The Ottawa Hospital | L'Hôpital d'Ottawa

Calcium Channel Blocker Overdose

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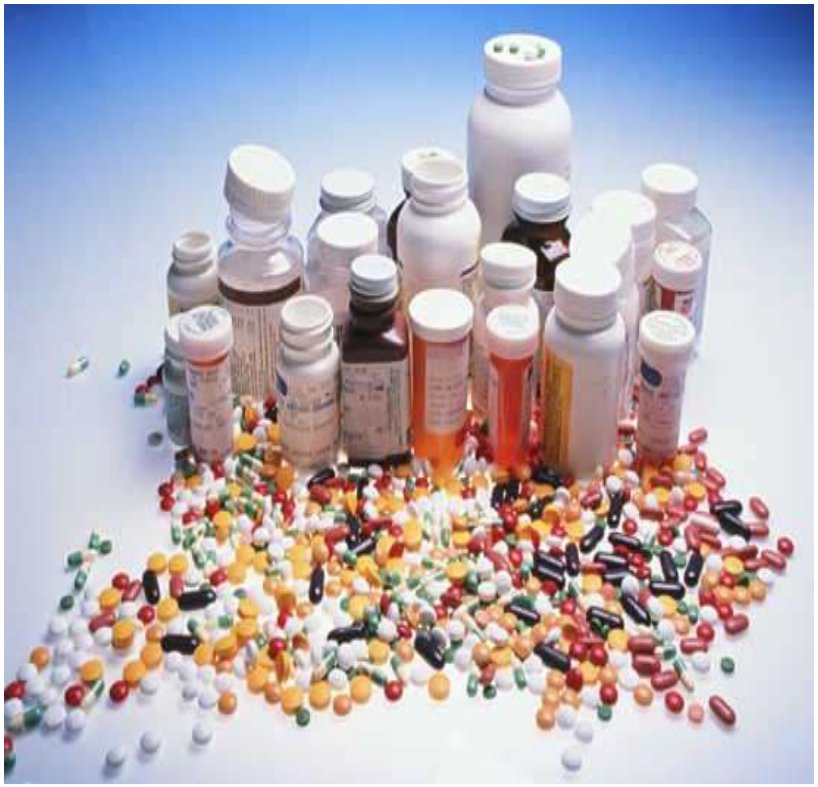
Case Study (Day 0)

- 57 year old 100 kg male
- PMHx: hypertension, high cholest., NIDDM, depression
- After a night of drinking came home and took ALL of his recently filled medications (3 month supply)
- Discovered by family vomiting…to hospital

Case Study

Meds ingested:

- Diltiazem HCL SR 240mg x 90 tabs
- Atorvastatin 900mg x 90 tabs
- Ramipril (ACE)900mg x 90 tabs
- Chlorthalidone (thiazide; undetermined amount)
- Metformin (undetermined amount)



Case Study

In ER

- Initially alert and oriented, vomiting +++pills
- Gradual hypotension with decreased LOC/unresponsive
- Intubated for airway protection (CPAP10/10 40%)
- Vitals: HR 80-90 SR progressing to bradycardia 40-60, BP 70-90/30-40
- ABG: 7.04/41/93/11/-18/96
- 4 large bore peripheral IV's inserted

Case Study

- Phenylephrine IV infusion, titrated up to 300mcg/min
- Intralipid 20% 150ml IVP/infusion started @.25ml/kg/min
- Calcium Gluconate 60mg/kg IVP over 5 minutes
- Glucagon 10mg IVP, infusion 2mg/hr
- Sodium bicarbonate 1 amp IVP
- Transported to ICU

Case Study

- in ICU decreased LOC but obeying commands, nodding
- Trilumen CVAD, introducer sheath inserted
- Rapid deterioration in vitals
- Progressively hypotensive, bradycardic
- Vitals: BP 60-105/35-40, HR 22-80 3rd degree CHB
- ABG 6.98/41/79/10/-22/97

Case Study

Medications (rapid escalation):

