Anti-Arrhythmics and antihypertensives
Curriculum

- **PR_BK_46**  
  Antiarrhythmics: Classification. Indications for use, including use in resuscitation

- **PB_BK_40**  
  Rhythmicity of the heart; cardiac impulse generation

- **PR_BK_47**  
  Hypotensive agents: Classes of drugs to produce acute hypotension in theatre. Therapeutic antihypertensive agents: classification according to mechanism of action. Adverse effects of drugs.
Physiology

- Cardiac myocytes are electrically excitable

- Resting intracellular potential -90mV
Physiology

• **Action potential** occurs when $\text{Na}^+$ enters the cell and sets up a depolarising current

• Stimulation of a single muscle fibre causes electrical activity to spread across the myocardium
Action potential of cardiac myocyte

- **Phase 0** rapid depolarisation (inflow of Na$^+$)
- **Phase 1** partial repolarisation (inward Na$^+$ current deactivated, outflow of K$^+$)
- **Phase 2** plateau (slow inward calcium current)
- **Phase 3** repolarisation (calcium current inactivates, K$^+$ outflow)
- **Phase 4** Na/K ATPase restores ion gradients. Pacemaker potential due to slow Na$^+$ inflow (autorhythmicity)

- **Refractory period** (phases 1 to 3)
  - Absolute
  - Relative
Sinus rhythm

- SA node – pacemaker
- SAN depolarisation $\rightarrow$ atrial depolarisation (P-wave)
- Slow conduction through AV node (P-R interval)
- Rapid conduction through His bundles and Purkinje fibres (QRS)
- Repolarisation (R-wave)
Pacemaker cells (SAN, AVN)

- Depolarisation due mainly to slow Ca$^{2+}$ influx
- No fast Na$^+$ channels
- Resting potential -60mV (SAN)
- Phase 4: slow Na$^+$ influx ("funny" currents - $I_f$) → transient (T-type) Ca$^{++}$ channels open → further depolarisation
- At -40mV L-type, voltage-gated Ca$^{2+}$ channels open → full membrane depolarisation → action potential
- K$^+$ outflow & closure of Ca$^{2+}$ channels → repolarisation
Classification of arrhythmias

Site of origin: Atrial
  Junctional
  Ventricular

Rate: Bradycardia (< 60/minute)
  Tachycardia (> 100/minute)
Mechanisms of arrhythmia

Abnormal impulse generation
(abnormal or ectopic pacemaker activity)

• ‘Enhanced Automaticity’

• Non-conducting or conducting tissue

• Increased rate of spontaneous depolarisation in affected cells → more rapid rate of discharge than SA node

• Often seen in ischaemia and hypokalaemia
Mechanisms of arrhythmia

Abnormal impulse conduction (Re-entry)
- Circuit may be in atria, ventricles or AV node
- May be due to myocardial ischaemia or damage
- May involve accessory pathway as one limb (WPW)
- Re-entry when transient or unidirectional conduction block occurs
Mechanisms of arrhythmia

Abnormal impulse conduction

- Atrial fibrillation due to multiple, atrial re-entrant circuits
- Re-entry responsible for sustained VT
Classification of antiarrhythmic drugs

- **Electrophysiological action** - Vaughan Williams

- **Site of action** - atrial or ventricular

- **Sicilian Gambit** – Vulnerable parameter (excitability, conduction, refractory period) and target of treatment \((\text{Na}^+, \text{K}^+, \text{Ca}^{2+} \text{ channels})\)
Vaughan Williams Classification

• Based on action of drug on cardiac action potential
• Physiological classification
• In use for over 30 years
• Simple to understand and use (too simple?)
• Excludes digoxin, adenosine, atropine, magnesium
• Some drugs (amiodarone) in more than 1 class
**Vaughan Williams Classification**

- **Class I: Sodium channel blockers**
  - inhibit sodium influx during phase 0
  - reduce rate of depolarisation
    - Ia (quinidine, procainamide, disopyramide) \( \uparrow \) AP
    - Ib (lignocaine) \( \downarrow \) AP
    - Ic (flecainide) \( \leftrightarrow \) AP

- **Class II: Beta Blockers**

- **Class III: K+ channel blockers**
  - prolong action potential and prolong refractory period (suppress re-entrant rhythms)
    - amiodarone, sotalol

