Beta blockers

**Types**

Selective
- $\beta_1$ (e.g. atenolol, bisoprolol, metoprolol, carvedilol, timolol)
- $\beta_2$ (e.g. butoxamine) – not used therapeutically

Non-selective (e.g. propranolol)

Other classifications:
- **Lipid solubility**: propranolol $>$ atenolol
- **Route of elimination**: atenolol = renal, propranolol = hepatic
- **Speed of elimination**
  - Atenolol – long half-life, od dosing
  - Propranolol – short half-life, bd/tds dosing
  - Esmolol – ultra-short half-life (9 min), need to give by continuous infusion
- **Intrinsic sympathomimetic activity**
  - Acebutolol, oxprenolol, pindolol

**Indications**

Chronic
- **Cardiovascular**
  - Angina: first line after GTN
  - MI: first line after event and for secondary prophylaxis
  - HT: first line if concomitant IHD or angina
  - Heart failure: traditionally accepted as CI because of negative inotropic effect. However, recent trials have demonstrated survival benefit (CIBIS, CIBIS-II, MDC, USCHFTP) for certain agents (bisoprolol, metoprolol, carvedilol). Note: start on very low dose, very gradual dose escalation, patients may get worse before they get better and many will not tolerate even a gentle regime.
  - Arrhythmias: esp. rate control in AF; prophylaxis and treatment
- **CNS**
  - Anxiety: propranolol for GAD and panic disorder. Symptomatic treatment, should be supplemented with psychotherapy to address underlying problems.
  - Migraine: propranolol is first-line in prophylaxis, together with pizotifen, a 5-HT$_2$ antagonist. Treat for 3-6 months and attempt withdrawal, which often leads to prolonged remission.
  - Tremor: propranolol for essential tremors
- **Eye**
  - Glaucoma: topical timolol is a first-line agent in acute angle closure glaucoma.
- **Endocrine**
  - Hyperthyroidism: propranolol inhibits peripheral T$_4$ de-iodination and provides immediate symptomatic relief. Used in chronic hyperthyroidism to supplement anti-thyroid medication, and acutely as below.
  - Phaeochromocytoma: after $\alpha$-blockade

Acute
- Akathisia: give propranolol.
- Hyperthyroidism: thyroid operations/crisis
- Malignant HT

**Adverse effects and their basis**

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<tr>
<th>Contraindications</th>
<th>Adverse effects</th>
<th>Pharmacological basis</th>
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<tbody>
<tr>
<td>Asthma, COPD (even if $\beta_1$-selective/’cardioselective’, or topical for glaucoma)</td>
<td>Bronchoconstriction</td>
<td>Block of bronchodilatory $\beta_2$-receptors</td>
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Heart failure (if acute, or β-blocker intolerant) | Bradycardia, hypotension: common but rarely symptomatic; heart block | Negatively chronotropic and inotropic effects
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PVD | Peripheral vasoconstriction, Raynaud’s phenomenon | Block of vasodilatory β₂-receptors (no β₁-receptors in periphery)
Hyperkalaemia | Block β-dependent K⁺ transport into cells (converse for salbutamol)

Pregnancy | Stillbirth, IUGR | ?
Breastfeeding – can affect infant (atenolol and sotalol excreted in greater amounts into milk)

Depression | Malaise, fatigue, vivid dreams, nightmares, hallucinations (esp. with lipid-soluble agents such as propranolol) | Outflow from locus coeruleus to cortex, thalamus and limbic system is important in controlling mood and motivation.
Worsened glucose tolerance | Masking of hypoglycaemia (esp. non-selective agents) | Many are sympathetically mediated.
Increase in lipids | ?

**Management of beta-blocker overdose**

**Clinical features**

<table>
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<th>CV</th>
<th>Bradycardia, heart block, hypotension, low cardiac output heart failure/cardiogenic shock</th>
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<tr>
<td>RS</td>
<td>Severe bronchospasm in patients with asthma</td>
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<tr>
<td>CNS</td>
<td>Loss of consciousness with lipid soluble agents</td>
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Seen 5min after administration, last approx. 6h (atenolol).

**Treatment**

- Atropine (to remove all vagal tone)
- If no effect: glucagon 1mg slow IV injection; can be repeated twice or followed by infusion (physiological antagonism)
- Isoprenaline infusion: 10mg/500ml, 0.5-20μg/min (high doses to overcome block)
- Cardiac pacing
- Salbutamol for bronchospasm (consider if wheeze may be cardiac)