- Phenylephrine, norepinephrine, dopamine, vasopressin, epinephrine infusions
- Intralipid infusion, glucagon infusion
- High dose insulin @150 units/hr with D50W infusion
- Methylene blue IVP, with an infusion

Case Study

- Midazolam infusion started for comfort
- Large bore nasogastric tube inserted; gastric lavage initiated followed by activated charcoal and Pegalyte 4L NG
- Patient having prolonged recurrent episodes of complete heart block with ventricular response in 20's

Case Study

- Transcutaneous pacing initiated as a bridge to transvenous pacing
- Odd!..after a few minutes of tv pacing, reverted to SR 80-90
- Dual lumen CVAD inserted, CRRT initiated

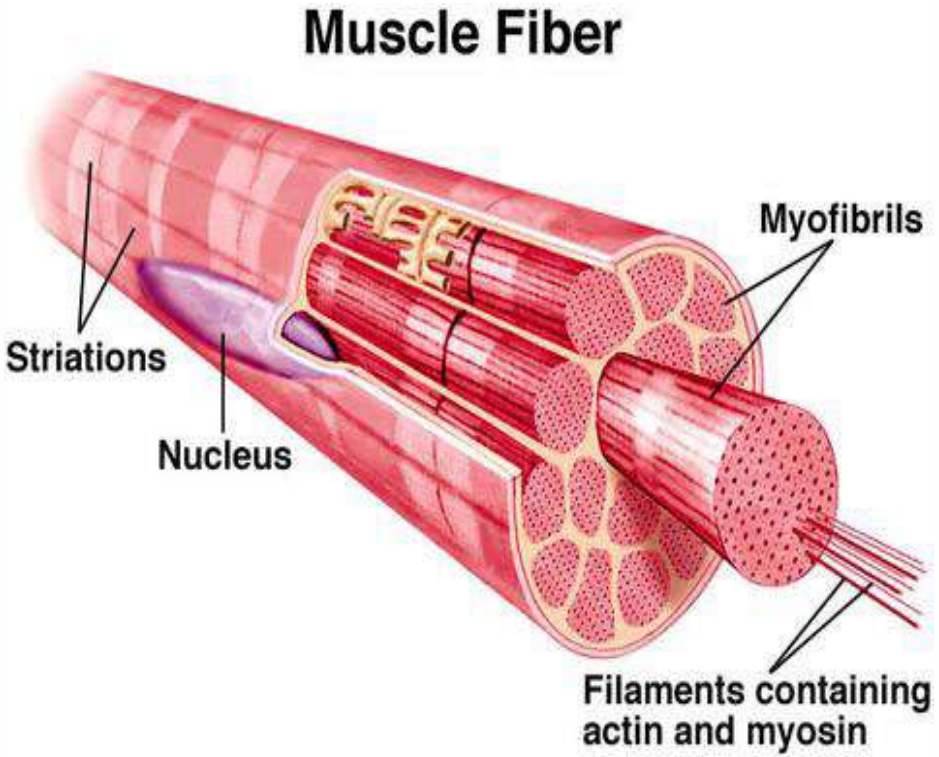
Physiology/Pharmacology (sorry)

Overview

- Calcium channel blockers used to treat HTN, angina, arrythmias
- Wide clinical use, commonly prescribed
- Examples: amlodipine, diltiazem, verapamil
- Available in immediate and extended release
- Substantial toxicity, CCB account for ~40% of deaths in cardiovascular drug OD

