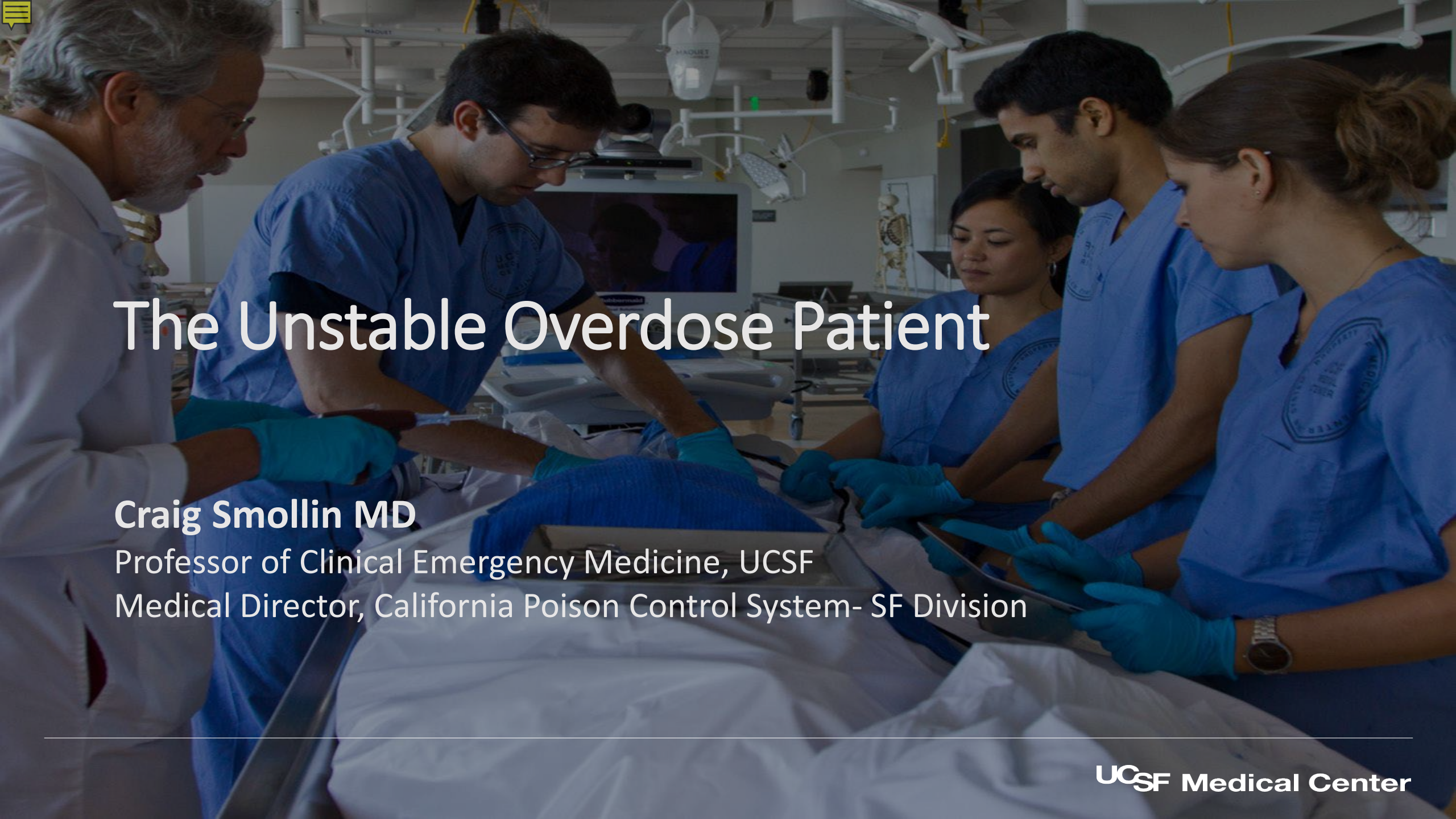


# The Unstable Overdose Patient

**Craig Smollin MD**
Professor of Clinical Emergency Medicine, UCSF
Medical Director, California Poison Control System- SF Division

UCSF Medical Center

# Disclosure

- I have no relevant financial relationships with the manufacturers of any commercial products discussed in this presentation.
- I will not discuss any unapproved or investigative uses of any commercial product in this presentation

# Objectives

- Review two cases exemplifying uniquely unstable overdose patients

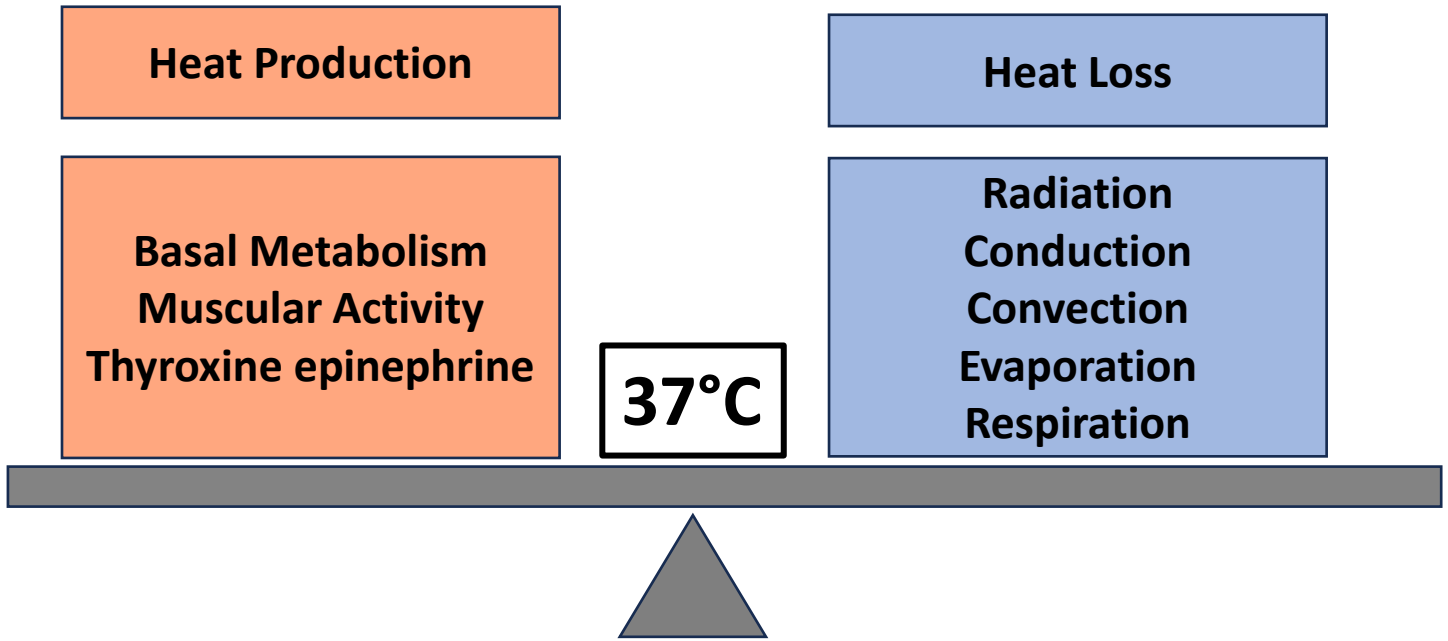
# Case #1

- A 33-year-old female presents to the ED with altered mental status.
- She was at a concert with friends and suddenly became less responsive.
- In the ED, the she has a witness generalized tonic clonic seizure and is now post ictal.

