TOX/ENVIRONMENTAL 24TH March 2020

CASE ONE

75 year old woman presents with 2 days of lethargy and diarrhoea. She has a background of mild CHF, hypertension, but is otherwise fully independent and active. Her obs are:

HR 50, RR 18, SBP 90, GCS 14, afebrile, BGL 8, Sats 92%

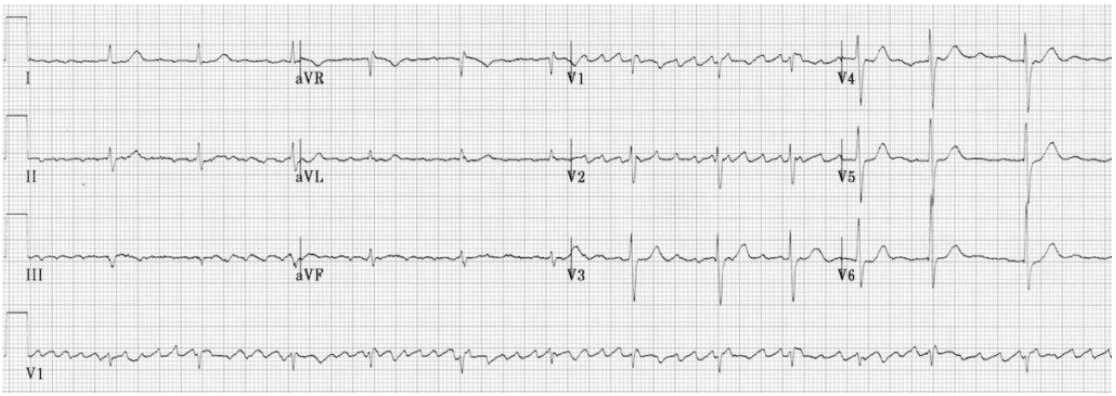
Medications: Furosemide, cilazapril, simvastatin, aspirin, digoxin, felodipine

1. **What are your differentials and your investigations?**

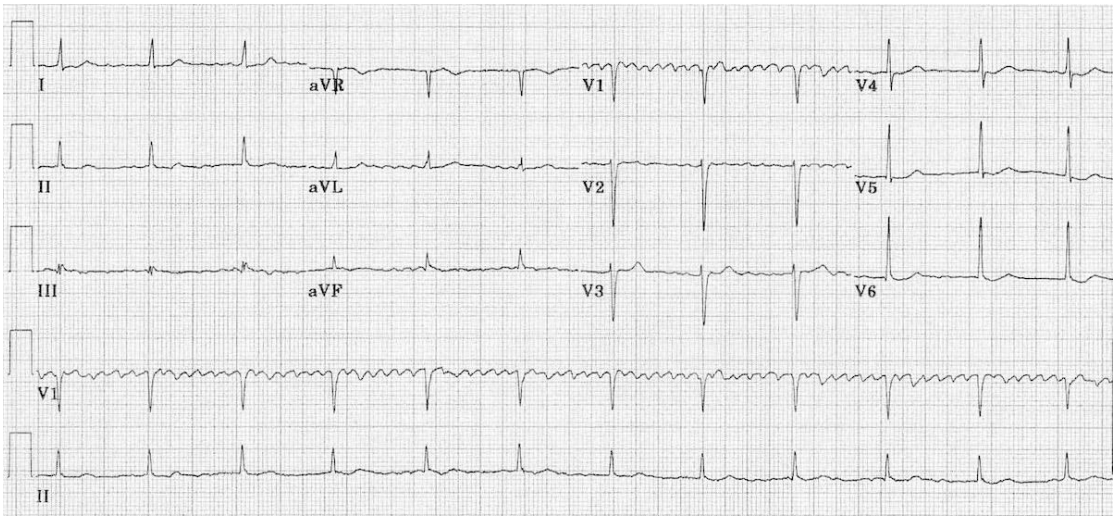
- Broad: Infective, cardiac, ischaemic bowel, drugs?

