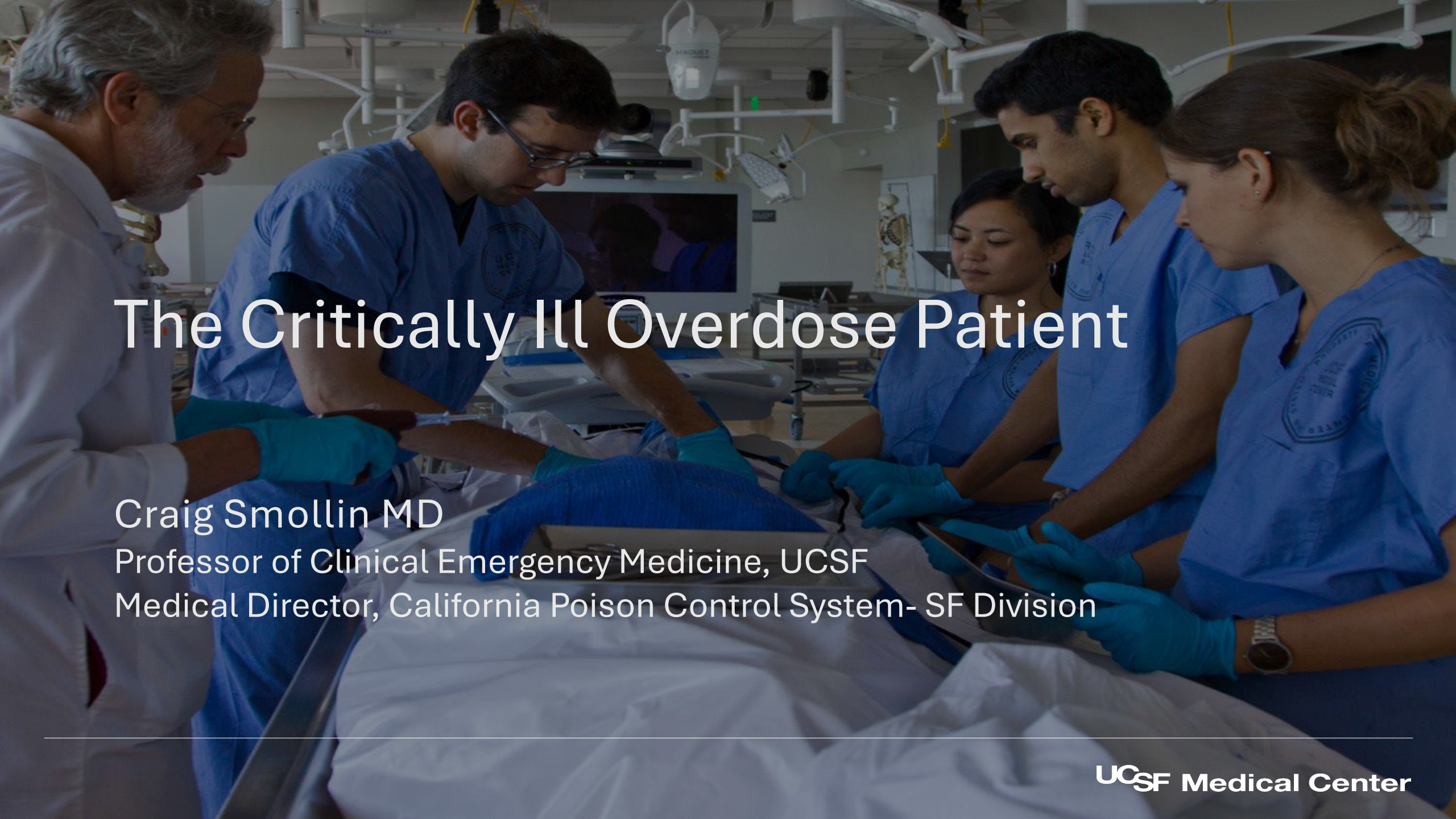


The Critically Ill Overdose Patient

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

UCSF Medical Center