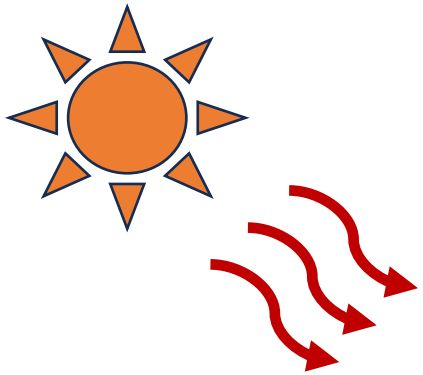
# Case #1

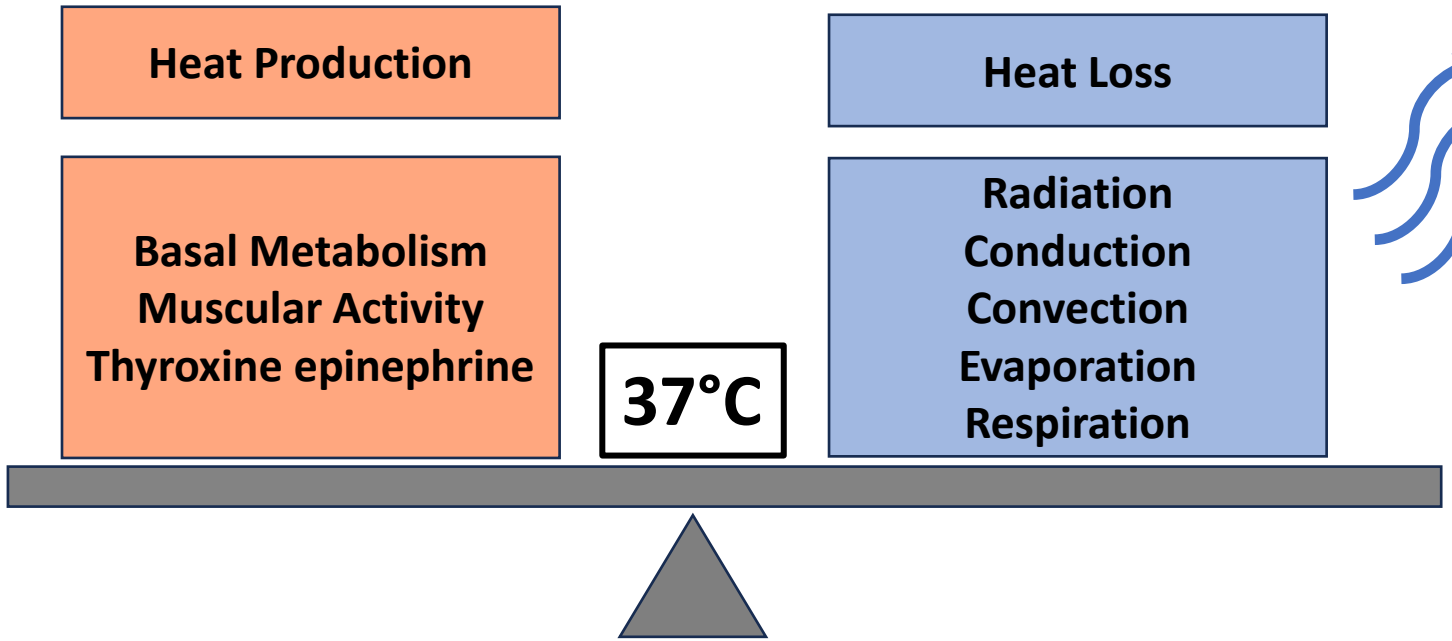
- Physical Exam:
- Vitals: BP 170/100 mmHg, HR 132, RR 24, O2 sat 99%, Temp **42 C**
- Pupils 7 mm and reactive bilaterally
- Skin hot to touch and diaphoretic
- Neuro eyes closed, not following commands, localizes to painful stimuli.

# Thermoregulation



# Thermoregulation








- Vasodilation
- Tachycardia
- Increased CO
- Sweating

# Risk Factors Associated with Heat Related Illness

- **Environmental Factors:** High humidity, high thermal radiation, low wind speed.
- **Individual variation in core temperature:** Obesity, metabolic heat production, movement economy, aerobic fitness
- **Age:** Extremes of age more susceptible
- **Clinical factors:** Disruption of sweat glands (e.g., burn history), heart failure, peripheral vascular diseases, medications, drugs of abuse.

# Drug-induced Hyperthermia

| Drug-induced syndrome | Associated drugs |
|---|---|
| Neuroleptic malignant syndrome | Antipsychotics (haloperidol, olanzapine), some antiemetics (metoclopramide), withdrawal of antiparkinson drugs |
| Serotonin toxicity | Serotonin reuptake inhibitors, monoamine oxidase inhibitors, dextrometorphan, tramadol, tapentadol, linezolid, St John's wort (toxicity most often occurs when the drugs are used in combination) |
| Anticholinergic toxicity | Antispasmodics, anticholinergic drugs, plant alkaloids (such as belladonna, *Brugmansia*) and mushrooms (e.g. *Amanita*) |
| Sympathomimetic syndrome | Phenthylamines, e.g. amphetamines, methamphetamines (MDMA), cocaine, monoamine oxidase inhibitors |
| Malignant hyperthermia | Volatile anaesthetics and depolarising muscle relaxants, e.g. suxamethonium |
| Uncoupling of oxidative phosphorylation | Salicylates in overdose, dinitrophenol |

***Jamshidi N et. al Aust Prescr. 2019***

# Heat Stroke

- Life-threatening illness
- Uncontrolled rise in core body temperature > 40°C

  **AND**
- Central nervous system dysfunction (e.g., delirium, seizures, coma)
- From exposure to high environmental temp = ***Classic Heat Stroke***
- From strenuous physical activity = ***Exertional Heat Stroke***