- ECG
- Bloods : VBG, U+E, FBC, LFT, ? trop, **Digoxin** level
- CXR
- MSU

2. **This is her ECG's describe and discuss?**



Slow AF ? block



Slow regularised type AF

- Slow regularised AF, AF with block common in digoxin toxicity
- AVB, AF rate < 60bpm
- Increased automaticity : PVC, bigeminy
- SVT with AV block
- VT

2. Her bloods are below please interpret in the clinical setting?

Na 150, K 6.1, Cr 240, Hb 130, Gluc 8, Digoxin level 3 nmol/L

- Hyperkalaemia and renal impairment with elevated digoxin level; in clinical setting of non-specific GIT illness, hypotension and bradycardia consistent with possible chronic digoxin toxicity. High risk mortality!

3. What are the clinical manifestations of digoxin toxicity and the mechanism?

- Membrane Na-K-ATPase pump inhibition
- Increase intracellular Ca (+ve automaticity, +ve inotropy)
- Increase extracellular K (hyperkalaemia esp with renal impairment)
- Enhanced vagal tone reduced SA/AV node conduction

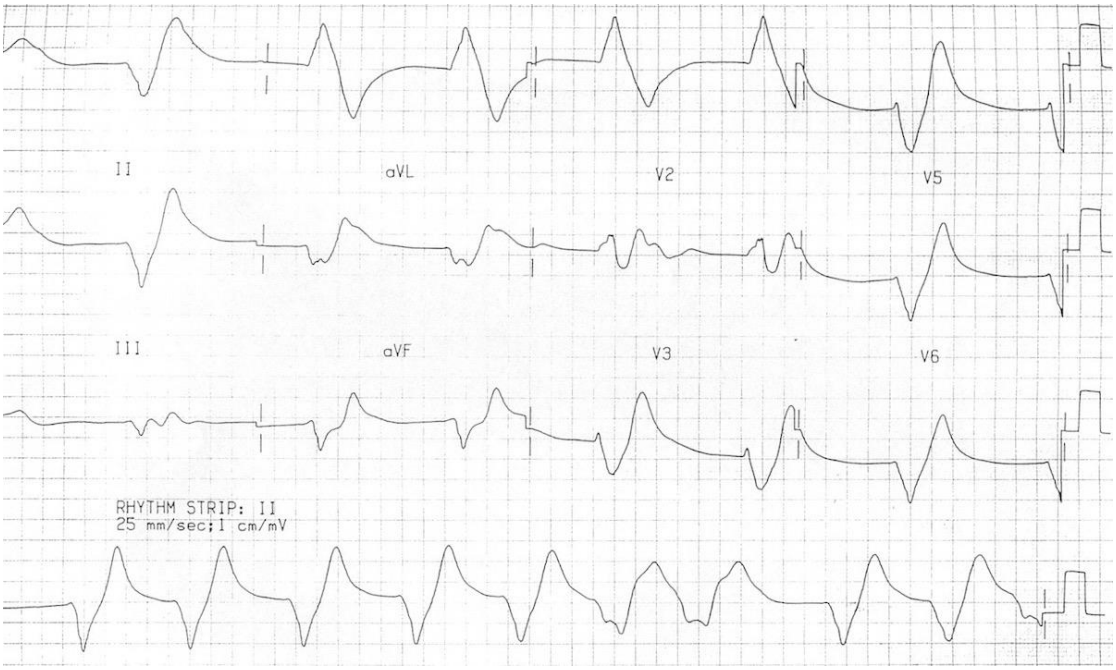
- CVS – brady, tachy, hypotension
- GIT- mild N/V/D/abdo pain (more prominent in acute OD)
- CNS- confusion, lethargy
- Vision- blurred, yellowing (chromatopsia), yellow halos (xanthopsia)

- Probability of toxicity predicted by considering digoxin level and clinical manifestations

4. How would you manage this patient?

- Get help, Tox input, ICU
- Early treatment with Digoxin immune Fab reduces mortality
- 1-2 ampoules usually sufficient
- Hyperkalaemia
- NaHCO3
- Insulin dextrose
- Ca contraindicated
- AVB
- Atropine 0.6mg (20mcg/kg) rpt up to 1.8mg max
- Pacing rarely effective
- Vent tachydysrhytmias
- Lignocaine 1mg/kg (100mgmax)
- Correct ypotension
- Correct hypokalaemia
- Treat any intercurrent illness ? Abs etc

5. Despite 500ml saline, and 2amps of immune Fab she has a brady-arrest. Her ECG is below. How would you manage this patient?