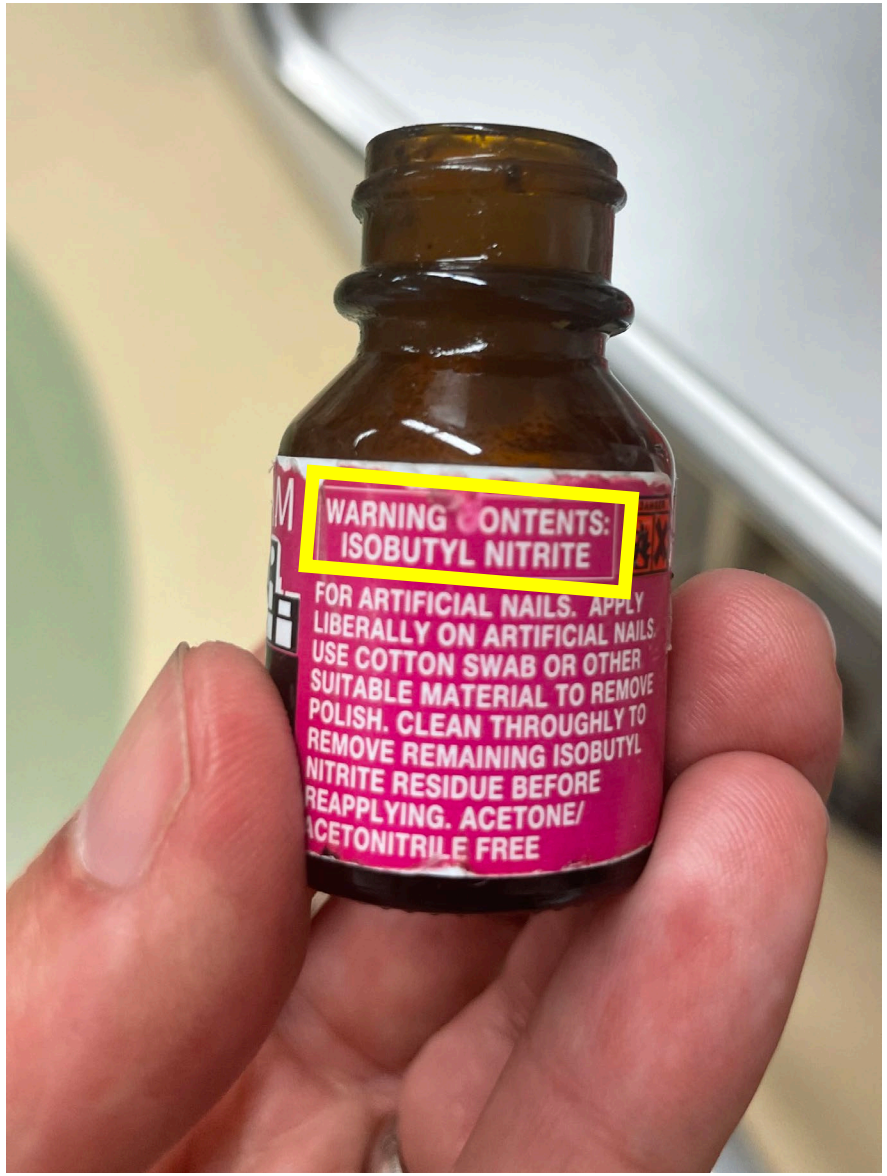
Disclosure

- I have no relevant financial relationships with the manufacturers of any commercial products discussed in this presentation.

