ELECTROCARDIOGRAMS (ECG):

ECG TOXIDROMES: looking for signs of cardiac toxicity

QT prolongation	• Potassium efflux blockers
QRS prolongation	• Sodium channel blockers
Other	• Sodium-potassium ATPase blockers • Calcium channel blockers • Beta-adrenergic blockers

ECG TO HELP …

DIAGNOSE	• CNS depression & QT prolongation → *Quetiapine? Citalopram? Antipsychotics?* • Opioid toxidrome with runs of torsades → *methadone?* • Oropharyngeal burns & ECG showing evidence of hyperkalemia or hypcalcemia → *hydrofluoric acid ingestion?*
PREDICT	• If patient has overdosed on a TCA • If QRS > 0.1 sec → 30% likelihood developing sz • If QRS > 0.16 sec → 50% likelihood developing ventricular dysrhythmias

GUIDE MANAGEMENT	• If QRS > 0.1 sec
	  ○ Give 2-3 amps of IV sodium bicarbonate
	  ○ Can repeat boluses every 3-5 minutes until QRS interval narrows or until serum pH reaches 7.55
	• If QT prolonged
	  ○ Check lytes & top up (K, Ca, Mg especially)
	  ○ Consider IV Mg^{2+} if QT > 500-550
	  ○ Fix cause

ECG IN THE POISONED PATIENT:

- Abnormal ECG is common in the poisoned patient (approx. 70%)
  - 62% rhythm abnormality
    - Sinus tachycardia (51%), sinus bradycardia (7%)
    - AV block (7%), non-sinus atrial tachycardia (3%)
    - Nodal bradycardia (3%)
  - 38% morphological abnormality
    - Abnormal QRS (35%), QRS widening (33%)
    - QT prolongation (33%), PR prolongation (12%)
    - ST elevation (9%), ST depression (25%)
    - T wave inversion (20%)

PR INTERVAL PROLONGED	• Toxins that ↓ interatrial or AV nodal conduction lead to AV dissociation or blocks • **↓ conduction =** CCBs, BBs • **↑ vagal tone** = cholinergics • Both **vagal tone & direct effects** = digoxin

QRS WIDENED	• Results of blocking fast sodium channels
	• Leads to ventricular dysrhythmias
	• Cyclic ADs
	• Venlafaxine
	• Citalopram
	• Carbamazepine
	• Diphenhydramine / dimenhydrinate
	• Cocaine
	• (Hydroxychloroquine
	• Class 1A
	  ○ Disopyramide
	  ○ Quinidine
	  ○ Procainamide
	• Class 1C
	  ○ Propafenone
	• Propranolol
	• Verapamil/diltiazem

ST SEGMENT CHANGES	• Characterizes myocardial ischemia or MI • Seen w/ toxins that cause **vasoconstriction/ischemia** ○ Cocaine, other α-agonists, ergots • Also seen following **severe hypotension or hypoxia**

T WAVE PEAKED	• Evidence of early hyperkalemia
	• As hyperK^+ worsens (6.5-8 mEq/L) → "sine wave"
	  ○ PR & QRS interval prolong and QRS merges with T waves
	• Hyperkalemia can occur with **chronic use**
	  ○ Spironolactone, ACEI/ARBs, K^+ supplements
	• **Acute hyperkalemia** with digoxin
	  ○ T wave changes uncommon

ECG CONTINUED:

QT INTERVAL PROLONG	• Typically prolongs with slower HR • If sufficiently long, can lead to v tach, v fib or TdP	
CAUSES	• Congenital • Na channel blockers • K channel blockers • Electrolyte disturbance (Ca, K esp.)	

DRUG CAUSES	• Antidysrhythmics
	• Antifungals
	• Antibiotics
	  ○ Quinolones
	  ○ Macrolides
	• Antipsychotics
	  ○ Risperidone
	  ○ Haloperidol
	  ○ Quetiapine
	  ○ Olanzapine
	  ○ Ziprasidone
		• Antidepressants
		  ○ TCAs
		  ○ Citalopram
		  ○ Venlafaxine
		• Other
		  ○ Methadone
		  ○ Cocaine
		  ○ Diphen-hydramine

HEMODYNAMIC ABNORMALITIES IN THE POISONED PATIENT:

HEART RATE:

BRADYCARDIA	• CNS depression: sedatives, opioids, clonidine • ↑ vagal tone: digoxin, cholinergics • Na channel *activation*: aconitine • **Direct depressant effects on cardiac pacemakers:** beta blockers, calcium channel blockers • Direct & indirect: metabolic acidosis, severe hyperK