- **Class IV: Calcium channel antagonists.**
  - slow impulse propagation in nodal and damaged areas (verapamil)
Class IA
Procainamide/ Quinidine/ Disopyramide

• **Mode of action:**
  – Na\(^+\) Channel Blockers (prolong AP)
  – Depress conduction and **prolong refractoriness**
  – Atrial, His/Purkinje, ventricular tissue
  – Act on re-entry and enhanced automaticity mechanisms

• **ECG changes:**
  – PR, QRS, QTc

• **Adverse and other effects:**
  - Local anaesthetic, myocardial depression, vagolytic, anticholinergic (disopyramide, quinidine), lupus (procainamide)
  - Prolonged QT → torsade de pointes (avoid quinidine if QT > 400ms)

• **Uses:**
  – Rarely used because of side effects
  – Atrial or ventricular arrhythmias
  – Procainamide safe in AF due to WPW syndrome
Class IB
Lidocaine/ Mexiletine/ Phenytoin

- **Mode of action**
  - Na\(^+\) Channel Blockers (shorten AP)
  - **Shorten refractory period**
  - Action on Purkinje Cells (little action on other cardiac cells)
    - \(\downarrow\) enhanced automaticity
    - Increases VF threshold
- **ECG changes**
  - Slight \(\downarrow\) QTc (Lidocaine/Phenytoin)
  - *Used in congenital long QT syndromes (Mexiletine)*
- **Adverse effects**
  - Lignocaine toxicity - drowsiness, convulsions
  - Hepatic clearance of lignocaine – reduce dose in hepatic disease, CCF, cardiogenic shock
  - Hypotension/ bradycardia only in high dosage
- **Uses:**
  - Effective and safe
  - Ischaemia-induced arrhythmia with automaticity (post-MI VT)
  - Not effective in re-entry and atrial tachycardias.
  - Digoxin toxicity (lidocaine, phenytoin)
Class IC
Flecainide/ Propafenone/ Ethmozine

• **Mode of action:**
  - Na\(^+\) Channel Blockers (no effect on AP)
  - ↓ abnormal automaticity
  - Slow conduction in all cardiac cells

• **ECG changes**
  - PR, QRS
  - QTc → toxicity

• **Adverse effects**
  - Pro-arrhythmic (sudden death due to VF after MI)
  - Myocardial suppression

• **Uses:**
  - Atrial and ventricular arrhythmias (ventricular ectopics, PAF, paroxysmal SVT)
  - Rarely used because of side effects
Class II Agents
Beta-blockers – Esmolol, Sotalol

• Mode of action:
  – Suppress phase 4 depolarisation & prolong phase 4
  – Slow AV conduction
  – Sotalol also class III
  – Esmolol is cardioselective, short acting, metabolized by red cell esterases.

• Uses:
  - Effective in arrhythmias induced or exacerbated by sympathetic activity
  – Abolish re-entry and automaticity
  – Atrial and ventricular arrhythmias - reduce arrhythmia post MI
  - Sotalol useful in paroxysmal AF and life-threatening ventricular arrhythmias

• Side effects:
  - Bradycardia, fatigue, myocardial suppression, exacerbate heart failure
  – Bronchoconstriction (even cardioselective agents)
Class III

K⁺ - channel blockers: Amiodarone, Sotalol, Bretylium

- **Mode of Action:**
  - Potassium Channel Blockade
  - Prolonged repolarisation and action potential
  - Other effects: Class Ia and II activity, calcium channel blockade

- **ECG changes:**
  - Prolonged QT

- **Adverse effects:**
  - Negligible haemodynamic effects
  - Torsade de pointes (prolonged QT)

- **Uses:**
  - Very effective antiarrhythmics
  - Amiodarone is a first-line agent for a broad spectrum of ventricular and atrial arrhythmias (AF, SVT, VF, VT, WPW syndrome)
  - Amiodarone recommended for shock-refractory VF (UKRC)
  - Acute treatment/ prophylaxis
Amiodarone

- \( t_{1/2} \) 30-110 days – accumulates, loading dose required
- Large volume of distribution
- Hepatic metabolism- biliary and intestinal excretion

- Photosensitive rashes
- Grey/blue discolouration of skin
- Thyroid abnormalities 2%
- Pulmonary fibrosis
- Corneal deposits
- CNS/GI disturbance
- Torsade de pointes
- Heart block
- Nightmares 25%
- Abnormal LFT 20%
- Interacts with digoxin, warfarin (reduces clearance)
- Phlebitis via peripheral veins
Class IV
Ca\textsuperscript{2+} Channel Blockers: Verapamil, diltiazem