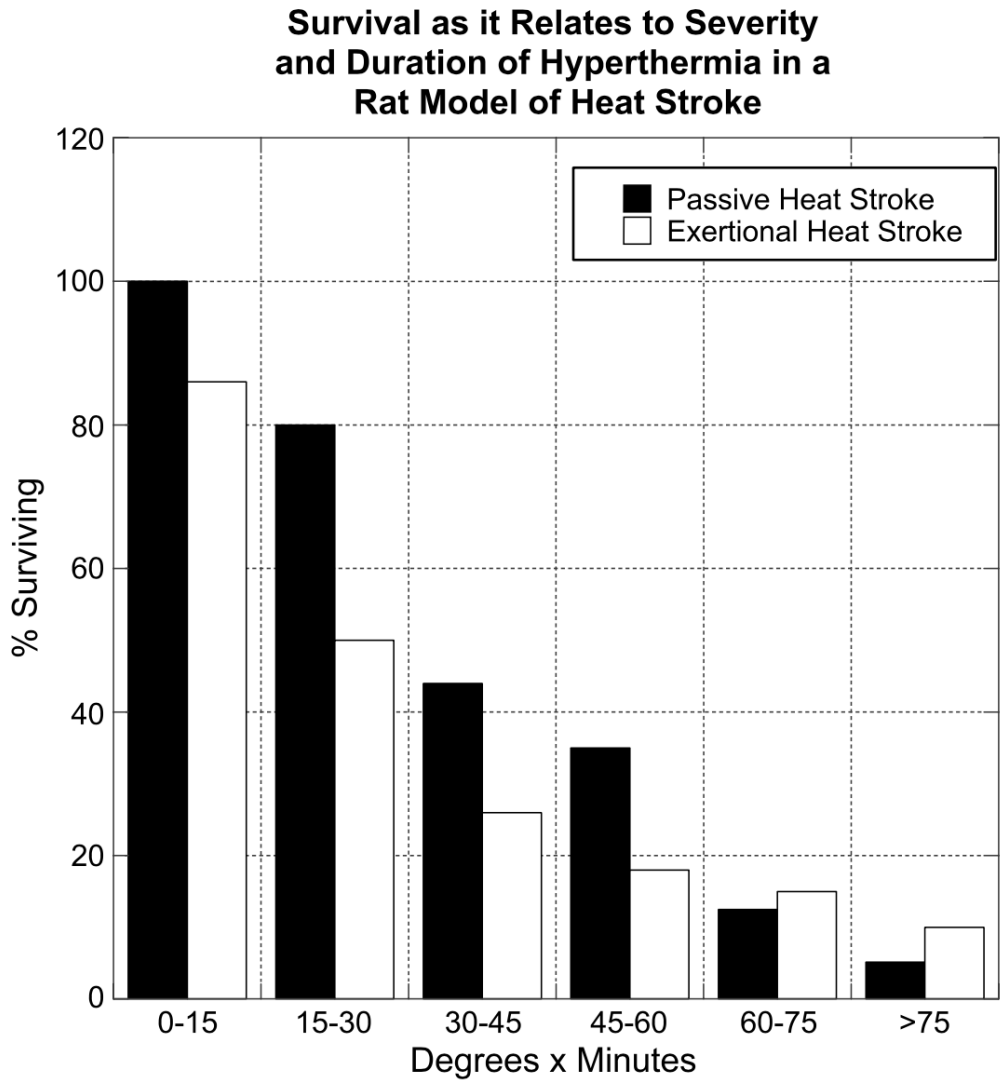
# Main physiological effects of severe hyperthermia

| System | Parameter | Clinical Implications |
|---|---|---|
| **CV** | • Tachycardia<br>• Volume depletion<br>• Hypotension | • Adequate fluid resuscitation |
| **CNS** | • Encephalopathy<br>• Seizures<br>• Coma | • Treat seizures with benzodiazepines<br>• May be confused with meningitis |
| **Renal/Met** | • Acute Kidney Injury<br>• Rhabdomyolysis<br>• Electrolyte disturbances (hyponatremia, hyperkalemia) | • Adequate fluid resuscitation<br>• Treat hyperkalemia |
| **Heme** | • Disseminated intravascular coagulation<br>• Thrombocytopenia | • Risk of bleeding with invasive procedures |
| **GI** | • Edema and hemorrhage (regional ischemia)<br>• Elevation of liver function tests | • Will contribute to hypovolemia |

Multi-organ system dysfunction!!

# Heat Stroke – Management

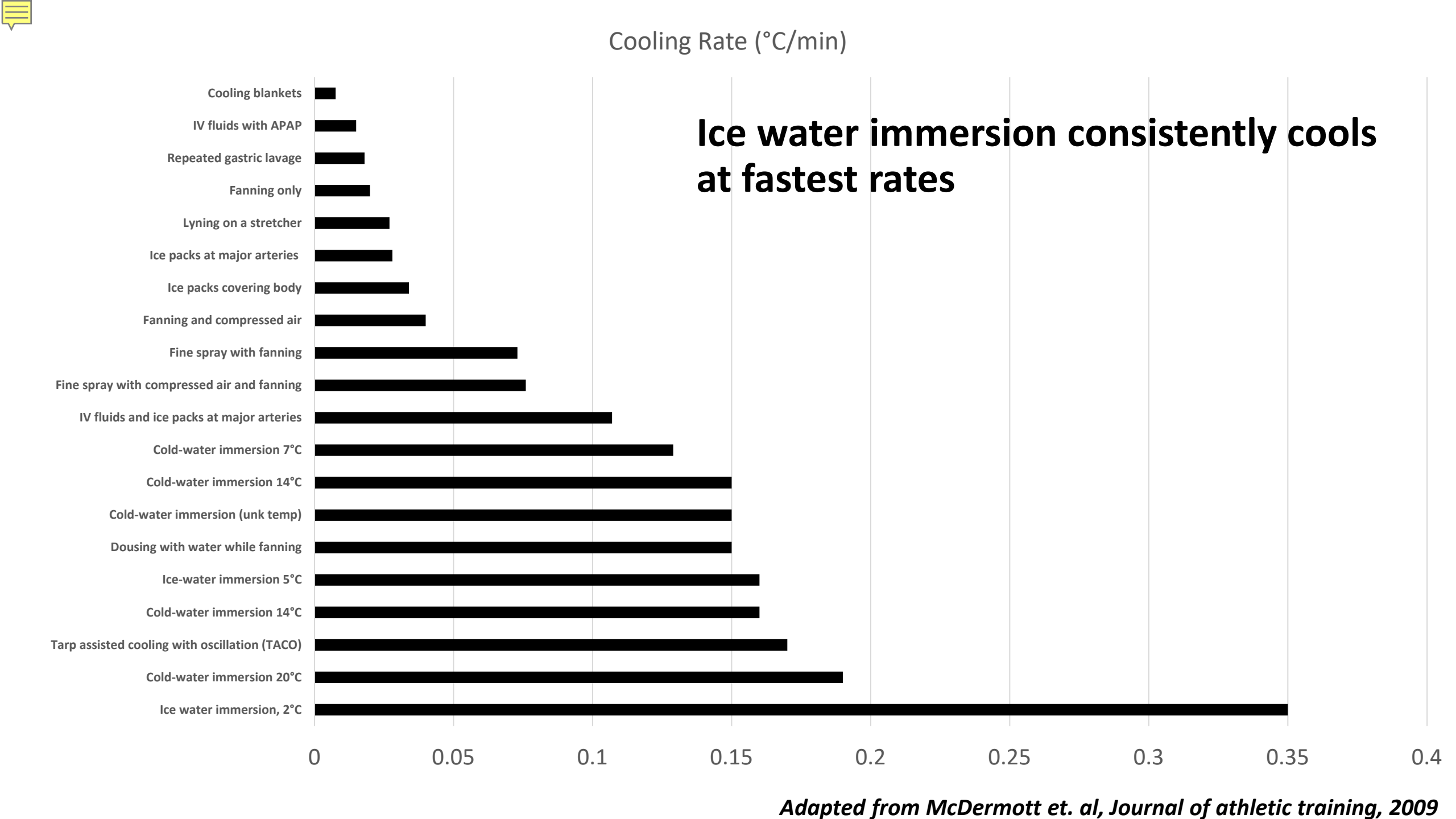
- Severity of damage is related to the **degree** and **duration** of hyperthermia.