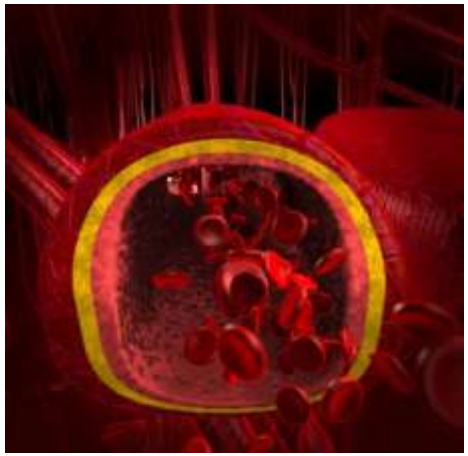
Physiology/Pharmacology

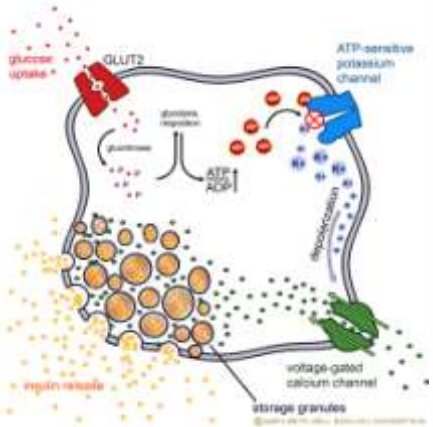
- Calcium is critical for myocardial contractility and conduction
- Maintains tonic constriction in vascular smooth muscle; contraction of skeletal and cardiac muscle cells
- CCB block calcium channels causing vasodilation, depressed myocardial contractility or altering conduction and pacemaker cells