Principles For Managing The “Sick” Poisoned Patient

- Don’t forget the ABC’s and good supportive care
- The history is often unreliable
- Collateral information is critical (What, Where, When, How?)
- Look for clues on the physical examination
- Look for clues in the laboratory data (something feels off)

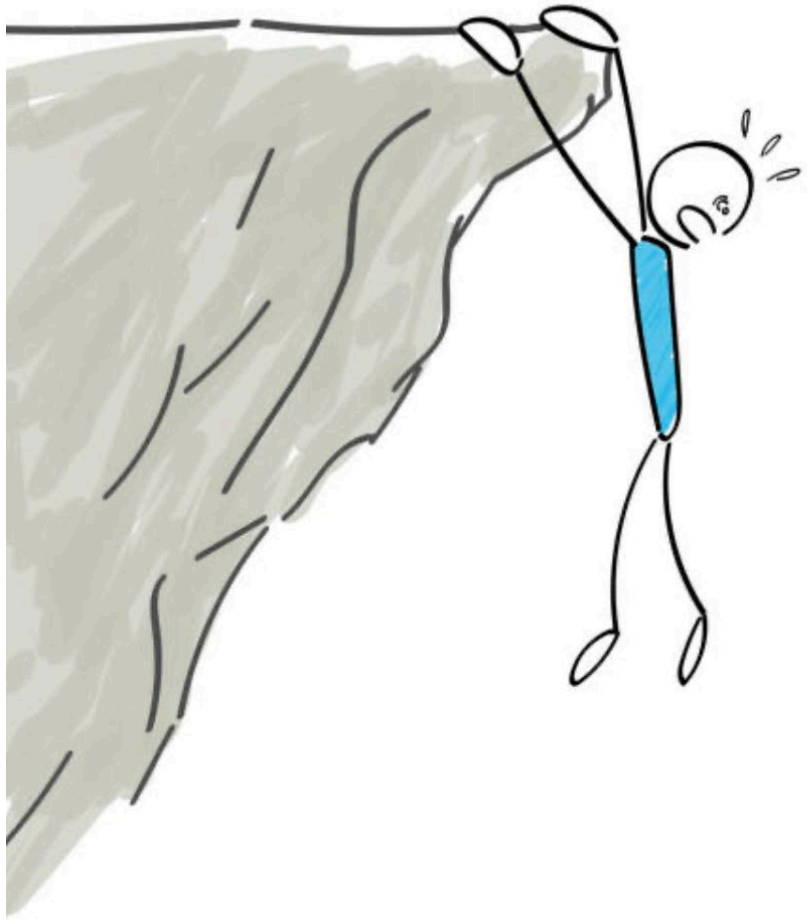

AMSTERDAM
NAIL POLISH REMOVER
Acetone/Acetonitrile Free Nail Polish
Remover/Conditioner/Adhesive Promoter
Containing Isobutyl Nitrite
For Artificial Nails.
[Food, Drug and Cosmetic Act;
and 21 United States Code §201 (q)]
Patented- US Patent # 7625532
.345 fl
/ 10 ml


WARNING CONTENTS:
ISOBUTYL NITRITE
FOR ARTIFICIAL NAILS. APPLY
LIBERALLY ON ARTIFICIAL NAILS.
USE COTTON SWAB OR OTHER
SUITABLE MATERIAL TO REMOVE
POLISH. CLEAN THROUGHLY TO
REMOVE REMAINING ISOBUTYL
NITRITE RESIDUE BEFORE
REAPPLYING. ACETONE/
ACETONITRILE FREE


AutoZone 4134
3783 S MARYLAND
LAS VEGAS, NV
(702) 836-3148
oyalty Card 910100XXXXXX0115
VDP PART 1 @ 1/209.99
VDP PARTS PO # 002619
#844584 621-071 209.99 P
621-071 Dorman
Radiatur Fan Assembly, EA
#391379 AF-2100 15.99 P
Prestone Prediluted
Antifreeze/Coo t, 1 GAL
SUBTOTAL 225.98
COURTES UNT: 10.00%
DISCOUNT AMOUNT 1.60-
DISCOUNTED SUBTOTAL 224.38
TOTAL TAX @ 8.250% 18.51
TOTAL 242.89
CASH 300.00
CHANGE 57.11
REG #02 CSR #51 RECEIPT #380285
STR- TRANS #688947
STORE #4134
DATE 06/22/2017 10:44
OF ITEMS SOLD 2

Three Crashing Toxicology Patients…

- Hyperthermia
- Acidosis
- Hypotension



Case #1 – “Hot and Bothered”

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


FREE HUGS
edc

Case #1: What would you do?

