improvement
- MgSO₄ 2g IVI over 20min
- Salbutamol 3-20 ug/min IVI
- Aminophylline
  - If not already on theophylline
  - Load then IVI

Acute COPD

Initial Rx
- 24% O₂
  - Blue venturi mask
  - Aim for 88-92% SpO₂
- Hydrocortisone 200mg IV
- Doxy 200mg PO STAT if evidence of infection

No Improvement
- Consider aminophylline
- BiPAP

PE
- Oxygen
- Morphine + metoclopramide
- Massive PE: alteplase 50mg bolus STAT
- Stable: anticoagulate
  - Enoxaparin 1.5mg/kg/24hr SC
  - Warfarin: 5mg PO
Endocrine

DKA

Dx
- Acidosis (↑ AG): pH <7.3 (± HCO₃ <15mM)
- Hyperglycaemia: ≥11.1mM (or known DM)
- Ketonaemia: ≥3mM (≥2+ on dipstix)

Fluids
- 0.9% NS infusion via large-bore cannula
  - SBP<90 → 1L stat + more until SBP >90
  - SBP>90 → 1L over 1h
  - Then: 1L over next 2h, 1L/2h, 1L/4h, 1L/4h, 1L/6h
  - Switch to 10% dex 1L/8h when glucose <14mM

Insulin Infusion
- 0.1u/kg/h Actrapid (6u if no wt., max 15u)
- Transfer to sliding scale when resolved
  - Ketones <0.3mM
  - Venous pH >7.3 (HCO₃ >18mM)
- Transfer to SC insulin when eating

Start Potassium Replacement in 2nd Bag of Fluids
- >5.5mM → Nil
- 3.5-5.5mM → 40mM
- <3.5mM → consult senior for review

Additional Therapy
- LMWH
- Consider NaHCO₃ if pH <6.9
- Find and Rx any infection

HONK
- Rehydrate 0.9% NS over 48h
  - May need ~9L
- Wait 1h before starting insulin
  - It may not be needed
  - Start low to avoid rapid changes in osmolality
    - e.g. 1-3u/hr
- LMWH

Thyroid Storm
- Fluid resuscitation + NGT
- Bloods: TFTs + cultures if infection suspected
- Propranolol PO/IV
- Digoxin + LMWH if AF
- Carbimazole then Lugol's iodine 4h later to inhibit thyroid
- Hydrocortisone 100mg QDS IV
- Rx cause

Myxoedema Coma
- Correct any hypoglycaemia
- T3/T4 IV slowly (may ppt. myocardial ischaemia)
- Hydrocortisone 100mg IV
- Rx hypothermia and heart failure

Addisonian Crisis
- Check CBG: glucose may be needed
- Hydrocortisone 100mg IV 6hrly
- IV crystalloid
- Rx underlying cause

Phaeochromocytoma Emergencies
- 1st α-block
  - Phentolamine: repeat to safe BP
  - Phenoxybenzamine: exchange for phentolamine
    - Longer t½
- 2nd β-block
  - Only after α-blockade
  - Avoids unopposed α-adrenergic stimulation
- Surgery
  - Electively after 406wks to allow full α-blockade and volume expansion
  - Phenoxybenzamine ↑d until significant postural hypotension.

Hypoglycaemia

Alert and Orientated: Oral Carb
- Rapid acting: lucozade
- Long acting: toast, sandwich

Drowsy / confused but swallow intact: Buccal Carb
- Hypostop / Glucogel
- Consider IV access

Unconscious or Concerned re Swallow: IV dextrose
- 50ml 50% or 100ml 20% glucose

Deteriorating / refractory / insulin-induced / no access
- 1mg glucagon IM/SC
- Won’t work in drunks + short duration of effect (20min)
- Insulin release may → rebound hypoglycaemia
**Metabolic**

**Hyperkalaemia**

**ECG Features (in order)**
- Peaked T waves
- Flattened P waves
- ↑ PR interval
- Widened QRS
- Sine-wave pattern → VF

**Mx**
- Calcium gluconate 10ml 10%
- 50ml 50% glucose + 10u insulin (Actrapid)
- Salbutamol 5mg nebulizer
- Calcium resonium 15g PO or 30g PR
- Haemofiltration (usually needed if anuric)

**Hypokalaemia**

**ECG Features**
- Result from delayed ventricular repolarisation
- Flattened / inverted T waves
- Prominent U waves (after T waves)
- ST depression
- Long PR interval
- Long QT interval

