LOCAL ANAESTHETIC TOXICITY

NEARLY ALWAYS DUE TO THERAPEUTIC MISADVENTURE → WRONG DOSE, ROUTE OF ADMINISTRATION OR TECHNIQUE

CARE IS PRIMARILY SUPPORTIVE, BUT INTRALIPID MAY HAVE A ROLE IN SEVERE CASES

RISK ASSESSMENT:

- Onset of clinical manifestations is RAPID
- Toxicity can occur when lower doses are administered by direct IV or intra-arterial route
- METHAEMOGLOBINAEMIA can occur with BENZOCAINE, LIGNOCAINE OR PRILOCAINE → not dose-related
- MAXIMAL DOSES (in mg/kg):
    - BUPIVACAINE → 1-2.5
    - LIGNOCAINE → 4-5
    - ROPIVACAINE → 2.5-3
    - PRILOCAINE → 5-7

TOXIC MECHANISM:

- LA agents bind reversibly to sodium channels and act on peripheral nerves to inhibit the sodium flux necessary to initiate and propagate action potentials

TOXICOKINETICS:

- Systemic toxic effects correspond to peak concentrations and are influenced by multiple factors:
    - Total dose
    - Rate of administration
    - Route and location of administration
- Toxicity is RARE following oral ingestion due to extensive first pass metabolism
- Small volumes of distribution, half-life ~2 hours (longer for bupivacaine)

CLINICAL FEATURES:

- Earliest symptoms are neurologic → tinnitus, dizziness, anxiety, confusion, perioral numbness
- More severe toxicity:
    - CNS → seizures, coma (usually precedes CVS unless massive OD, then arrest may be first manifestation)
    - CVS → bradycardia, hypotension, dysrhythmia, cardiovascular collapse and asystole
    - Respiratory → respiratory depression, apnoea
- BUPIVACAINE is particularly cardiotoxic due to prolonged binding to myocardial tissue
- Methaemoglobinaemia is NOT DOSE-RELATED → blue discolouration of mucous membranes but may progress to CNS and CVS manifestations of cellular hypoxia → death when MetHb concentrations 70%

INVESTIGATIONS:

- Serial ECG → evidence of sodium channel blockade → pronged PR/QRS and large terminal R wave in aVR)

MANAGEMENT:

- Standard resuscitation algorithms
- SODIUM BICARBONATE for ventricular dysrhythmia
- Fluid resus for hypotension
- ANTIDOTES:
    - INTRAVENOUS LIPID EMULSION:
        - Indicated for cardiac arrest refractory to standard resuscitation
        - Can also be used as a rescue therapy for refractory cardiac arrest in context of acute poisoning with other highly lipophilic agents (TCAs, propranolol, verapamil)
        - Proposed mechanisms include extraction of agent from tissue binding sites by introduction of intravascular lipid phase, increased myocardial ATP synthesis due to reversal of inhibition of fatty acid delivery to miochondria and restoration of myocyte function by activation of calcium and potassium channels
        - Give 1-1.5mL/kg as bolus and repeat 1-2x at 3-5 minute intervals
        - Infuse 0.25mL/kg/minute until stability is restored
        - Pulmonary hypertension, ALI and haematuria have been described
    - METHYLENE BLUE → antidote for methaemoglobinaemia:
        - Administered to all symptomatic patients (chest pain, dyspnoea or confusion)
        - Consider in asymptomatic patients with MetHb >20%
        - Contraindicated in those with G6PD deficiency as haemolysis may occur.
        - Dramatically increases the natural rate of reduction of MetHb to haemoglobin
        - 1-2mg/kg slowly over 5 minutes, usually a single dose is sufficient but MetHb production can continue for days with dapsone poisoning
        - Have a lower threshold for administration in those with conditions that interfere with oxygenation (i.e. anaemia, IHD)