TACHYCARDIA	• Most common rhythm disturbance in poisoned pt
	• Direct effect:
	  ○ Cocaine, sympathomimetics, anticholinergics, methylxanthines
	  ○ Agitation, withdrawal states
	• Indirect states: secondary to
	  ○ Hypotension, hypoxia, acidosis, fever
	  ○ Electrolyte disturbances, metabolic derangements

BLOOD PRESSURE:

INCREASED	• Direct α-adrenergic agonists: epinephrine, NE • Indirect acting: cocaine, amphetamines, MAOIs • Direct & indirect : dopamine, imidazoline decongestants, psuedoephedrine • Not α adrenergic receptors : nicotine, vasopressin
DECREASED	• Commonly from volume depletion • Substances that affect venous tone : sedative / hypnotics, clonidine • Co-existing states: hypoxia, acidosis, volume depletion, dysrhythmias

PUTTING THIS ALL TOGETHER: approach to management requires integration of

- Vital signs
- Electrocardiogram
- What else is going on in patient

CYCLIC ANTIDEPRESSANTS:

MECHANISMS	• Anticholinergic (coma, tachycardia) • Antihistaminic (coma) • Inhibits reuptake of NE & 5-HT (sz, hypotension) • α-adrenergic blockade (hypotension) • Na channel blocker (prolonged QRS, asystole)

TOXICITY	• Severe toxicity results in coma, seizures, hypotension, dysrhythmias and death
	• Onset within 4-6 mins; can be 30 min
	• Death usually within first several hours
	  ○ First 6 hours most critical, then next 6 hours
	• Toxic dose: > 5 mg/kg in child and adult
	  ○ > 1 g = life threatening in an adult

ANTIDEPRESSANTS (CONTINUED):

TREATMENT	• GI decontamination
	  ○ Can use charcoal > 2 hours post, if intubated
	• QRS widening (QRS > 0.1 sec) and other conduction abnormalities
	  ○ IV sodium bicarbonate boluses (2-3 amps or 1-2 mEq/kg) → repeat boluses every 3-5 mins until QRS interval narrows or until pH 7.55
	  ○ IV sodium bicarbonate boluses > infusions
	  ○ $NaHCO_3$ produces alkalemia → reduces ionization of TCA molecules and may reduce binding to sodium channels
	  ○ Monitor for hypokalemia and fluid overload
	• Ventricular dysrhythmias refractory to IV $NaHCO_3$, lidocaine may be useful
	  ○ Competes with TCA for Na channel → fewer Na channels blocked, conduction improved
	  ○ NOTE: lidocaine lowers seizure threshold and should be used with *caution*
	• Hypotension unresponsive to IV fluids
	  ○ IV sodium bicarbonate boluses
	  ○ If persists, use norepinephrine (likely more effective than dopamine)
	• IV lipid emulsion therapy can be considered in patients *refractory* to standard resuscitation measures
	• Seizures & agitation should be controlled with IV BDZ
	• Seizures refractory to high-dose BDZ should be treated with propofol, barbiturates, general anesthesia or neuromuscular paralysis (with continuous dosing)

CALCIUM CHANNEL BLOCKERS:

MECHANISM	• Inhibit L-type calcium channels in myocardium and smooth muscle • Also block Ca channels in pancreas → hyperglycemia

CLASSES	• Non-dihydropyridines (verapamil, diltiazem)
	  ○ Inhibit SA and AV node
	• Dihydropyridines (amlodipine, felodipine)
	  ○ Peripheral vasodilators
	  ○ *Lose selectivity in overdose*

TOXICITY	• Extension of therapeutic effects
	  ○ Hypotension - most common & life-threatening
	  ○ Bradycardia
	  ○ CNS effects are secondary to ↓ BP & hypoxia
	• Toxicity determined by
	  ○ Formulation and dose
	  ○ Co-ingestions – especially BBs
	  ○ Co-morbidities – CHF, cardiac disease
	  ○ Age

TREATMENT	• GI decontamination
	• Hypotension/bradycardia
	  ○ IV fluids
	  ○ Atropine
	  ○ Calcium boluses (3-4 boluses, infusion?)
	  ▪ 10-20 mL of 10% Ca chloride
	  ▪ 30-60 mL of 10% Ca gluconate
	  ○ Vasopressors – often multiple
	  ○ High-dose insulin glucose therapy

OTHER TREATMENTS	• Methylene blue
	  ○ Case reports for refractory vasodilator shock amlodipine overdose (↓ nitric oxide activity)
	• Fat emulsion
	  ○ Only if failing other therapies
	  ○ Case report evidence only; weak evidence
	• ECMO
	• Intra-aortic balloon pump

HIGH-DOSE INSULIN GLUCOSE THERAPY:

RATIONALE	• Healthy heart uses free fatty acids for energy • Stressed heart relies on carbohydrates • CCBs inhibit insulin release from pancreas which ↓ glucose being actively transported into heart • Providing energy to heart so it can respond to all other therapies being given (pressors, etc) • Also, insulin has inotropic effects
DOSE	• **Loading dose:** 1 U/kg regular insulin • **Infusion:** 1 U/kg/hr regular insulin along with 0.5 g/kg/hr **dextrose** (5 mL/kg/hr of D10W or 2 mL/kg/hr of D25W) • Can titrate up to 10 U/kg/hr insulin PRN BP

MONITOR	• K, glucose, BP
	• NOTE: if develop hypoglycemia, ↑ dextrose
	  ○ Do not decrease insulin dose
	  ○ Not sliding scale monitoring

BETA BLOCKERS:

- Similar approach except may get some response from glucagon infusion
- Still use high-dose insulin glucose even though not hyperglycemic initially, as with CCBs
- NOTE: propranolol can cause seizures and QRS prolongation, as well as ↓BP and ↓ HR

DIGOXIN:

MECHANISM	• Inhibits NaK-ATPase resulting in
	  ○ ↑ Na intracellularly, which disrupts Na gradient → ↓ Ca extrusion from cell and ↑ intracellular Ca
	  ○ ↑ Ca → ↑ contractility & automaticity
	  ○ At toxic levels, ↑ automaticity → dysrhythmias
	• Also, ↑ vagal tone → ↓ HR and blocks
	• *Chronic* digoxin toxicity more common than *acute OD*
	  ○ Risk factors: elderly, AKI, drug interactions	

TOXICITY	**CARDIAC**	• Bradycardia (usually severe) • Heart block – all degrees • Atrial or ventricular dysrhythmias • Death is secondary to asystole
	NON-CARDIAC	• Visual disturbances • GI disturbances • Confusion, agitation, weakness • Hyperkalemia (common) • Hypokalemia may occur in chronic OD
DIAGNOSIS	• History, ECG, lytes, renal function, digoxin level	
TREATMENT	• GI decontamination if recent, acute overdose • Digoxin-specific antibodies (DigiFab) • Hyperkalemia responds to antidote	
MONITOR	• ECG, clinical status, VS, potassium • No digoxin level after give DigiFab	

DIGIFAB INDICATIONS	• Any potential digoxin-related life-threatening dysrhythmia, including:
	  ○ Severe ventricular dysrhythmias (v tach, v fib)
	  ○ Progressive bradydysrythmias (severe sinus bradycardia or 2nd – 3rd degree heart block not responsive to atropine)
	• Serum digoxin level > 12.8 nmol/L measured > 6 hrs post-ingestion in an *acute* ingestion
	• *Acute* ingestion of > 10 mg in an adult (4 mg in child)
	• Serum potassium > 5.5 mmol/L in *acute* ingestion	

HYDROXYCHLOROQUINE:

OVERVIEW	• Highly toxic in overdose • Rapid onset of hypotension, ventricular dysrhythmias, cardiac arrest • Hypokalemia, seizures, and coma common • Death possible within 1-3 hours	
MOA OF TOXICITY	**CVS**	• Dose-related sodium and potassium channel blocking properties • Direct cardiodepressant effects • Delays repolarization, slows conduction
	HYPOK⁺	• Direct membrane effect
	CNS	• Direct sodium channel effect and hypoperfusion
TOXIC DOSE	• Therapeutic dose: 200 – 400 mg/day • Death: 11 – 12 g (teens) • Survival: 4, 12, 22 g after aggressive care	
KINETICS	• Rapidly absorbed • Peak 2 – 4.5 hours • Highly tissue bound (large Vd) • Distributional half-life: 15-30 hours • Elimination half-life: 4-40 days `	

INTRAVENOUS LIPID EMULSOIN (ILE)	• Consider for drug-induced cardiotoxicity **not** responding to standard measures
	• Proposed mechanisms still not clear
	  ○ Intracellular vs. intravascular vs. Membrane
	• Case reports of use with variety of toxins
	• ADRs
	  ○ Acute pancreatitis
	  ○ Analytical interferences
	  ○ May bind other resuscitative drugs `	

TAKE HOME POINTS	• Uncommon, clinicians often unfamiliar • May have to rapidly manage simulatensous QTc and QRS prolongation • Requires aggressive supportive care	

KEY POINTS:

- ECG is one of investigative tools to:
  - Establish diagnosis
  - Predict toxicity
  - Guide management
- Drugs with varying indications can share common cardiac toxicology
- Approach to management and monitoring can be systematic

SUMMARY:

- Ingestion was propafenone and digoxin
  - Na channel blocker and Na-K ATPase blocker
- Treatment directed at
  - VS, ECG, clinical signs
- Often don't know history or have labs initially when to have begin txt
- ECG will help guide therapy and decision making
- Use ECG info along w/ everything else you have learned from tox module