- Commence CPR
- 5amps immune Fab
- NaHCO3 for hyperkalaemia
- CPR continue for at least 30min post digoxin immune Fab

CASE TWO

32 year old male is brought into the resus via ambulance after collapsing during a long distance mountain run. He has no known past history or medications. His obs on arrival are:

Temp 40.1, SBP 110, HR 120, Sats 98% oa, RR 30, BGL 6, GCS 12 (E3, V3, M6)

Only treatment so far from the ambulance has been 1L of Saline.

1. What are your likely differential diagnoses?

- Heat Stroke – severe hyperthermia
- Consider : drugs (stimulants), seizures, medical events, CNS event

2. What are your management priorities?

- Cooling prevention of organ damage
- Cold IVF
- Evaporative cooling (fan and cold mist spray)
- Ice packs
- Cooling blankets
- Anti-pyretic
- BDZ for seizures and agitation control

- Manage metabolic disturbance – electrolytes, glucose

- Investigate and prevent rhabdomyolysis, ARF, and Hyperkalaemia

3. He is agitated and repeat temperature is 41 despite cold IVF and ice packs. His VBG is below. What is your next step in his management?

pH 7.1, CO2 3.2, HCO3 15, Na 155, K 5.8, Gluc 5, Lactate 6

- Severe hyperthermia with metabolic acidaemia and hyperkalaemia needs aggressive management.
- RSI (avoid suxamethonium) maintain low normal ETCO2
- Sedation and paralysis on going
- Cooling (cooling blanket)
- IVF to maintain diuresis (IDC monitor U/O)
- Consider urinary alkalinisation (controversial) in setting of rhabodmyolysis/myoglubinuria/hyperkalaemia

CASE THREE

An unwell 23 year old male is brought into the ED by the ambulance; he is hypotensive, poorly responsive, and is placed in the resus area. The Ambulance staff report a history of being found confused and poorly responsive in his bedroom by his family. There is no history of trauma. They noted a number of empty pill packets and containers. He does have a history of depression and previous self-harm attempts. He has been given 2L N saline on route but remains hypotensive. BSL was 10.

Initial Obs:

- BP 70/40
- HR 70
- Sat 92% o/a
- GCS M 4, E 2, V 2-3

1. **What important history do you want to determine about his presentation?**

- Risk Stratification:
- Potential ingestants and co-ingestants, access to medication, regular medications
- Potential timing of ingestion and max dosing
- Regular medications
- Past medical and social history

- Pre hospital interventions and responses

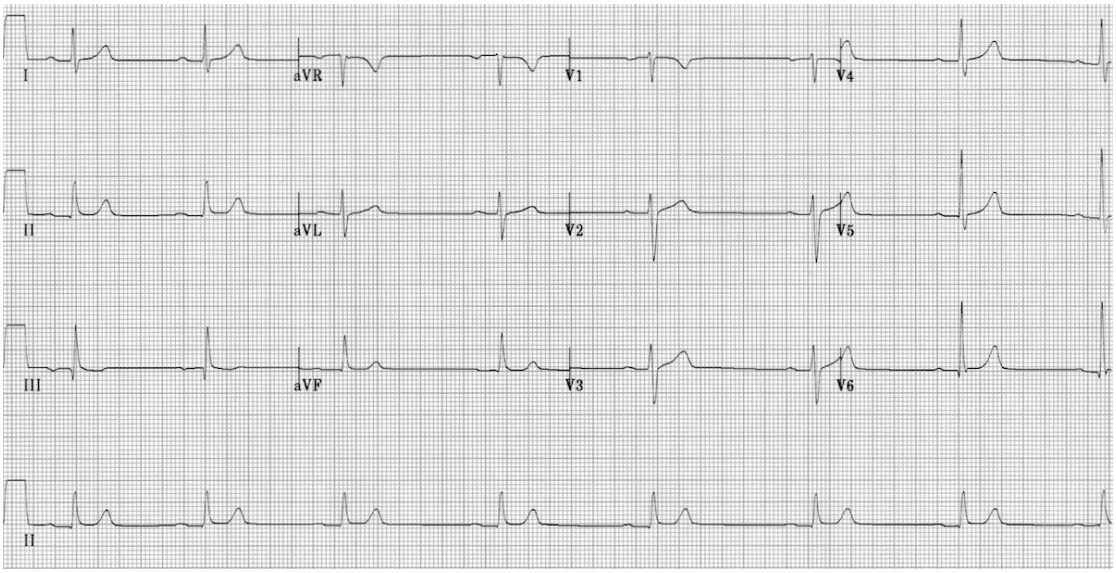
2. **It is determined that an empty bottle of Diltiazem CD 240mg was found (His Father's medication) along with a sheet of cilazapril tablets . Discuss the risk of Calcium channel blocker overdose and clinical features.**