• **Mode of Action:**
  – Ca\textsuperscript{2+} channel blockade
  – Prolongs conduction and refractoriness in AV node
  – Slows rate of conduction of SA node

• **Use:**
  – Supraventricular arrhythmias only
  – Ineffective and dangerous in ventricular arrhythmias
  – Interrupts re-entry in paroxysmal SVT involving AV node
  – Acute treatment /prophylaxis
  – IV/oral

• **Side effects:**
  – May precipitate VF in WPW syndrome
  – Do not use IV verapamil with β- blocker (heart block)
  – Bradycardia
  – Heart failure
  – Grapefruit juice increases serum levels
Digoxin

- Cardiac glycoside (digitalis, foxglove)
- Inhibits Na\(^+\)/K\(^+\) pump in myocardial cell membrane → intracellular Na\(^+\) and Ca\(^{2+}\)
- Positive inotrope
- Increases vagal activity
- Slows AV conduction by increasing AV node refractory period and vagal effect
- Shortens refractory period and increases automaticity in atria and ventricles
Action of Digoxin
Digoxin

- AF or flutter (for ventricular rate control)
- \( t_{1/2} \) 36 hours (loading dose needed)
- Renal excretion
- Narrow therapeutic index – (plasma level 1-2ng/ml)
- Therapeutic drug monitoring required
- Reduce dose in elderly/renal impairment
Digoxin – adverse effects

- Arrhythmias if levels high (bigemini, VT, VF)
- AV block
- Anorexia, nausea, diarrhoea
- Xanthopsia,
- Gynaecomastia,
- Confusion, agitation
Digoxin – adverse effects

• Adverse cardiac effects potentiated by hypokalaemia and hypomagnesaemia

• Overdose:
  - Digibind (digoxin binding antibody fragments)
  - Lidocaine, phenytoin for ventricular arrhythmias,
  - Pacing, atropine for bradycardia, AVB
Adenosine

- Purine nucleotide (activates adenosine (A1) receptors)
- Slows AV nodal conduction
- Used in termination of SVT/ diagnosis of narrow-complex tachyarrhythmias
- Rapid IV bolus (6mg, 12mg, 12mg)
- Short $t_{1/2}$. Effects last 20-30 seconds
- Taken up by RBCs and metabolised by enzymes on vascular endothelium
Adenosine - adverse effects

- Feeling of impending doom!
- Flushing, dyspnoea, chest pain
- Transient arrhythmias – prolonged bradycardia
- Contraindicated in asthma, heart block
- Heart transplant recipients very sensitive – $\frac{1}{2}$ dose
- Theophyllines inhibit action (block A1 receptor)
- Dipyridamole prolongs action (blocks uptake)
Other anti-arrhythmics

Magnesium sulphate
• Used in life-threatening arrhythmias associated with hypokalaemia or hypomagnesaemia
• Effective in torsade de pointes
• 2g (8mmol Mg\(^{2+}\)) by slow IV injection
• Large doses $\rightarrow$ hypotension, respiratory depression, muscle weakness, coma

Atropine
• Blocks M2 muscarinic receptors in heart (antivagal)
• SA node rate, AV node conduction
• Used in symptomatic bradycardia - 0.5mg IV
• No longer recommended for routine use in asystole or PEA (2010)
• Side effects unimportant in management of acute arrhythmias
### Classification by site of action

More useful clinically

<table>
<thead>
<tr>
<th>Supraventricular</th>
<th>Ventricular</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Digoxin</td>
<td>- Lignocaine</td>
<td>- Amiodarone</td>
</tr>
<tr>
<td>- Adenosine</td>
<td>- Mexilitine</td>
<td>- Sotalol</td>
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<tr>
<td>- Verapamil</td>
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<td>- Flecainide</td>
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<tr>
<td>- B-Blockers</td>
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<td>- Procainamide</td>
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<tr>
<td>- Quinidine</td>
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<td>- Disopyramide</td>
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<td>- Propafenone</td>
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</table>
Management of arrhythmias