**Mild:** K > 2.5
- Oral K supplements
- ≥80mmol/d

**Severe:** K < 2.5 and/or dangerous symptoms
- IV K cautiously
- 10mmol/h (Max 20mmol/h)
- Best to give centrally (burning sensation)
  - Max central conc: 60mM
  - Max peripheral conc: 40mM

**Hypercalcaemia**

**Rehydrate**
- 1L 0.9% NS / 4h
- Monitor pts. hydration state

**Frusemide**
- Only start once pt. is volume replete
- Causing + makes room for more fluids

**Bisphosphonates**
- Ca bisphosphonate can’t be resorbed by osteoclasts
- Used to prevent recurrence
  - Can obscure Dx as ↓Ca, ↓PO4 and ↑PTH
- E.g. Pamidronate, Zoledronate (IV)

**Acute Poisoning**

<table>
<thead>
<tr>
<th>Poison</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Alkaline urine: NaHCO₃ + KCl</td>
</tr>
<tr>
<td>Benzodiazipine</td>
<td>Flumazenil</td>
</tr>
<tr>
<td>β-B</td>
<td>Atropine, glucagon</td>
</tr>
<tr>
<td>Cyanide</td>
<td>Dicobalt edentrate</td>
</tr>
<tr>
<td>CO</td>
<td>Hyperbaric O₂</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Digibind</td>
</tr>
<tr>
<td>Ethylene Glycol</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Heparin</td>
<td>Protamine</td>
</tr>
<tr>
<td>Iron</td>
<td>Desferrioxamine</td>
</tr>
<tr>
<td>Lead</td>
<td>Sodium calcium edentate</td>
</tr>
<tr>
<td>Methanol</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Opiates</td>
<td>Naloxone</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Atropine + pralidoxime</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>NAC</td>
</tr>
<tr>
<td>TCA</td>
<td>NaHCO₃ + O₂</td>
</tr>
<tr>
<td>Warfarin: major bleed</td>
<td>PCC + Vit K IV</td>
</tr>
</tbody>
</table>
# Revision

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**Prescribing Scenarios**

### Scenario 1

68 year old man with T2DM and hypertension is brought to the A&E department with AF which started less than 2 hours earlier. His ventricular rate is about 130/min. DC cardioversion is unsuccessful and he remains in hospital. He says he would prefer not to have a further attempt at the procedure. BP is consistently higher than 150/90 during the daytime. Electrolytes, creatinine, and thyroid function are normal. Fasting blood glucose is 7.9, fasting total cholesterol is 6.6, HDL cholesterol is 0.96 and TGs 3.4

**Answer**
- Metformin 500mg x1 daily c β breakfast
- Simvastatin 20mg x1 nocte
- Verapamil 80mg x3 daily
- Lisinopril 10mg x1 daily
- Warfarin 5mg x1 daily
  - Check INR on day 5 and adjust dose according to Tait Regimen, aiming for an INR of 2.5.

### Scenario 2

72 year old woman is admitted with a fractured neck of femur following a fall. She has successful surgery but despite appropriate prophylaxis develops a DVT in one calf. While she is being treated for this, she undergoes bone densitometry which reveals vertebral and femoral osteoporosis. She also has a lower UTI.

**Answer**
- Paracetamol 1g x4 daily
- Codeine phosphate 30mg every 4 hours as required
  - Maximum daily dose 240mg
- Enoxaparin 1.5mg/kg x1 daily SC until INR = 2.5
- Warfarin 5mg x1 daily
  - Check INR on day 5 and adjust dose according to Tait regimen, aiming for an INR of 2.5.
  - Continue warfarin for 6 weeks – 3 months.
- Alendronate 70mg x1 weekly
- Trimethoprim 200mg x2 daily for 7d

### Scenario 3

A 62-year-old man is admitted with a 3-day-history of increasing shortness of breath. On examination his temperature is 37.7 C, he has right lower lobe consolidation and also pitting oedema to his knees and JVP +6 cm. He is in sinus rhythm at 88 bpm and his BP is 133/76 mm Hg and oxygen saturation is 92%.

**Answer**
- Oxygen 4L via nasal cannula: aim for SpO₂ 94-98%
- Amoxicillin 500mg x3 daily for 7d
- Clarithromycin 500mg x2 daily for 7d
- Frusemide 40mg x1 daily

### Scenario 4

A 59-year-old woman presents with a several year history of increasing shortness of breath and a productive cough. She has a smoking history of at least 30 pack years but no other medical history. On examination of the chest there is widespread wheeze and coarse crackles cleared by coughing, but the sputum is very viscous though clear. Spirometry confirms a mixture of obstructive and restrictive abnormalities.

