ADRENALINE (Intravenous, intramuscular and endotracheal)

SCOPE (Area): FOR USE IN: Critical Care Unit, ED and Theatre
EXCLUSIONS: Paediatrics (seek Paediatrician advice) and General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES
No brand names.

PHARMACOLOGY AND PHARMACOKINETICS
Adrenaline is a naturally occurring sympathomimetic agent acting as a nonselective agonist at adrenergic receptor sites. Adrenaline is a positive inotrope and chronotrope (beta_1 receptors); vasodilator at low doses (beta_2 receptors); vasoconstrictor at high doses (alpha receptors); bronchial smooth muscle relaxant (beta_2 receptors) and stabilises mast cells. Adrenaline also mobilises liver glycogen resulting in hyperglycaemia and possibly glycosuria. It has a rapid onset of action, a short duration of action and fast elimination when the infusion is ceased due to the short half-life of 2 minutes. Adrenaline is predominantly metabolised by monoamine oxidase (MAO) and catechol-o-methyl transferase (COMT) in the liver and tissues. Sodium metabisulfite or sodium bisulfite is present as a preservative.

INDICATIONS
- Anaphylaxis.
- Cardiac arrest including ventricular fibrillation, pulseless ventricular tachycardia, asystole and electromechanical dissociation.
- Hypotension – as an inotrope.
- Bradycardias - as a chronotrope.
- Bronchospasm and laryngeal spasm causing respiratory distress.
- Life threatening angioneurotic oedema.
- Inotropic support in acute heart failure and cardiogenic shock, acute exacerbation of chronic heart failure, septic shock.
- Other indications of adrenaline are not covered by this guideline.

CONTRAINDICATIONS
Absolute:
- Phaeochromocytoma.

Relative:
- Shock (other than anaphylactic).
- Organic brain damage.
- Cardiac dilation.
Known hypersensitivity to sympathomimetics.

PRECAUTIONS
- **Hypovolaemia** - correct before using adrenaline.
- **Extravasation** – can cause tissue necrosis and sloughing.
- **Local ischaemic necrosis** – can occur with repeated injections to the same site.
- **Tachyarrhythmias**.
- **Pulmonary hypertension** – may be worsened by adrenaline-induced pulmonary vasoconstriction.
- **Hyperthyroidism, diabetes, hypertension or the elderly** - increased risk of adverse effects with adrenaline.
- **Occlusive or cerebrovascular disease** – increased risk of peripheral ischaemia and stroke.
- **Acidosis, hypercapnia or hypoxia** – can decrease adrenaline’s effectiveness and/or increase its adverse reactions. Correct before commencing adrenaline where possible.
- **Ischaemic heart disease, heart failure or arrhythmias** - increased risk of arrhythmias, angina and myocardial ischaemia with adrenaline use.
- **Aortic stenosis and hypertrophic cardiomyopathy** - adrenaline may increase outflow obstruction.
- **Closed angle glaucoma** – adrenaline increases intraocular pressure due to pupillary dilation.
- **Parkinson’s Disease** – adrenaline increases rigidity and tremor.
- **Allergy** – adrenaline ampoules and minijets contain sodium metabisulfite or sodium bisulfite, which can cause severe allergy in susceptible patients (asthmatics are of greatest risk).

PREGNANCY AND BREASTFEEDING
Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS
**Do not withhold use of adrenaline due to concerns surrounding drug interactions.**
- **Beta blockers (anaphylaxis)** – beta2 blockade of receptors in the lungs can prevent adrenaline-induced bronchodilation. Anaphylaxis in patients taking beta-blockers may be refractory to treatment with usual doses of adrenaline; increase dose of adrenaline (being alert for possible hypertension) and give glucagon.
- **Drugs with arrhythmogenic, hypertensive or vasoconstrictive effects** – adrenaline increases the risk of these effects when co-administered with these drugs. Use combinations cautiously, monitoring ECG, blood pressure and haemodynamic parameters.
- **Cocaine** - risk of fatal arrhythmias with adrenaline when cocaine misused in the previous 24 hours. Avoid where possible.
- **Beta blockers (general)** - may allow the alpha receptor-mediated effects of adrenaline (vasoconstriction) to predominate, leading to marked hypertension followed by bradycardia. Reduce adrenaline dose if using a nonselective beta-blocker (oxprenolol, pindolol, propranolol). Monitor heart rate and blood pressure closely when adrenaline is used with any beta blocker.
- **Tricyclic antidepressants** - dysrhythmias and hypertension may result when used with adrenaline. Avoid combination if possible, otherwise reduce adrenaline dosage and monitor for dysrhythmias and hypertension.
- **Drugs that cause hypokalaemia** - may worsen the hypokalaemic effect of adrenaline, monitor potassium carefully.
- **Alpha blockers** - may decrease vasoconstrictive effects of adrenaline.
- **Entacapone** – may inhibit the metabolism of adrenaline, increasing heart rate and potential for arrhythmias. Reduce adrenaline dosage and monitor carefully.
Monoamine oxidase inhibitors (phenelzine, tranylcypromine, moclobemide), selegiline and linezolid – may inhibit the metabolism of adrenaline resulting in hypertension. Use with caution and monitor heart rate/blood pressure.