Treat the patient, not the rhythm

• **Cardiovascular compromise:**
  
  Hypotension
  Myocardial ischaemia
  Cardiac failure
  Organ hypoperfusion

• **Risk of deterioration**
  
  Extreme bradycardia or tachycardia
  2\textsuperscript{nd} or 3\textsuperscript{rd} degree heart block
Management of arrhythmias

• **Treat the cause:**  
  \[ \downarrow K^+, \downarrow Mg^{2+} \]
  - Ischaemia
  - Hypoxia
  - Heart failure
  - Hypotension
  - Acidosis
  - Thyrotoxicosis

• **Physical methods:**  
  - Defibrillation/ cardioversion
  - ICD
  - Pacing/ overdrive
Treating acute arrhythmias

AV nodal re-entrant tachycardia
• Vagal manouevres (carotid sinus massage, valsalva)
• Adenosine 6mg, 6mg, 12mg IV (terminates AVNRT in 90%)
• Verapamil 5-10mg IV slowly (beware side effects)
• Beta-blocker

Atrial flutter
• DC cardioversion (anticoagulate if duration > 48 hours)
• If stable, ventricular rate control (B-blocker, digoxin, verapamil, diltiazem)
Treating acute arrhythmias

Acute atrial fibrillation

- DC cardioversion if unstable
- Pharmacological cardioversion (amiodarone) if resistant to DCC or if haemodynamically stable

- Rate control if stable or duration > 48 hours (diltiazem, esmolol, digoxin)

- Consider anticoagulation prior to electrical or pharmacological cardioversion, if AF > 48 hours duration
Treating acute arrhythmias

**Arrhythmias in WPW syndrome**

- AF or A.flutter may → V. rapid ventricular response due to conduction through accessory pathway
- Agents which slow AVN conduction will not slow ventricular response (verapamil, diltiazem, digoxin, beta-blockers)
- Digoxin and verapamil may accelerate ventricular response and precipitate VF
- DC cardioversion indicated
- Use drugs which slow accessory pathway conduction – amiodarone, flecainide, disopyramide, procainamide
Treating acute arrhythmias

**Ventricular tachycardia**
- If associated with cardiac arrest – defibrillation
- If cardiac output maintained – DC cardioversion
- For shock-resistant VT – amiodarone 300mg + 900mg/24 hours
- If haemodynamically stable – amiodarone (sotalol, flecainide, lignocaine are alternatives)

**Torsade de pointes**
- Magnesium sulphate 2g IV
- Beta-blocker (not sotalol) in congenital prolonged QT syndrome
- Overdrive pacing
- Defibrillation if associated with cardiac arrest
Treating acute arrhythmias

Ventricular fibrillation

- Defibrillation

- Amiodarone if shock-resistant (following 3rd shock) – 300mg IV

- Lignocaine if amiodarone not available (not if amiodarone already given) – 1-1.5mg/kg
Remember!

Antiarrhythmics can cause arrhythmias
- Torsade de Pointes (Class 1a > 1c > Class III)
- Bradycardias (adenosine, amiodarone, B-blocker, verapamil, digoxin)

Antiarrhythmics may cause/exacerbate hypotension or heart failure
- All classes except amiodarone and digoxin

Treat the patient rather than the arrhythmia
- Is the patient compromised by the rhythm?

Treat precipitating factors
- Electrolyte abnormalities, ischaemia, hypoxia

Consider non-pharmacological methods
- Electrical cardioversion
- Pacing/overdrive pacing
MCQs

- With regard to antiarrhythmic agents:
  A. Class I drug block sodium channels
  B. Class III drug prolong the refractory period of the myocardium
  C. Lidocaine belongs to class I
  D. B-Blockers belong to more than one group
  E. Class I drugs have a wide variety of clinical applications.
With regard to antiarrhythmic agents:

A. Class I drug block sodium channels — True
B. Class III drug prolong the refractory period of the myocardium — True
C. Lidocaine belongs to class I — True
D. B-Blockers belong to more than one group — True
E. Class I drugs have a wide variety of clinical applications. — True
• Digoxin toxicity
  A. Is associated with ventricular bigemini
  B. May be alleviated by giving Calcium
  C. May be partly controlled by giving B-blocker
  D. Is more likely to occur in hypokalaemia
  E. Is unlikely to occur at concentrations <2ng/ml
Digoxin toxicity