**Answer**
- Formoterol inhaler 12 micrograms x2 daily + extra doses for symptom relief (maximum total dose 48 micrograms daily)
- Carbocysteine 750mg x3 daily

### Scenario 5

73 year old woman is admitted with congestive heart failure. She has pitting oedema to the umbilicus and is almost immobile. Her BMI is 28 and BP is 121/65. On admission she is found to have a UTI, bacteriology results are awaited. Other investigations show creatinine 133, fasting Glucose 5.1, total cholesterol 4.8, HDL cholesterol 1.1. CXR confirms pulmonary congestion.

**Answer**
- Oxygen 4L via nasal cannula: aim for SpO₂ 94-98%
- Frusemide 40 mg IV x1 daily
- Lisinopril 2.5mg x1 daily
- Bisoprolol 1.25mg x1 daily
- Simvastatin 20mg x1 nocte
- Aspirin 75mg x1 daily
- Cephalexin 250mg x4 daily for 7 days
- Enoxaparin 40mg x1 daily SC until mobile
Scenario 6

A 73-year-old woman is admitted with a fractured neck of femur following a fall. She had been lying on the floor of her flat for at least 24 hours and was found to have a calf deep vein thrombosis and a lower urinary tract infection. There were no other abnormalities found on admission and she was not known to have any other illnesses before her accident. She has moderately severe pain and surgery is planned but for the moment she is not “nil by mouth”.

Answer
- Paracetamol 1g x4 daily
- Tramadol 50mg every 4 hours as required
  - Maximum daily dose 300mg
- Enoxaparin 1.5mg/kg x1 daily SC
  - **No warfarin before surgery**
- Trimethoprim 200mg x2 daily for 7d

Scenario 7

A 62-year-old man with type 2 diabetes and hypertension is admitted with a 3-day history of increasing cough and shortness of breath, and a temperature of up to 38.2°C. His BMI is approximately 31kg/m². On examination there are signs of right lower lobe consolidation. Blood pressure varies between 144/91 and 163/103 mm Hg. Electrolytes and creatinine are within the normal range. Random blood glucose is 14.3 mmol/L, fasting total cholesterol is 6.1 mmol/L, HDL cholesterol 0.96 mmol/L and triglycerides 3.4 mmol/L.

Answer
- Oxygen 4L via nasal cannula: aim for SpO₂ 94-98%
- Amoxicillin 500mg x3 daily for 7d
- Clarithromycin 500mg x2 daily for 7d
- Lisinopril 2.5mg x1 daily
- Nifedipine MR 20mg x1 daily
- Metformin 500mg x1 daily 6 breakfast
- Simvastatin 20mg x1 nocte
Prescriptions for Comment

Prescription 1

69 year old man has COPD with heart failure. He also has BPH with obstructive symptoms. He is admitted with an infective exacerbation of the COPD.

Bendroflumethazide 5mg OD
Bisoprolol 5mg OD
Ciprofloxacin 500 mg BD
Doxazosin 8mg OD
Enalapril 5mg OD
Ipratropium Bromide 40 ug QDS inhaled

Comments
- **Bendroflumethazide**
  - Not the preferred diuretic in heart failure. Switch to frusemide.
- **Bisoprolol**
  - High dose for heart failure. Titrate up slowly from 1.25mg OD.
  - COPD was considered a relative contraindication in COPD, but this is now controversial. A recent trial in the BMJ suggested that cardioselective β-blockers may be beneficial.
- **Ciprofloxacin**
  - Not the preferred choice for acute exacerbation of COPD. Switch to amoxicillin.
- **Doxazosin**
  - High dose for treatment of BPH. Either reduce to 2-4mg x1 daily or switch to tamsulosin which may be more effective.
- **Enalapril**
  - Dose is low. Gradually increase to 10-20mg BD if tolerated.
- **Ipratropium bromide**
  - May exacerbate BPH. Switch to formoterol inhaler.

Prescription 2

68 year old woman has PD for at least 5 years. She suffers a TIA affecting her speech and the right hand side of her face lasting about 6 hours. BP is 158/62 seated and 132/54 standing, in sinus rhythm. Total cholesterol is 7.8, HDL 1.2. She is not diabetic and her renal and liver function are normal. There is 60% stenosis of the left internal carotid and 15% of the right.