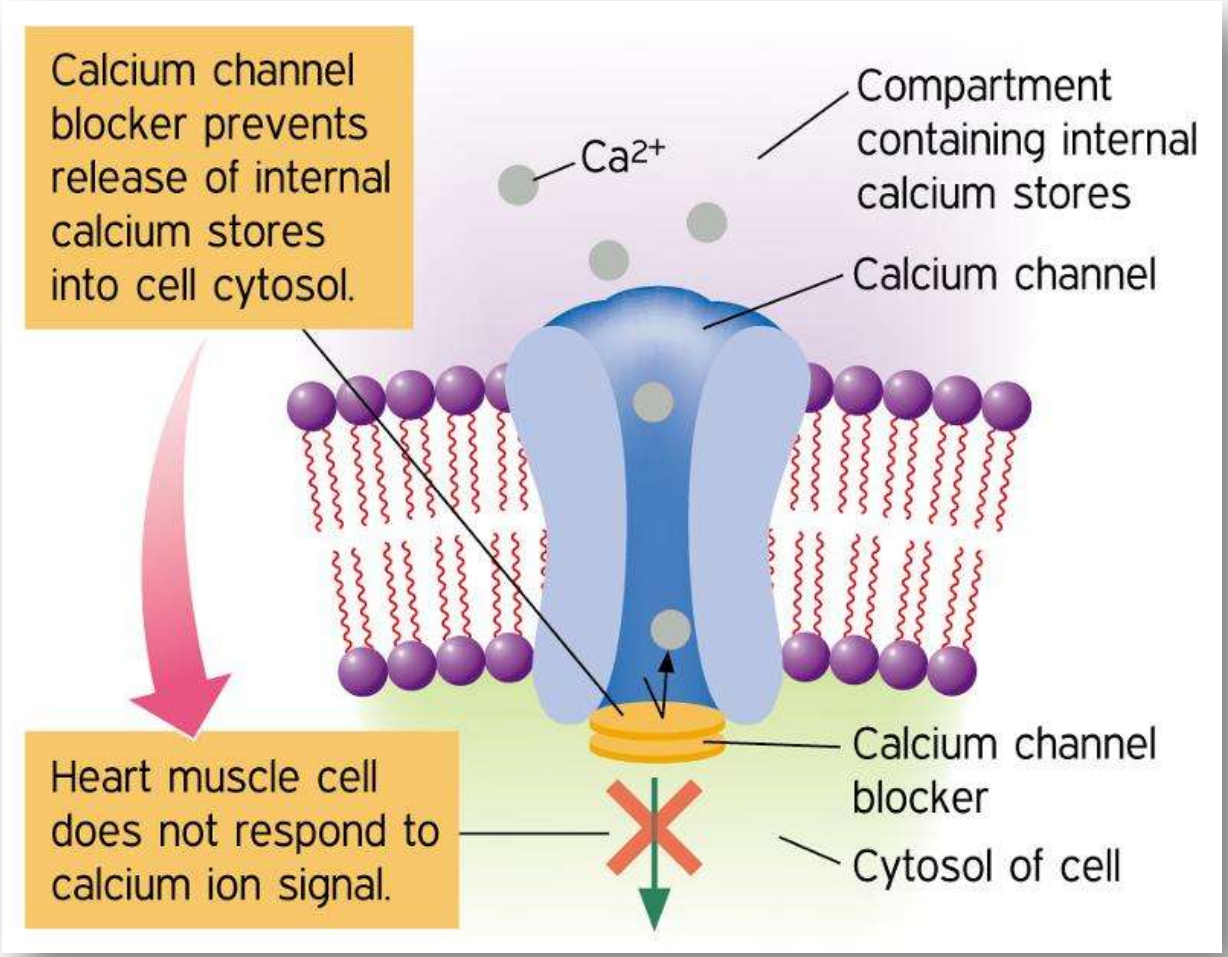
Physiology/Pharmacology

- CCB are chosen based on their primary target tissue or "selectivity" (myocardial vs. vascular)
- Selectivity is lost with overdose
- Negative inotropic and chronotropic effects, as well as "vasoplegia" (widespread vasodilation)
- At toxic levels will also inhibit insulin release from pancreas by blocking calcium channels in beta cells





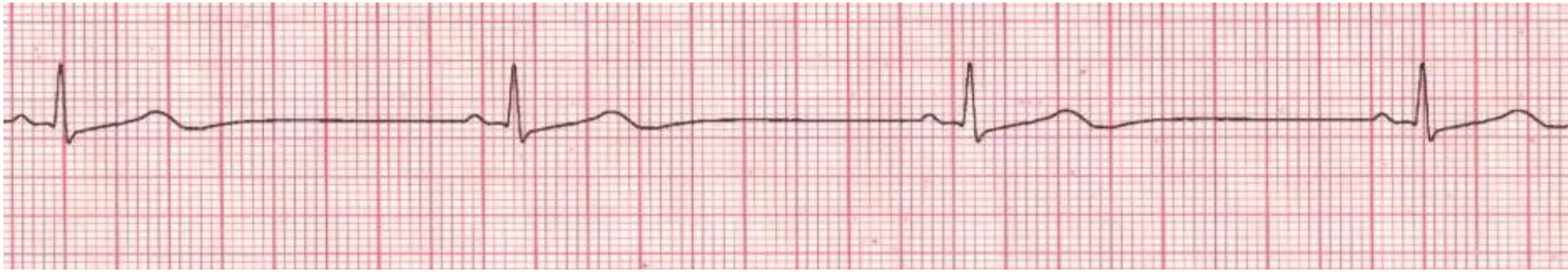
Physiology/Pharmacology



Physiology

Typical Symptoms of CCB toxicity

- Drowsiness/confusion (can be surprisingly lucid)
- hypotension and bradycardia (prolonged PR, blocks)
- Pulmonary crackles, signs of failure
- Hyperglycemia
- Initially stable may deteriorate quickly



Toxicity

- Usual max single dose of sustained release 360mg
- Pt took 21,600mg (~22g)
- In addition to other antihypertensive meds

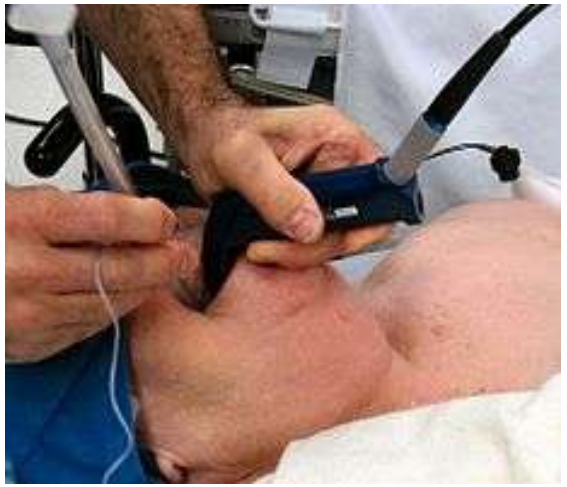
Treatment

Focus on 4 Elements

- STABILIZATION – ABC's
- DECONTAMINATION
- ANTIDOTE(S)
- SUPPORTIVE THERAPY

Stabilization

- Correct immediate life threatening complications
- For CCB overdose most commonly hypotension and bradycardia
- Intubation (Atropine)
- IV access, fluids