- >10 tabs verapamil/diltiazem SR in adult or any deliberate ingestion potentially lethal
- 1-2 tabs in child of slow release potentially lethal
- Onset up to 2 hrs immediate and 16hrs Slow release
- Co-ingestants of other cardiotoxic agents are additive effect
- Co morbidities

- Block L-type Ca channels : slowed conduction, vasodilation, reduced cardiac contractility, hypo-insulinaemia
- Clinical features :
- CVS: bradycardia, 1st HB, hypotension (SBP< 95) early signs; accelerated AV node conduction, 2nd and 3rd degree heart block, sinus arrest with nodal escape, asystole
- CNS: not directly affected
- Metabolic: Hyperglycaemia marker severity , metabolic acidaemia

3. **How would you manage this man? Bloods/ECG (see VBG/ECG) have been completed and he has received a total of 3L saline now without change in his BP.**

VBG pH 7.26, PCO2 6.2, HCO3 18, Na 140, K 4, Gluc 11, Lactate 2.6



- Obvious fluid resistant shock with bradycardia – life threatening CCB toxicity
- Get help ASAP – ED SMO/TOX/ICU
- Establish large bore multiple IVL and plan for CVL and ART line

- CCB specific therapy aim SBP > 90, HR > 50min :
- Calcium 60ml 10% gluconate, 20ml Calcium chloride and repeat boluses, consider infusion aim serum Ca 2.0
- High dose insulin euglycaemia therapy (HIET)

2 Recommended high-dose insulin euglycaemic therapy protocol,[3,4,9] based on the clinical experience of the Western Australian Toxicology Service, published case reports, reviews and animal studies

Commence therapy with:

- Glucose 25 g (50 mL of 50% solution) IV bolus, unless marked hyperglycaemia (blood glucose > 22 mmol/L) is present
- Short-acting insulin 1 IU/kg bolus to maximally saturate insulin receptors

Continue therapy with:

- Short-acting insulin infusion starting at 0.5 IU/kg/h and titrated every 30 min to a maximum of 5 IU/kg/h*
- Dextrose 25 g/h IV infusion titrated to maintain euglycaemia (blood glucose, 5.5–14 mmol/L); central venous access may be required to allow use of concentrated solutions (eg, 50% dextrose) and limit excess volume administration

Monitor:

- Glucose — every 20 min for first hour, then every 1 h
- Potassium — replace only if < 2.5 mmol/L and there is a source of potassium loss

Therapeutic end points:

- Improvement in myocardial ejection fraction (> 50%); increased BP (systolic BP > 90 mmHg in adults)
- Adequate heart rate (> 60 beats/min)
- Resolution of acidaemia; euglycaemia; adequate urine output (1–2 mL/kg/h)
- Reversal of cardiac conduction abnormalities (QRS interval < 120 ms)
- Improved mentation

Therapy is weaned after the withdrawal of other vasopressors, as cardiotoxicity resolves. Dextrose may be required after cessation of insulin.