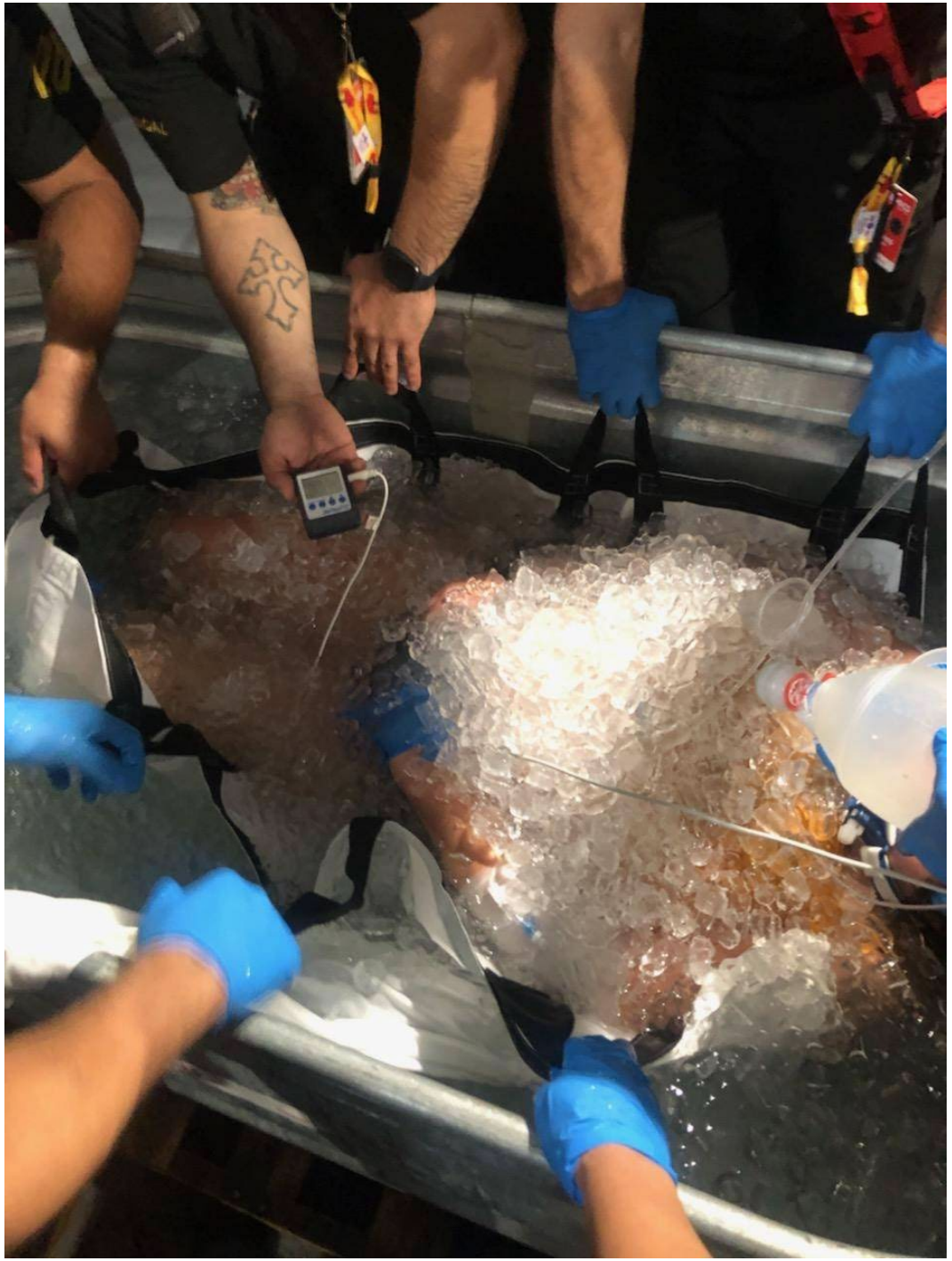

*Casa DJ, et. al. Med Sci Sports Exerc. 2010 PMID:20559063.*

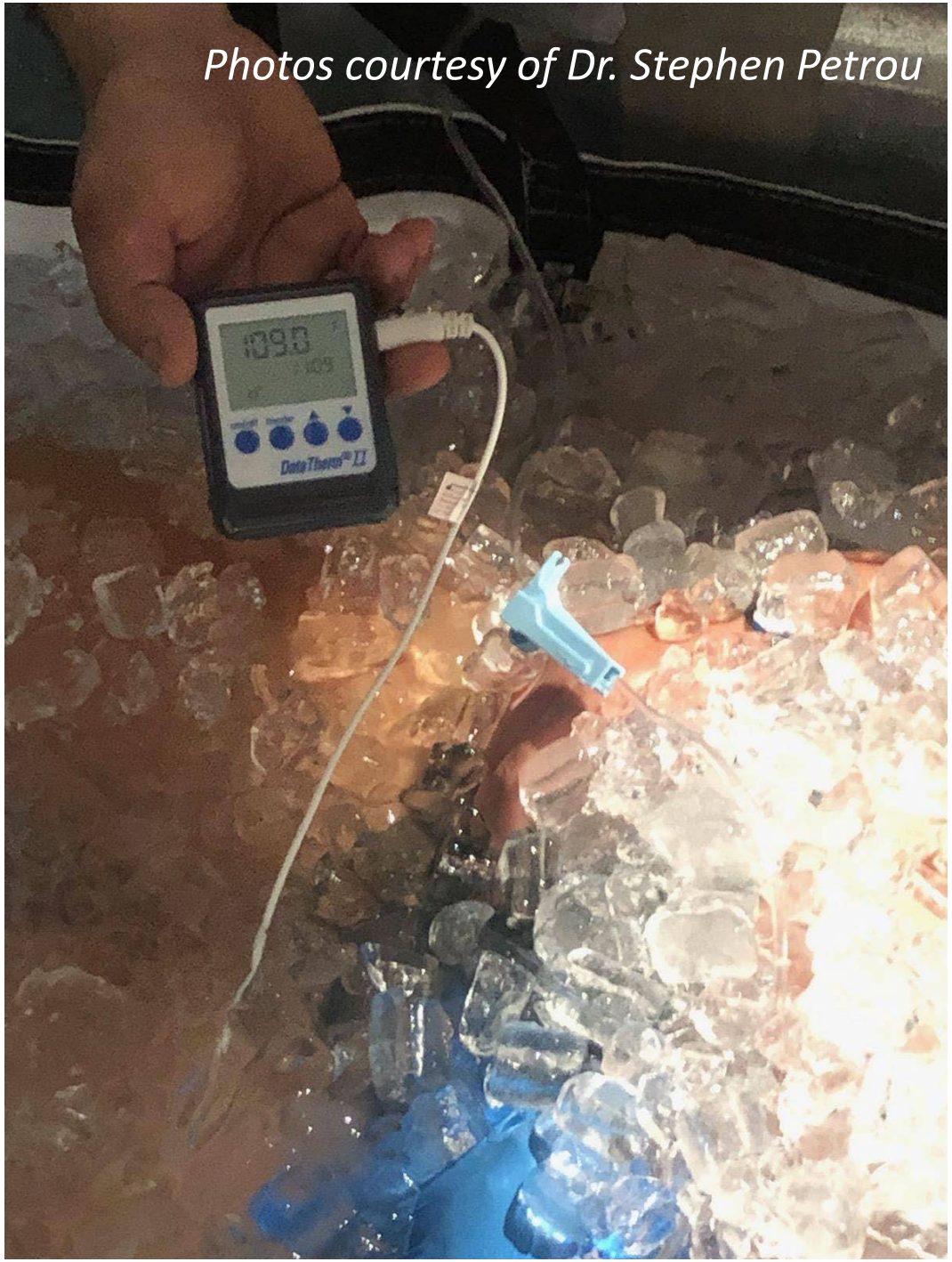
# Heat Stroke – Management

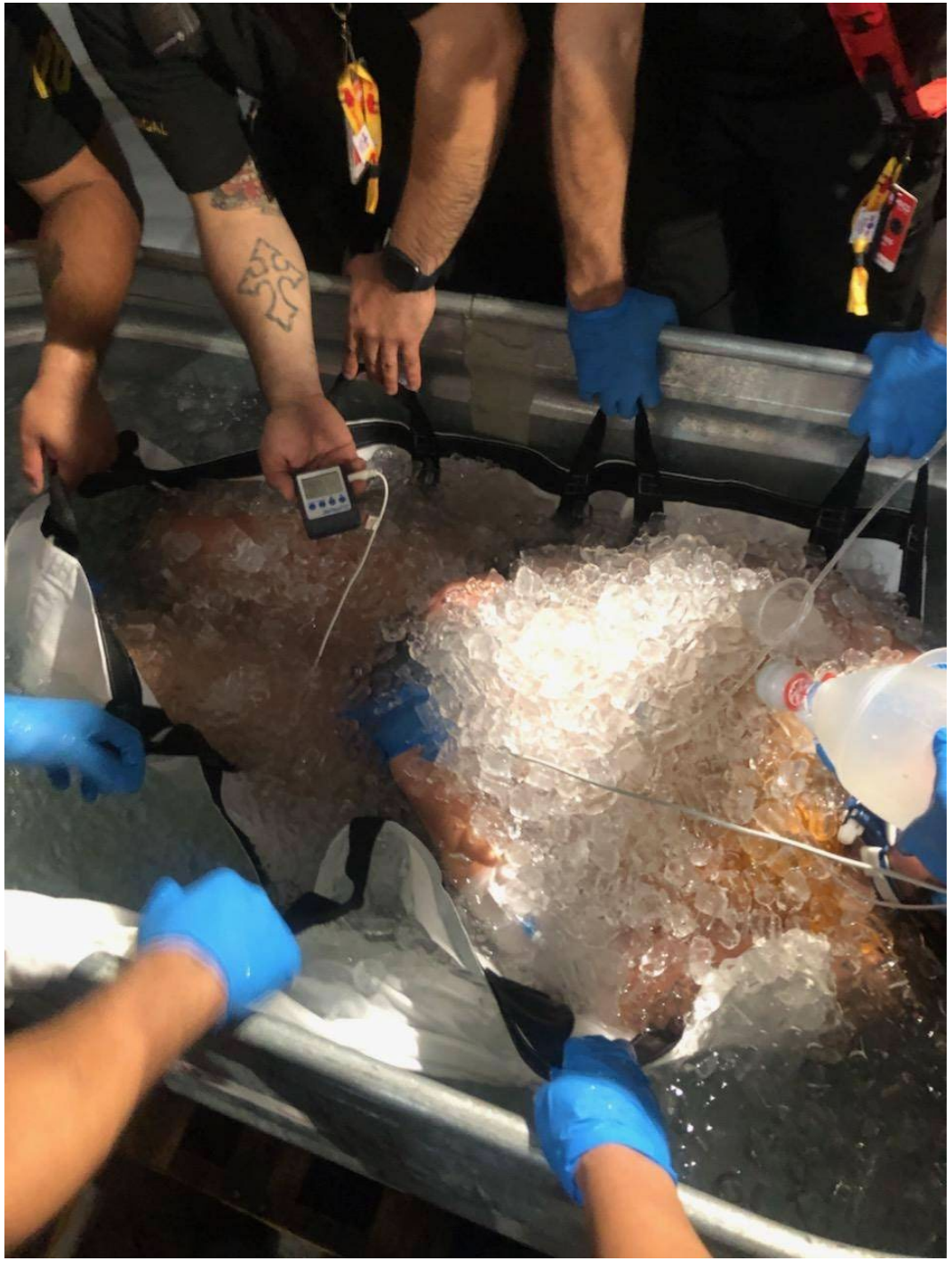
- Target = 39°C (102.2°F)
- Within 30 minutes
- **Ideally within 15 minutes!!**




***Adapted from McDermott et. al, Journal of athletic training, 2009***




Photos courtesy of Dr. Stephen Petrou




*Photos courtesy of Dr. Stephen Petrou*


Photos courtesy of Dr. Stephen Petrou

GENERAL MEDICINE/ORIGINAL RESEARCH

# Tarp-Assisted Cooling as a Method of Whole-Body Cooling in Hyperthermic Individuals

Yuri Hosokawa, PhD, ATC*; William M. Adams, PhD, ATC; Luke N. Belval, MS, ATC; Lesley W. Vandermark, PhD, ATC; Douglas J. Casa, PhD, ATC

*Corresponding Author. E-mail: yuri.hosokawa@uconn.edu, Twitter: @K_S_Institute.