- A) Immediate intubation
- B) Tylenol 1 gram IV
- C) Start cold IV fluids
- D) Cool mist with fans
- E) Ice water bath

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

Main physiological effects of severe hyperthermia

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

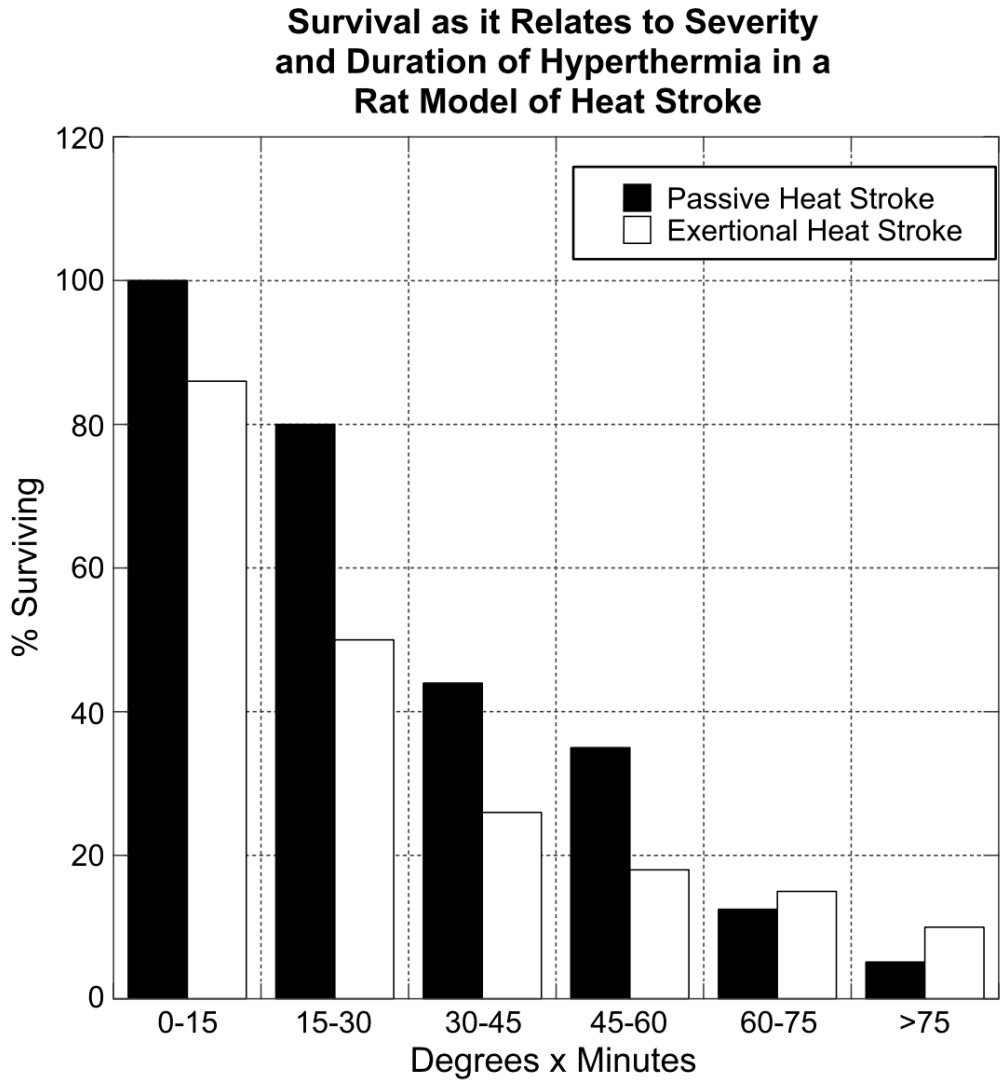
Multi-organ system dysfunction!!

Case #1 – Hot and Bothered

- Physical Exam:
  - Vitals: BP 170/100, 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 stimulus.