IV = intravenous. BP = blood pressure. * The maximum safe and effective rate of infusion is unknown but may be even higher than 5 IU/kg/h. In animal studies, insulin infusions as high as 10 IU/kg/h have been safely used.[11] ◆

- Early high dose inotrope/vasopressor Adrenaline/Norad

- Early consideration intubation and ventilation (risks /drugs ?)

- Other:

- Atropine for bradycardia
- Intralipid
- Sodium bicarbonate for acidaemia
- Cardiac pacing : ventricular pacing to bypass AV block at rate max 60min
- VA ECMO/Bypass (CVICU)

4. What is the mechanism of high dose insulin therapy (HIET)?

- HIET may allow the heart to overcome the 'metabolic starvation' that results from calcium channel blocker toxicity (and other poisonings, such as beta blockers), which compounds the direct cardiotoxic effects.
- Catecholamine independent inotropy
- Increaesd intra cellular calcium and calcium ATPase activity
- Increased intracellular glucose availability

CASE FOUR

You are climbing the Inca trail to see Machu Picchu. The max elevation on the trail is 4220m reached on day 2. (O2 12-13% compared to sea level, lung capacity 50%)

You are at the top of the climb on day 2. A 24 year old man has collapsed with visible dyspnoea and some mild confusion. You are the only medical person available to help him.

1. **What are your differential diagnoses?**

- Broad range multiple medical causes
- Primary cardiac or neurologic or metabolic
- AMS related
- Dehydration
- Heat or cold related illness
- Envenomation

2. **What is the physiology for Acute Mountain Sickness (AMS)?**

- The cause of AMS and HACEis not entirely understood.
- A vasogenic mechanism is thought to be responsible for the cerebral oedema. Hypoxia-induced cerebral vasodilation and alteration of the permeability of cerebral capillaries are likely causes.
- Cytotoxic oedema may also play a role, with failure of the Na+-K+ ATPase due to oxygen radicals.

- HAPEis caused by heterogenous hypoxia-induced pulmonary vasoconstriction.
- HAPE prone individuals exhibit greater rises in their pulmonary artery pressure at altitude.
- The heterogeneity of the the response causes diversion of flow to the less constricted areas with subsequent capillary leakage.
- Diminished reabsorption of alveolar fluid is also likely to be important, with hypoxia inhibiting Na+ transport across the alveolar membrane.

3. **Who is at risk of AMS?**

Acute mountain sickness reflects lack of acclimatisation. Susceptibility to the condition is not related to physical fitness.

- Acute mountain sickness (AMS) is rare below altitudes of 2500m.
- It is similar to a bad hangover and is characterised by headache plus one or more of these other symptoms:
  nausea and/or vomiting, fatigue, lassitude, dizziness, and difficulty sleeping.
- Risk factors include:
  - previous AMS
  - rapid ascent
  - higher altitudes

    - strenuous physical exertion
- Recent altitude exposure can be protective. There is no simple way to identify who will suffer from AMS prior to arriving at altitude. Those over 50 years of age may be less prone to AMS than younger people.

4. Describe the potential severe conditions developing with AMS?

- High-altitude cerebral edema (HACE)
- Potentially fatal condition and represents the severe end of the AMS spectrum. It usually occurs over 3000m, with an estimated prevalence between 0.5% – 1.5% at altitudes between 4000-5000m.
- Symptoms include severe headache, confusion, ataxia, drowsiness, stupor and coma.
- Ataxia is the most sensitive sign, and should be considered an indication for descent.

- High-altitude pulmonary edema (HAPE)
- is the leading cause of death related to high altitude.
- HAPE usually occurs within the first 2-4 days of ascent to high altitudes.
- It is characterised by decreased exercise capacity, dry cough, cyanosis, dyspnoea at rest and pink, frothy sputum.
- HAPE and HACE can occur together.

The man has a RR of 25, coughing, palpable HR 120, and is not orientated to place or person.

5. What is your clinical concern and how will you manage this situation?

- Likely HACE and/or HAPE; can occur together. HACE more likely

- Key to management is rapid descent and avoiding further physical exertion

- O2 +/- portable CPAP if available
- Portable hyperbaric chamber
- Dexamethasone
- Nifedipine for HAPE, but if they have HACE risk of reducing cerebral perfusion which may worsen them.