**Cooling Rate = 0.17°C/min**

Tarp Assisted Cooling with Oscillation (TACO)

# Hyperthermia – Summary

- Drug induced hyperthermia is a life-threatening emergency.
- Defined by core body temp > 40°C **and** CNS dysfunction.
- Both modifiable and non-modifiable risk factors play a role in its development.
- Reduction in temp to **39°C** within **30 minutes** is critical.
- Cold water immersion is the most effective means of rapid cooling and can be practically implemented in both prehospital and clinical setting.
- Acetaminophen is ineffective for heat stroke.

# Case #2 Hypotension and Bradycardia

- 16-year-old female presents one hour after an intentional overdose of of an antihypertensive medication.
- Vital Signs: BP 73/50, HR 65, RR 18, O2 sat 98%

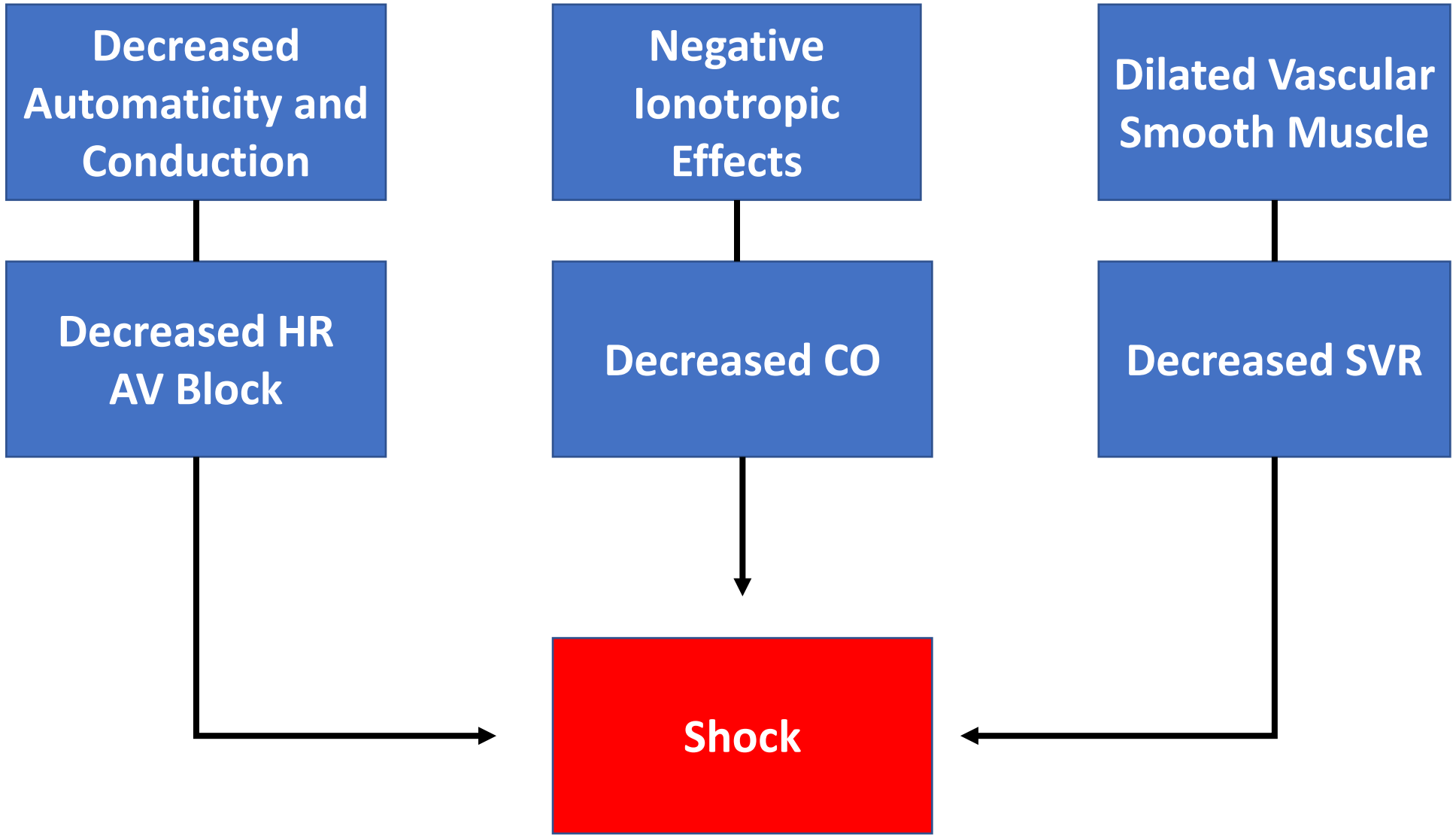
# Toxicology DDx Hypotension and Bradycardia