A. Is associated with ventricular bigemini  T
B. May be alleviated by giving Ca  F
C. May be partly controlled by giving B-blocker  F
D. Is more likely to occur in hypokalaemia  T
E. Is unlikely to occur at concentrations <2ng/ml  T

Therapeutic range 1-2ng/ml
Toxicity most arrhythmias: junctional bradycardia and ventricular bigemini common
Hypokalaemia, hypernatraemia, hypercalcaemia and hypomagnesia increase toxicity
Beta blockers should be avoided
phenytoin, lidocaine and digibInd
• Drugs used in the treatment of paroxysmal SVT include:
  A. Verapamil
  B. Nifedipine
  C. Mexilitine
  D. Lidocaine
  E. Propranolol
• Drugs used in the treatment of paroxysmal SVT include:

  A. Verapamil  
  B. Nifedipine  
  C. Mexilitine  
  D. Lidocaine  
  E. Propranolol

Mexilitine and Lidocaine used in treatment of VT
• Flecainide:
  A. Is indicated in Supraventricular arrhythmias
  B. Increases QRS duration
  C. May be given orally
  D. Is a negative inotrope
  E. As a bolus the dose is 20-30mg/kg
• Flecainide:
  A. Is indicated in Supraventricular arrhythmias  T
  B. Increases QRS duration  T
  C. May be given orally  T
  D. Is a negative inotrope  T
  E. As a bolus the dose is 20-30mg/kg  F

As a bolus 2mg/kg is given by slow IV infusion over 10-30 mins
• Class I anti-arrhythmic drugs:
  A. May prolong the cardiac action potential
  B. May shorten the cardiac action potential
  C. May have no effect on the cardiac action potential
  D. Include B-Blockers
  E. Potentiate fast sodium current
• Class I anti-arrhythmic drugs:
  A. May prolong the cardiac action potential  T
  B. May shorten the cardiac action potential  T
  C. May have no effect on the cardiac action potential  T
  D. Include B-Blockers  F
  E. Potentiate fast sodium current  F

Are Na channel BLOCKERS
  1a prolong AP  T
  1b shorten AP  F
  1c no effect  F

Beta blockers are Class II
Antihypertensive Drugs
Definition of hypertension: NICE 2011

- **Stage 1 hypertension** Clinic blood pressure is 140/90 mmHg or higher and subsequent ambulatory daytime average 135/85 mmHg or higher.

- **Stage 2 hypertension** Clinic blood pressure is 160/100 mmHg or higher and subsequent ambulatory daytime average is 150/95 mmHg or higher.

- **Severe hypertension** Clinic systolic blood pressure is 180 mmHg or higher, or clinic diastolic blood pressure is 110 mmHg or higher.
• Beta-blockers may be considered for younger people if ACEI and ARBs are contraindicated or not tolerated or there is evidence of increased sympathetic drive, and for women of child-bearing potential.

• If calcium channel blocker not suitable (oedema, intolerance), or if there is evidence or high risk of heart failure, offer a thiazide-like diuretic.
Drugs for hypertension

• Angiotensin Converting Enzyme Inhibitors (ACEI)

• Angiotensin II Receptor Blockers (ARB)

• Calcium Channel Blockers

• Thiazide diuretics

• Beta blockers

• Alpha blockers

• Miscellaneous (hydralazine, methyldopa, clonidine)
## ACEIs and ARBs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Actions</th>
<th>Side effects</th>
</tr>
</thead>
</table>
| **ACEI**  
  Captopril  
  Enalopril  
  Lisinopril  
  Perindopril | ACE inhibition  
  Blocks conversion of angiotensin I to angiotensin II  
  Inhibits breakdown of bradykinin | Dry cough (↓ bradykin breakdown)  
  Loss of taste  
  Rashes  
  Agranulocytosis  
  Renal failure (RAS, NSAIDs, hypovolaemia)  
  Hyperkalaemia (K-sparing diuretics, CRF)  
  Hypotension (diuretics, GA, spinal/epidural)  
  Angioedema (delayed, resistant) |
| **ARBs**  
  Losartan,  
  Valsartan,  
  Candesartan | Block AT$_1$ receptor  
  No action on ACE | Similar to ACEIs  
  Cough rare (bradykinin unaffected)  
  Angioedema rare, but reported |
## Calcium channel blockers