Nonselective alpha-blocker (phenoxybenzamine, phenotamine) – may lead to hypotension rather than an increase in blood pressure due to unopposed beta effect.

Bromocriptine – co-administration with adrenaline may increase the adverse effects of bromocriptine, including hypertension, ventricular arrhythmia and seizure. Monitor carefully.

Acetazolamide – decreases urinary excretion of adrenaline, and may increase therapeutic effect of adrenaline. Monitor.

Spironolactone – may decrease the vasoconstricting effect of adrenaline by an unknown mechanism. Monitor.

**DOSAGE AND ADMINISTRATION**

Requires continuous ECG monitoring.

For administration only
- in Critical Care Unit, ED and Theatre
- by MET or Code Blue

Administer via CVC only – see Precautions re extravasation. A large bore peripheral line or midline may be used in an emergency where central access is planned, or short term to avoid insertion of a CVC. If administering peripherally a second peripheral line is required to ensure continuity of the infusion, and the site requires monitoring for extravasation. Avoid administration on lines where other infusions may be bolused.

**Anaphylaxis dosing:**

**Intramuscular**
Use adrenaline 1 mg/1 mL (1:1,000) ampoules.
Adrenaline 10 microgram/kg (maximum of 500 microgram = 0.5 mg = 0.5 mL from 1 mg/mL ampoule) IM.
May be repeated if IV access is unobtainable.

**Intravenous**
Use adrenaline 1 mg/10 mL (1:10,000) minijets.
Mild reaction: Adrenaline 10 microgram (0.1 mL from 1 mg/10 mL minijet) by slow IV injection. Repeat dose or escalate dose titrating to response.
Moderate reaction: Adrenaline 1-2 microgram/kg (e.g. 50 microgram = 0.5 mL from 1 mg/10 mL minijet) by slow IV injection. Repeat dose or escalate dose titrating to response.

**IV injection resuscitation dose (via CVC where possible):**
Use adrenaline 1 mg/10 mL (1:10,000) minijets OR 1 mg/1 mL (1:1,000) ampoules.
Adrenaline 1 mg/10 mL (1 minijet) OR 1 mg/1 mL (1 ampoule) by slow IV injection.
Repeat dose every 3-5 minutes if needed.
Intermediate doses of adrenaline 2-5 mg (2-5 mL from TWO to FIVE 1 mg/1 mL ampoules) by slow IV injection every 3-5 minutes may be considered in an arrest situation.
**Endotracheal resuscitation dose (rarely used):**
Use adrenaline 1 mg/10 mL (1:10,000) minijets.
Adrenaline 1-2 mg (10-20 mL from ONE to TWO minijets) undiluted. Wait until end of exhalation and then administer via endotracheal tube.

**IV infusion (via CVC):**
Use adrenaline 1 mg/1 mL (1:1,000) ampoules to prepare infusion.
Withdraw 6 mL from a 100 mL sodium chloride 0.9% minibag.
Adrenaline 6 mg (6 mL from SIX ampoules) added to remaining 94 mL sodium chloride 0.9% in the minibag.
**Total Volume:** 100 mL.
**Final concentration:** 60 microgram/mL.
**Starting rate:** 1-3 microgram/min (1-3 mL/hr).
**Rate increase:** Can increase rate every 3-5 minutes. Use blood pressure, heart rate and cardiac output to titrate dose.
**Usual rate range:** 1-20 microgram/min (1-20 mL/hr).
**Maximum rate:** Rates much higher than 20 microgram/min (20 mL/hr) may be used in an ICU setting.
**Bolus dose during infusion:** 25-50 microgram in an emergency.
**Ceasing infusion:** Wean slowly with clinical assessment to avoid hypotension.