- ABCD'S
  - A – Alpha 2 agonists (e.g. clonidine)
  - B – Beta Blockers
  - C – Calcium channel blockers
  - D – Digoxin
  - S – Sedative Hypnotics

# Hypotension and Bradycardia

- 16-year-old female presents one hour after an intentional overdose of of an antihypertensive medication.
- Vital Signs: BP 83/50, HR 65, RR 18, O2 sat 98%
- Further history – She ingested verapamil.

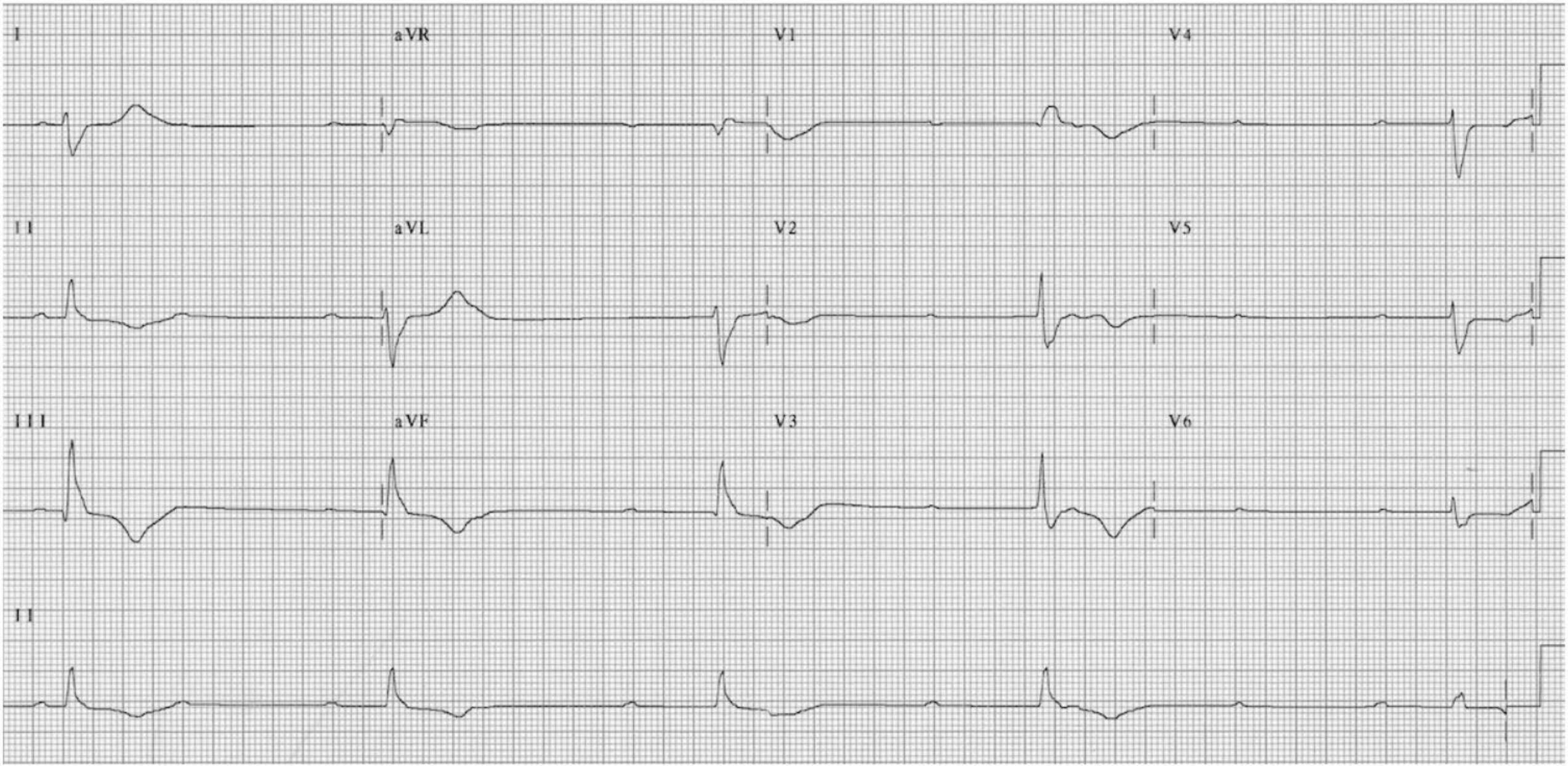
# Calcium Channel Blocker Toxicity

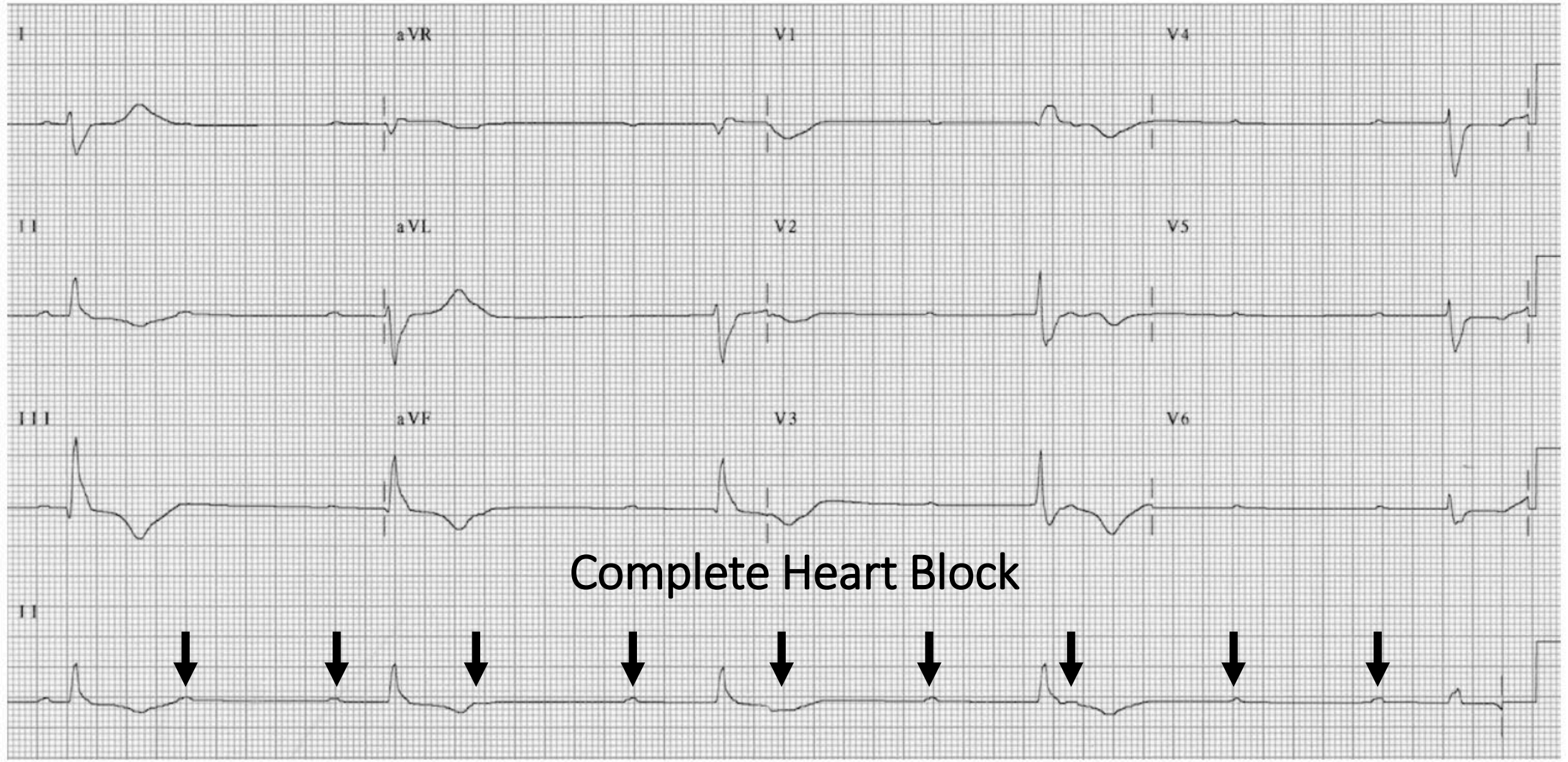


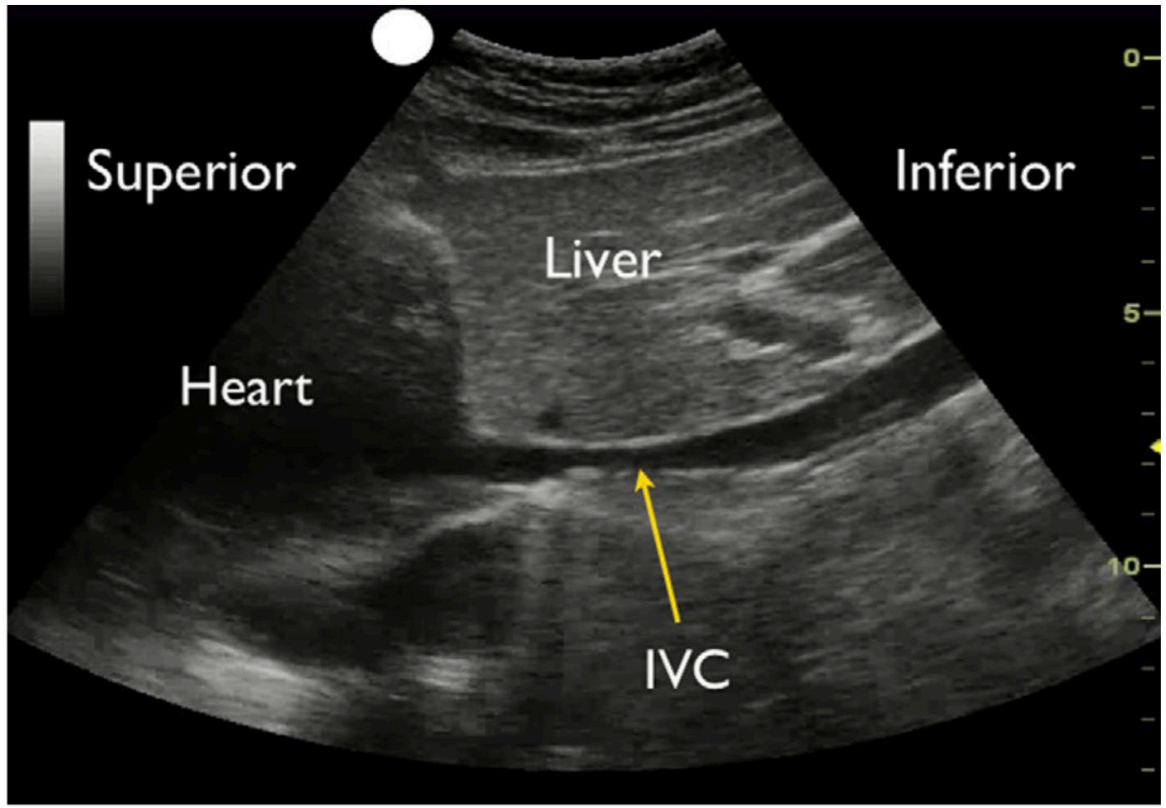