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Actions</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dihydropyridines</strong></td>
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<tr>
<td>Nifedipine</td>
<td>Competitive block of slow Ca(^{++}) channels in vascular smooth muscle $\rightarrow \downarrow$ intracellular Ca(^{++})</td>
<td>Reflex tachycardia, Headache, flushing, dizziness, Oedema</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Coronary and peripheral vasodilatation</td>
<td>Hypotension with GA (volatile agents $\downarrow$ intracellular Ca(^{++}))</td>
</tr>
<tr>
<td>Lacidipine</td>
<td></td>
<td>$\downarrow$ MAC, effect of NMBs</td>
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<tr>
<td>Felodipine</td>
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<tr>
<td><strong>Non-dihydropyridines</strong></td>
<td>Block Ca(^{++}) channels in vascular smooth muscle, myocardium, cardiac conducting tissue</td>
<td>As for dihydropyridines</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Coronary/ peripheral vasodilatation</td>
<td>Bradycardia, Heart block (verapamil)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Negative inotropy/ chronotropy</td>
<td>Heart failure, Bradycardia, hypotension with GA</td>
</tr>
<tr>
<td></td>
<td>Class IV antiarrhythmic (verapamil)</td>
<td>Caution with $\beta$-blockers, Digoxin levels (diltiazem)</td>
</tr>
</tbody>
</table>
### Thiazide diuretics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Actions</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bendroflumethiazide</td>
<td>Thiazide diuretics</td>
<td>Hyponatraemia</td>
</tr>
<tr>
<td></td>
<td>Inhibit Na+ reabsorption in distal convoluted tubule → diuresis</td>
<td>Hypokalaemia</td>
</tr>
<tr>
<td>Clortalidone (tenoret, tenoretic)</td>
<td></td>
<td>Hypomagnesaemia</td>
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<tr>
<td>Indapamide</td>
<td>Vasodilators</td>
<td>Hypercalcaemia</td>
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<tr>
<td>Hydrochlorthiazide (with ACEI, ARB)</td>
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<td>Postural hypotension</td>
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<td>Impaired diabetic control</td>
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<td></td>
<td></td>
<td>Hyperuricaemia/ gout</td>
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<td>Rashes</td>
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<td></td>
<td></td>
<td>Excerbate renal failure</td>
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<tr>
<td>Drug</td>
<td>Actions</td>
<td>Side effects</td>
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<tr>
<td><strong>Cardioselective</strong></td>
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<tr>
<td>Atenolol</td>
<td>Competitive block of cardiac $\beta_1$ and $\beta_2$ adrenoceptors</td>
<td>Cold peripheries (PVD)</td>
</tr>
<tr>
<td>Bisoprolol</td>
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<td>Bronchospasm</td>
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<tr>
<td>Metoprolol</td>
<td>Negative inotropy</td>
<td>Impaired diabetic control</td>
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<tr>
<td>Nebivolol</td>
<td>Negative chronotropy</td>
<td>↓ signs of hypoglycaemia</td>
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<tr>
<td></td>
<td>Anti-arrhythmic (class II)</td>
<td>Fatigue, impotence</td>
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<td></td>
<td>Alter baroreceptor sensitivity</td>
<td>Sleep disturbance</td>
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<td></td>
<td>May have central effects</td>
<td>Heart failure (rare)</td>
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<td></td>
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<td>Bradycardia/ heart block</td>
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<tr>
<td><strong>Non-cardioselective</strong></td>
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<tr>
<td>Propranolol</td>
<td>As above</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td>action at non-cardiac $\beta$-receptors</td>
<td>Heart failure/ heart block</td>
</tr>
<tr>
<td></td>
<td>Membrane stabiliser</td>
<td>Bronchospasm and vasoconstriction more likely</td>
</tr>
<tr>
<td><strong>Intrinsic sympathetic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>activity</td>
<td>Partial agonists at $\beta$-receptor</td>
<td>May cause less peripheral vasoconstriction and bradycardia</td>
</tr>
<tr>
<td>Oxprenolol</td>
<td></td>
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<tr>
<td>Pindolol</td>
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<tr>
<td>Acebutalol</td>
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Beta-blockers

- Numerous studies show improved perioperative morbidity and mortality in patients with ischaemic heart disease

- Importance of continuing beta-blockade perioperatively is indisputable

- Perioperative Ischemic Evaluation (POISE) (2008)

  Large randomized trial of metoprolol started immediately before noncardiac surgery in patients at high risk for atherosclerotic disease