GI Decontamination

Oro-gastric lavage

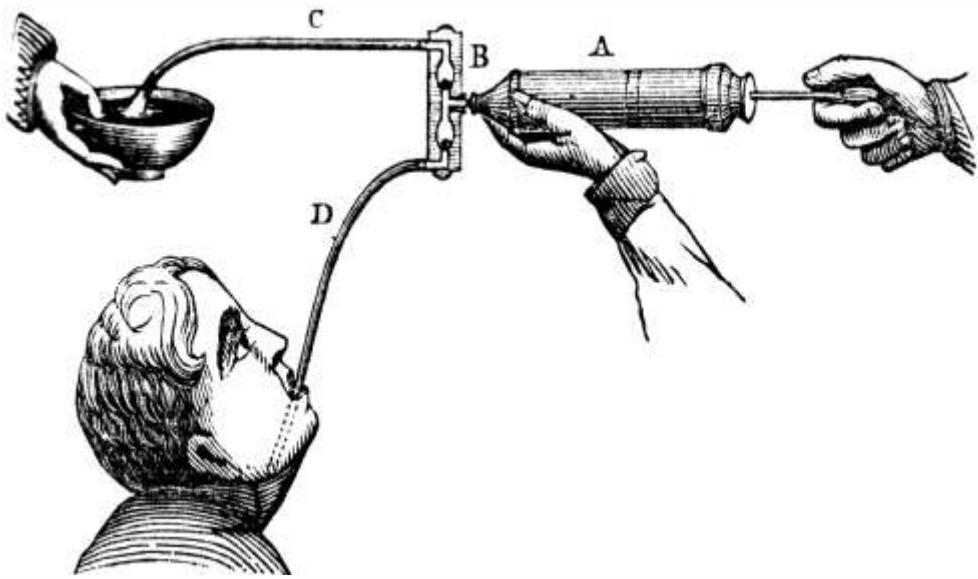
- Within 1-2 hours of ingestion

Activated Charcoal

- Within 1 hour of ingestion

Whole Bowel Lavage

- Pegalyte



Antidote Administration

Administration of calcium salts:

- Used to overcome CV effects of CCBs
- **Calcium chloride:** 3x bioavailable calcium than Ca-gluconate; nonacidotic patients
- **Calcium gluconate:** preferred in acidotic patients; less bioavailable calcium
- Often ineffective because CCB produce a non-competitive block

Supportive Therapy

Vasopressors

- Following fluid resuscitation: dopamine, phenylephrine, norepinephrine, epinephrine
- Positive inotropy, chronotropy and vasoconstrictive effects of agents

Supportive Therapy

Glucagon

- Increases intracellular cyclic AMP which activates calcium channels
- Increases heart rate
- 5mg IV push (repeat at 10 minute intervals)
- infusion

Supportive Therapy

Insulin and Glucose

- Mechanism is not clear
- CCB block FFA metabolism and produce insulin resistance in myocardial cells (carbohydrate dependence)
- Overcomes insulin resistance in myocardium and replaces insulin blocked at pancreatic level by CCB
- Not all patients will need glucose because CCB may cause hyperglycemia
- At high doses insulin will actually act as an inotrope
- 120-150 units/hr…monitor glucose