**Syringe Pump IV infusion (via CVC):**
**For use in ED only**
Use adrenaline 1 mg/1 mL (1:1,000) ampoules to prepare infusion.
Adrenaline 3 mg (3 mL from THREE ampoules) diluted to 50 mL with sodium chloride 0.9% in a luer lock syringe.
**Total Volume:** 50 mL.
**Final concentration:** 60 microgram/mL.
**Rate:** as for IV infusion above.

**General Administration Information**
- **Infusion preparation:**
  Mix infusion thoroughly after adding adrenaline to avoid inadvertently giving a more concentrated dose.
  Discoloured solutions (pink or brown) or solutions containing precipitates should not be used.
  Sodium chloride 0.9% can be substituted for different compatible IV fluid as requested by the Medical Officer.
  Infusion stable for 24 hours.
- **Infusion pump:** Volumetric pump.
- **Routes of administration:**
  IV injection: Yes
  IV intermittent infusion (15-60 minutes): No
  IV continuous infusion: Yes
  IM injection: Yes, but not in the buttocks. Avoid repeated injection to the same site.
  Subcut injection: Yes (but not in anaphylaxis). Avoid repeated injection to the same site.
- **Compatible/incompatible IV drugs/fluids:**
  Consult the Australian Injectable Drugs Handbook (‘Yellow book’) in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**
MONITORING (INCLUDING BLOOD TESTS)

- Observe the colour and temperature of the skin (especially of patients with occlusive vascular disease) for compromised peripheral circulation.
- Monitor electrolytes (especially potassium and magnesium) at baseline and at least daily.
- Dose range and clinical goals should be documented by the Medical Officer.
- A diminished therapeutic effect may occur with prolonged adrenaline infusions due to down-regulation of receptors.

NURSING PRACTICE POINTS

- Continuous ECG monitoring during infusion, look for arrhythmias and ECG changes.
- Baseline 12 lead ECG, and then daily and with rhythm changes or chest pain.
- When patient is unstable or infusion rate requires adjustment, monitor blood pressure every 2-5 minutes, or continuously via arterial line.
- When blood pressure stable, monitor blood pressure every 15-30 minutes, or continuously via arterial line.
- Record ALL vital signs at least hourly.
- Monitor and record neurovascular observations every 30-60 minutes, look for peripheral ischaemia.
- Consider 2 hourly glucose monitoring.

ADVERSE EFFECTS

- Common - anxiety, headache, fear, palpitations, tachycardia, restlessness, tremor, dizziness, dyspnoea, weakness, sweating, pupil dilation, pallor, hypokalaemia and hyperglycaemia.
- Infrequent - excessive increase in blood pressure, ventricular arrhythmias, pulmonary oedema, angina, urinary retention, hallucinations, psychosis, metabolic acidosis, peripheral ischaemia and necrosis (at infusion site).
- Rare - allergic reaction (sodium metabisulfite and sodium bisulfite in products).
- Overdose or rapid IV administration - arrhythmias (ventricular and supraventricular), severe hypertension, cerebral haemorrhage and pulmonary oedema.

DRUG PRESENTATIONS, LOCATION AND STORAGE

Adrenaline 1 mg/1 mL ampoules (1:1,000).
Adrenaline 1 mg/10 mL ampoules and minijets (1:10,000).

Imprest locations (at the time of guideline development):
Adrenaline 1 mg/1 mL: CCU, ED, Theatre, 2N, 2S, 3N, 3S, 4N, 4S, 5N, AAU, DPU, Dialysis, Oncology Day Ward, Radiology, Gandarra, JGU, MET/Code Blue resuscitation drug pack and ward resuscitation trolleys.
Adrenaline 1 mg/10 mL: 2S and 5N.
Adrenaline 1 mg/10 mL minijet: CCU, ED, Theatre, JGU, MET/Code Blue resuscitation drug pack and ward resuscitation trolleys.

Store below 25°C. Protect ampoules and minijets from light.