  Significantly reduced myocardial infarctions
  Significant increases in stroke and mortality
## Other antihypertensives

<table>
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<tr>
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<tbody>
<tr>
<td><strong>α₁-blockers</strong></td>
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<tr>
<td>Doxazosin</td>
<td>α₁-adrenoceptor antagonists</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Prazosin</td>
<td>Arterial and venous dilatation</td>
<td>Postural hypotension (1\textsuperscript{st}-dose)</td>
</tr>
<tr>
<td>Phenoxybenzamine</td>
<td>Use in phaeochromocytoma</td>
<td>Tachycardia + oedema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nasal congestion</td>
</tr>
<tr>
<td><strong>Hydralazine</strong></td>
<td>Direct peripheral vasodilator</td>
<td>Lupus syndrome (acetylator status)</td>
</tr>
<tr>
<td></td>
<td>Use in pregnancy, PET</td>
<td>Tachycardia + oedema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flushing, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypotension (care with GA)</td>
</tr>
<tr>
<td><strong>Methyldopa</strong></td>
<td>Central α₂ agonist</td>
<td>Postural hypotension, oedema, bradycardia, sedation, depression, dizziness, rash, haemolytic anaemia</td>
</tr>
<tr>
<td></td>
<td>↓ Central sympathetic discharge</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vasodilatation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Use in pregnancy, PET</td>
<td></td>
</tr>
<tr>
<td><strong>Clonidine</strong></td>
<td>Central α₂ agonist</td>
<td>Slight in BP initially (IV): α1 effect</td>
</tr>
<tr>
<td></td>
<td>↓ Central sympathetic discharge</td>
<td>Sedation (ICU sedative, ↓ MAC)</td>
</tr>
<tr>
<td></td>
<td>Vasodilatation</td>
<td>Rebound hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bradycardia</td>
</tr>
</tbody>
</table>
Peri-operative complications of hypertension

- Labile BP - increased response to laryngoscopy, risk of hypotension,
- Increased CVS morbidity and mortality: OR 1.3, CI 1.1-1.6 (Howell 2004)
- Myocardial ischaemia/ infarction
- Acute LVF
- Acute arrhythmia
- Cerebral haemorrhage/ infarction
- Renal failure

- Problems more likely in untreated hypertensives
- Treated hypertensives less labile
Pre-operative assessment

- Is the patient known to be hypertensive?
- Are they on antihypertensive medication?
- Is there a treatable cause for hypertension?
- Is this “white coat” hypertension?
- Is there evidence of end-organ damage
- Are there side effects from treatment?
- Should treatment be initiated/changed before surgery?
Pre-operative management

• Elective cases should receive regular medications on morning of surgery

• ACEI usually continued prior to anaesthesia. Consider stopping if major haemorrhage anticipated or using regional techniques such as epidurals

• If surgery cannot be postponed, consider single dose of atenolol pre-operatively
When is pre-operative treatment required?

- SBP>180mmHg or DBP>110mmHg
- SBP 160-179 or DBP 100-109, plus target organ involvement (coronary, renal, cardiovascular)
- Treatment optional for mild hypertension: SBP 140-159mmHg, DBP 90-99mmHg
- “White coat” hypertension not proven to increase risk. Repeat measurement
- Elderly patients with SBP< 180-190 mmHg should be considered for surgery, particularly if there is little evidence of end organ damage
- Adequate period of treatment before elective surgery ‘days to weeks’.
- Single pre-operative dose of atenolol may be effective, but also some evidence of morbidity from rapid control of BP with nifedipine)
Intra-operative hypertension

- Exclude and treat reversible causes: depth of anaesthesia, analgesia (remifentanil)
- Labetolol - Combined α and β-blocker (1:3 ratio). Rapid onset. Mean duration 45 minutes. 5-20mg boluses IV, titrated to response
- GTN – Nitric oxide donor. Rapid onset and short duration. Infusion 100-400mcg/min.
- Phentolamine – Competitive α –blocker. Useful in peri-operative control of phaeochromocytoma. 2-5mg IV bolus.
- Beta-blockers. Esmolol: infusion 50-150mcg/kg/min. Atenolol: 1mg/min IV up to 10mg. Metoprolol: 1mg/min IV up to 10mg.
- Hydralazine: 5-10mg, repeated after 20 minutes (infusion)
Bibliography: antihypertensives