# First Line Treatments and Desired Effects

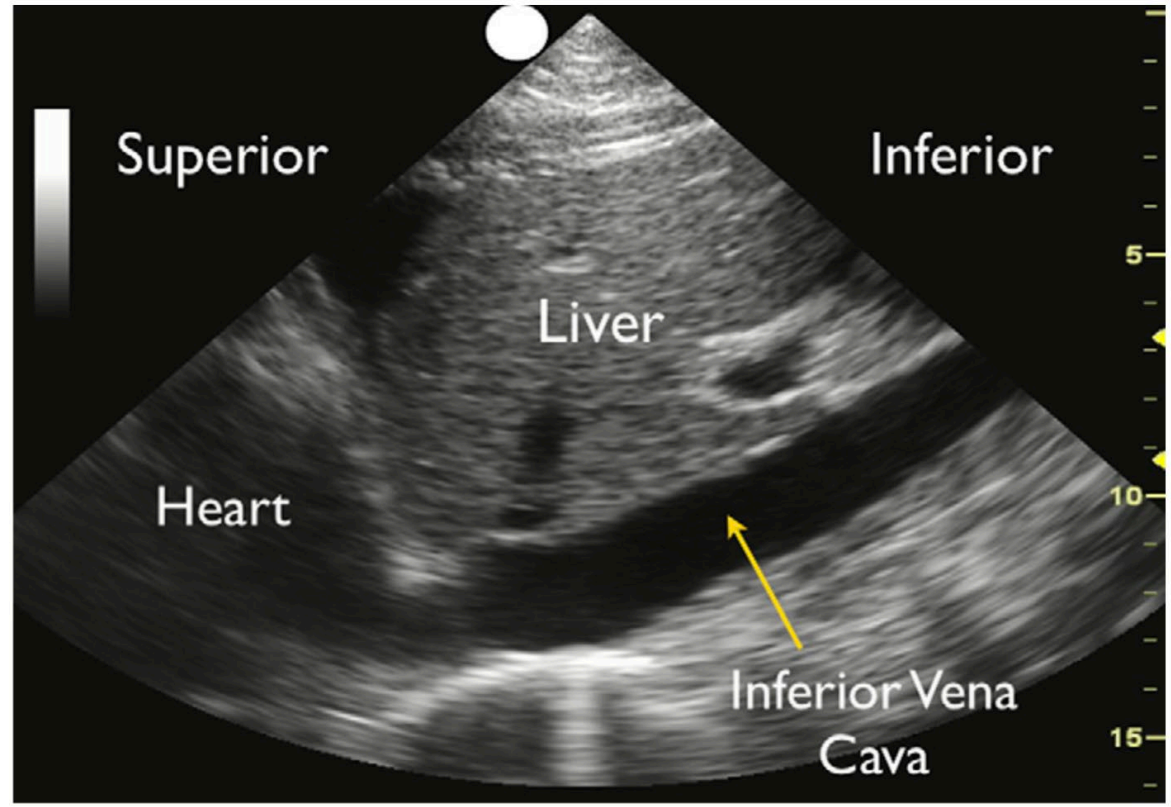
| Treatment | Desired Effect |
|---|---|
| Intravenous Fluids | Intravascular volume repletion, increase blood pressure |
| Intravenous Calcium | Increase cardiac contractility, increase blood pressure |
| Vasopressors<br>Norepinephrine<br>Epinephrine<br>Dobutamine | <br>Increase blood pressure<br>Increase cardiac contractility, increase heart rate<br>Increase cardiac contractility |
| High Dose Insulin with Glucose (HIE) | Increase cardiac contractility and blood pressure |
| Atropine | Increase heart rate |