Aspirin 75mg OD
Atenolol 50mg OD
Clopidogrel 75mg OD
Co-careldopa 250/25 BD
Pravastatin 20mg OD

Comments
- **Aspirin and Clopidogrel**
  - TIA occurred despite aspirin and clopidogrel. The MATCH trial found that the combination of aspirin and clopidogrel was not beneficial in neurovascular disease and resulted in increased bleeding risk. Stop the clopidogrel and add dipyridamole MR. The NASCET and ECST trials demonstrated benefit of carotid endarterectomy in symptomatic patients with 50-69% stenosis if the operative risk is low. This option should be considered.
- **Atenolol**
  - Not the first line drug for the treatment of hypertension in patients over 55 years. In addition she demonstrates a significant postural drop. Switch her antihypertensive to nifedipine MR 20mg x1 daily.
- **Pravastatin**
  - Cholesterol is high despite treatment with pravastatin. Pravastatin has a relatively low potency and the dose is low. Switch to simvastatin 20mg x1 nocte.
- **Co-careldopa**
  - Dose is expressed incorrectly: dose of carbidopa should be given first: i.e. 25/250 x2 daily.
  - Dose is quite high and not well spaced out (L-DOPA has a short t½). In addition she has postural hypotension. Change regimen to 25/100 x3-4 daily.
Prescription 3
A 65-year-old man has COPD and permanent atrial fibrillation with mild heart failure. He is admitted with an infective exacerbation of the COPD.

Verapamil modified release 120 mg x 1 daily
Bisoprolol 5 mg x 1 daily
Clarithromycin 500 mg x 2 daily
Warfarin 4 mg x 1 daily (INR 2.8)
Lisinopril 20 mg x 1 daily
Furosemide 40 mg x 1 daily

Answer
- Bisoprolol
  - High dose for heart failure. Titrate up slowly from 1.25 mg OD.
  - COPD was considered a relative contraindication in COPD, but this is now controversial. A recent trial in the BMJ suggested that cardioselective β-blockers may be beneficial.
  - β-B + verapamil contraindicated
- Clarithromycin + Warfarin
  - Clarithromycin is a Cyp450 inhibitor. The dose of warfarin may need to be reduced
- Verapamil + Furosemide + Lisinopril
  - Multiple drugs with antihypertensive effects may result in hypotension.
- There is no specific COPD therapy.

Prescription 4
A 72-year-old woman has Parkinson’s disease and develops nausea on initiation of treatment. She has had isolated systolic hypertension for at least 5 years. A few weeks later she develops distressing visual hallucinations. Her blood pressure is 117/62 mm Hg seated and 98/55 mm Hg standing.

Co-careldopa 250/25 1 tablet x 4 daily
Metoclopramide 10 mg x 3 daily
Prochlorperazine 5 mg x 1 at bedtime
Irbesartan 150 mg x 1 daily

Answer
- Co-careldopa
  - Dose is expressed incorrectly: dose of carbidopa should be given first: i.e. 25/250 x 2 daily.
  - Dose is quite high. In addition she is experiencing hallucinations and has postural hypotension. Reduce dose: e.g. 25/100 x 3-4 daily.
- Irbesartan
  - Dose is high and isn’t first line antihypertensive in this age. May not even be necessary at all given her blood pressure.
- Metoclopramide and prochlorperazine
  - Unnecessary to be on two anti-emetics and both are dopamine antagonists that cross the BBB and will worsen her parkinsonian symptoms. Stop them both and use domperidone to control her nausea.
  - If her psychiatric symptoms persist after the dose of co-careldopa has been reduced, 1st line treatment would be an atypical anti-psychotic, such as quetiapine.
## Useful Drugs to Know

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>500mg TDS PO</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500mg BD PO</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>200mg BD PO</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>1.2g TDS IV</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20mg OD nocte PO</td>
</tr>
<tr>
<td>Nifedipine MR</td>
<td>20mg OD PO</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>HTN: 10mg OD PO</td>
</tr>
<tr>
<td></td>
<td>HF: 2.5mg OD PO</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>HF: 1.25mg OD PO</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>1g QDS PO</td>
</tr>
<tr>
<td>Codeine Phosphate</td>
<td>30mg every 4h PRN PO</td>
</tr>
<tr>
<td></td>
<td>Max 240mg daily</td>
</tr>
<tr>
<td>Tramadol</td>
<td>50mg every 4h PRN PO</td>
</tr>
<tr>
<td></td>
<td>Max 300mg daily</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Treatment: 1.5mg/kg/24h SC</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis: 40mg OD SC</td>
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