Supportive Therapy

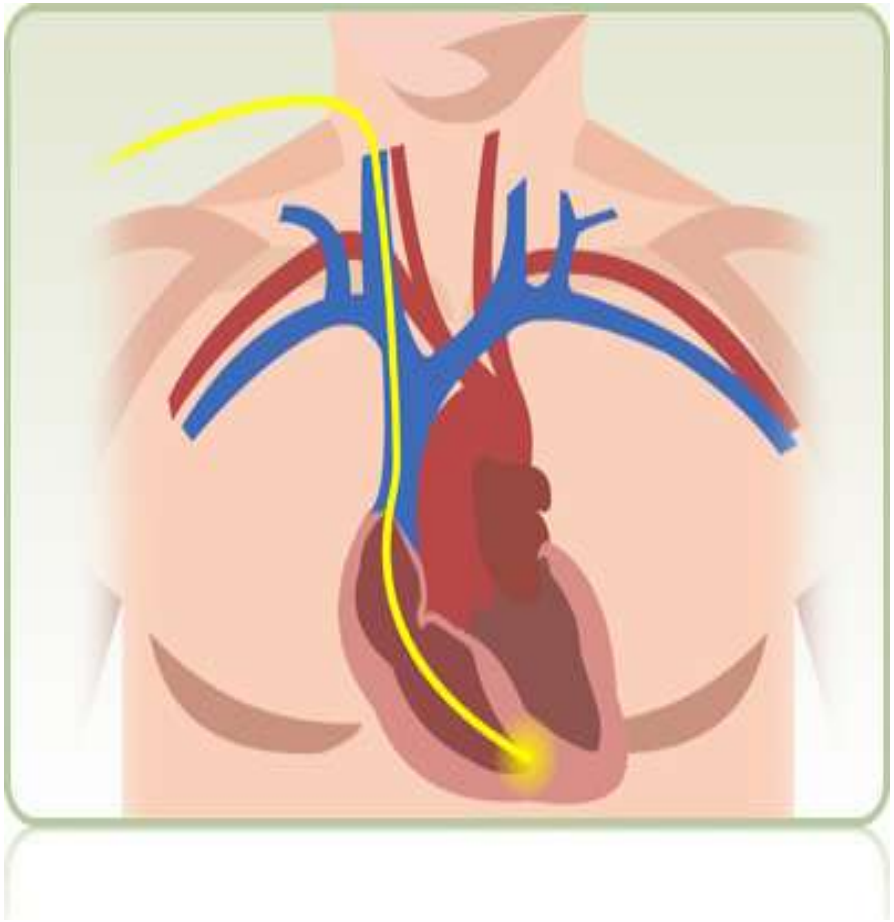
Lipid Emulsion Therapy

- Lipid surrounds CCB drug molecule
- Prevents it from binding to calcium channel
- Also proposed that lipid provides readily available energy source for myocardial cells
- Dosage 1.5 mg/kg IVP, infusion .25ml/kg/min

Supportive Therapy

Transvenous Pacing

- Assists with electrical conduction
- Does not correct negative inotropic effects of CCB or hypotension

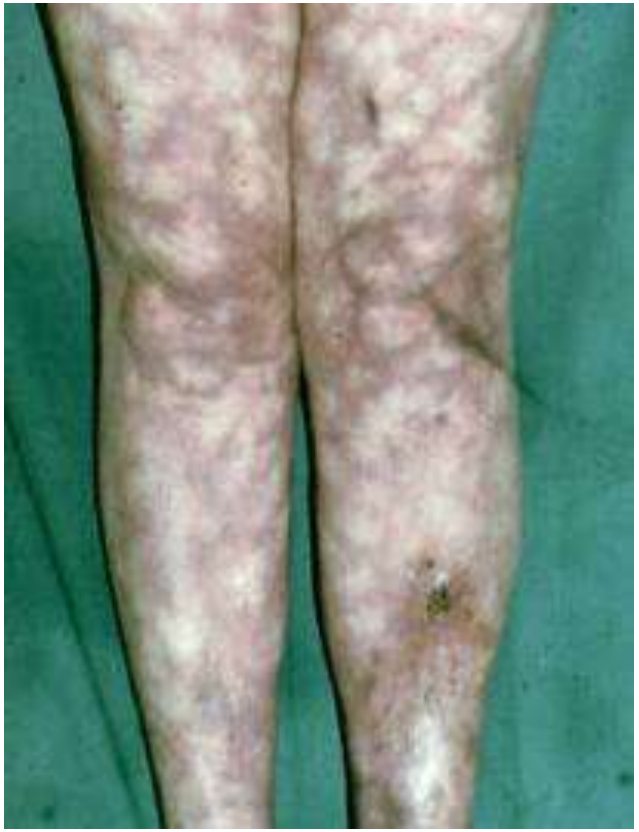


Case Study (Day 1)