*Maude et. al Critical Care Med. 2017 Mar; 45(3): e306–e315.*


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Complete Heart Block


Superior
Inferior
Liver
Heart
IVC
0
5
10


Superior
Inferior
Liver
Heart
Inferior Vena Cava
5
10
15

# Critical Care Management of Verapamil and Diltiazem Overdose With a Focus on Vasopressors: A 25-Year Experience at a Single Center

Michael Levine, MD; Steven C. Curry, MD; Angela Padilla-Jones, RN; Anne-Michelle Ruha, MD

- 48 patients with verapamil or diltiazem overdose
- IV fluids and vasopressors used almost exclusively
- Doses of vasopressors higher than usual
  - Norepinephrine 100 ug/min
  - Dopamine 100 ug/kg/min
- Many patients required more than one pressor (up to five)

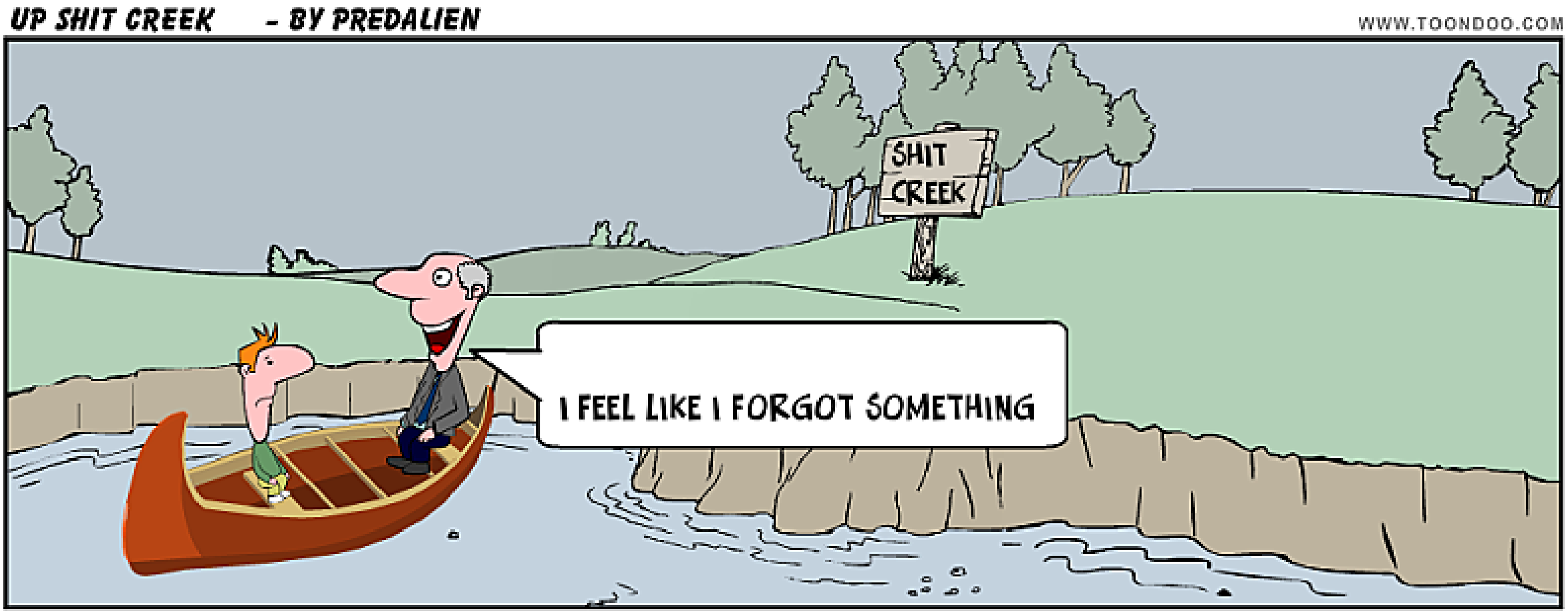
# High Dose Insulin (HIE)


- Bolus 1 unit/kg
- Start drip at 1 unit/kg/hour
- Start dextrose infusion (D10)
- Measure glucose at frequent intervals initially

# HIE Evidence?

- Case series
  - Espinoza TR, Bryant SM, Aks SE. Hyperinsulin therapy for calcium channel antagonist poisoning: A seven-year retrospective study. Am J Ther. 2013;20:29–31.
  - Boyer EW, Duic PA, Evans A. Hyperinsulinemia/euglycemia therapy for calcium channel blocker poisoning. Pediatr Emerg Care. 2002;18:36–37
  - Boyer EW, Shannon M. Treatment of calcium-channel-blocker intoxication with insulin infusion. N Engl J Med. 2001;344:1721–1722.
  - Yuan TH, Kerns WP, 2nd, Tomaszewski CA, et al. Insulin-glucose as adjunctive therapy for severe calcium channel antagonist poisoning. J Toxicol Clin Toxicol. 1999;37:463–474.
- Observational Studies
  - Bryant SM, Espinoza TR, Aks SE. Seven years of high dose insulin therapy for calcium channel antagonist poisoning. Clin Toxicol. 2009;47:751.
  - Greene SL, Gawarammana I, Wood DM, et al. Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: A prospective observational study.Intensive Care Med. 2007;33:2019–2024.
- Animal Studies

# Therapy for Patients Refractory to 1st Line Agents



# Therapy for Patients Refractory to 1st Line Agents

- “higher" dose insulin – up to 10 units/kg/hour
- Pacing
- Methylene Blue
- Intralipid
- **ECMO**

# CCB Overdose Summary

- Remember the ABCDS of hypotension and bradycardia.
- Ultrasound and can be a useful tool for directing management.
- High dose vasopressors may be necessary.
- High dose insulin therapy is also an important adjunct.
- Consider ECMO if available.

# Questions?