- Overnight patient aspirated pegalyte and charcoal (massive)
- By morning: PCV, rate 28, 12/28, Vt 490ml (was 700ml)
- Vasopressors all at maximum, with the addition of methylene blue infusion

Case Study

- BP 80/30 on pressors
- Tni risen from 10.7 to >40, lactate 17
- CK 4000
- WBC 28.6
- Gross mottling noted to extremities and torso
- Consult to CSICU cardiac anesthesia for possible ECMO



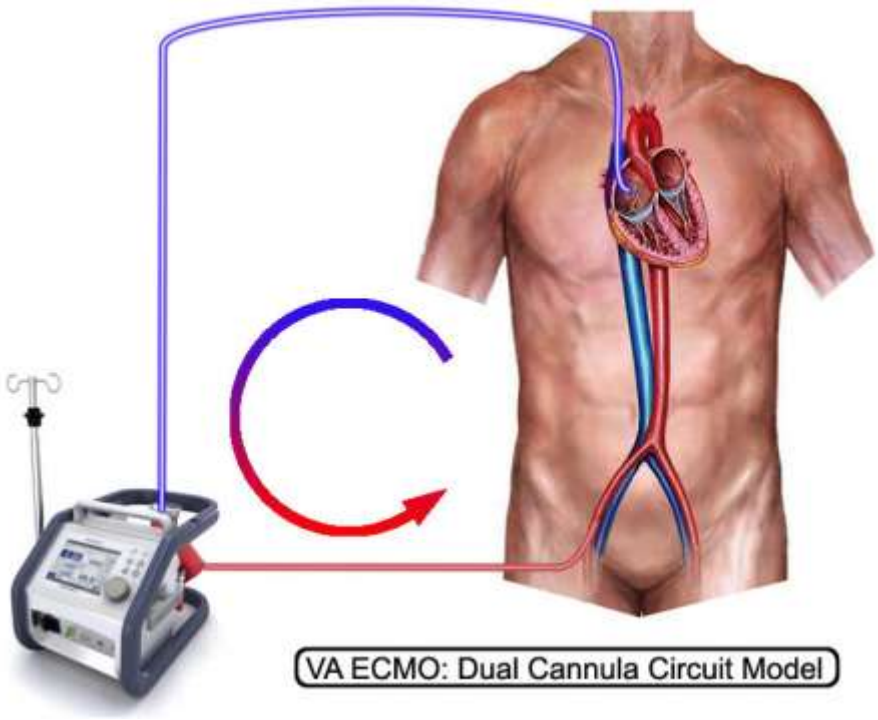
Case Study

- Transvenous pacer removed, PA catheter inserted (C.O. 5 l/min, C.I. 2.0, SVR 300)
- Prior to availability of ECMO, patient continued to deteriorate
- Idioventricular rhythm with sustained pauses
- Patient asystolic, no resuscitation attempted
- CTB almost exactly 24 hrs post ingestion

Other Therapies

ECMO/CP Bypass

- Some reports of favourable outcome for patients placed on prolonged ECMO/CPB
- Anecdotal only



Other Therapies

Methylene Blue?

- "hail Mary?"
- Has some efficacy in sepsis; not validated for CCB toxicity
- MB inhibits the nitric oxide cycle and vasodilation
- Improves SVR and MAP

Other Therapies

Levosimendan (calcium "sensitizer")

- Used in severe CHF
- Not recommended for use in CCB OD
- Sensitizes calcium channels and promotes influx into cell; increases contractility
- Theoretical benefit only
- Conflicting animal studies

Other Therapies

Dialysis

- In this case CRRT initiated to assist with correction of acid/base imbalance
- CCBs are highly protein bound
- Ineffectively removed by dialysis

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