Hyperthermia – Management

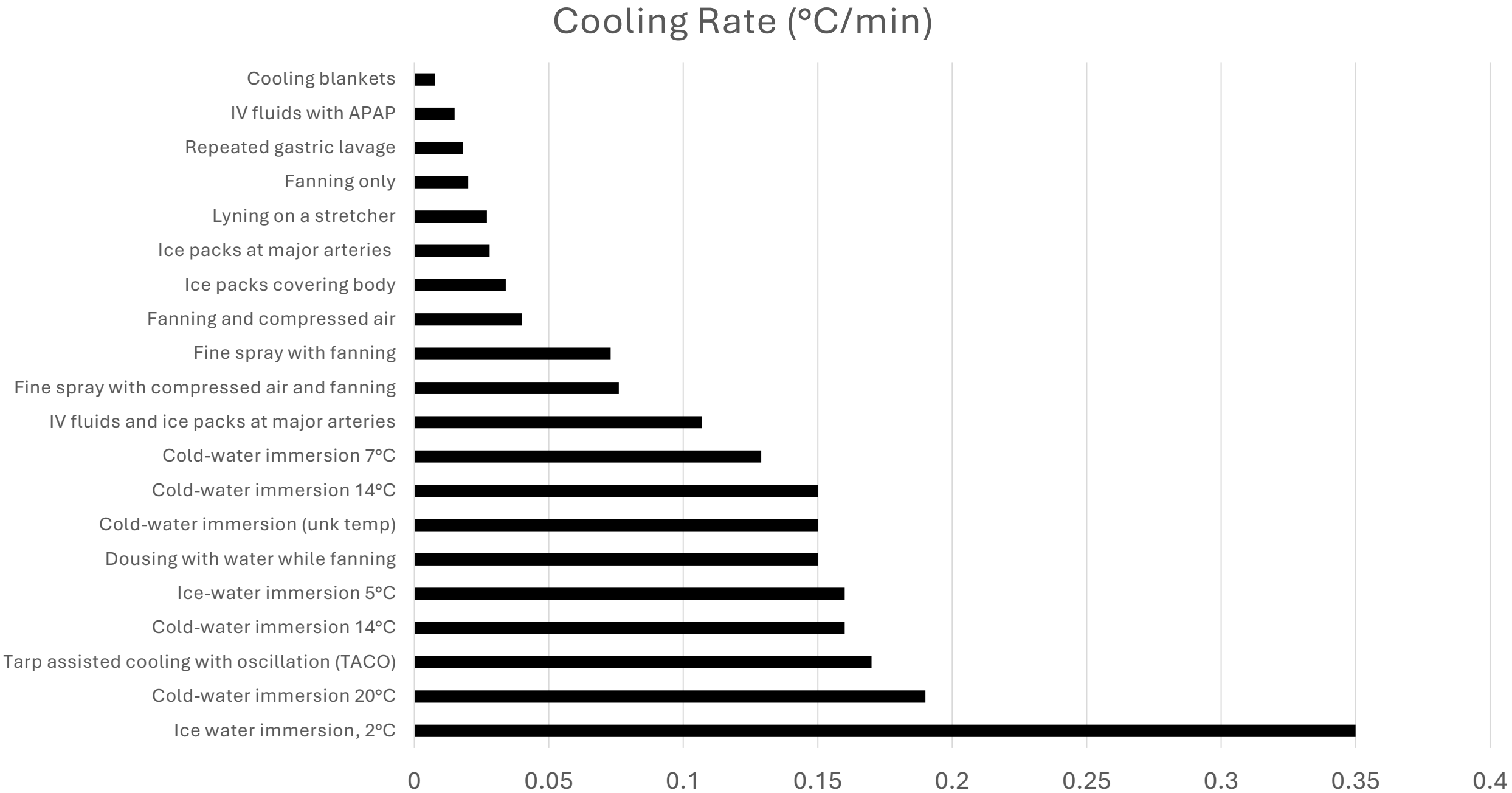
- Severity of damage is related to the degree and duration of hyperthermia.



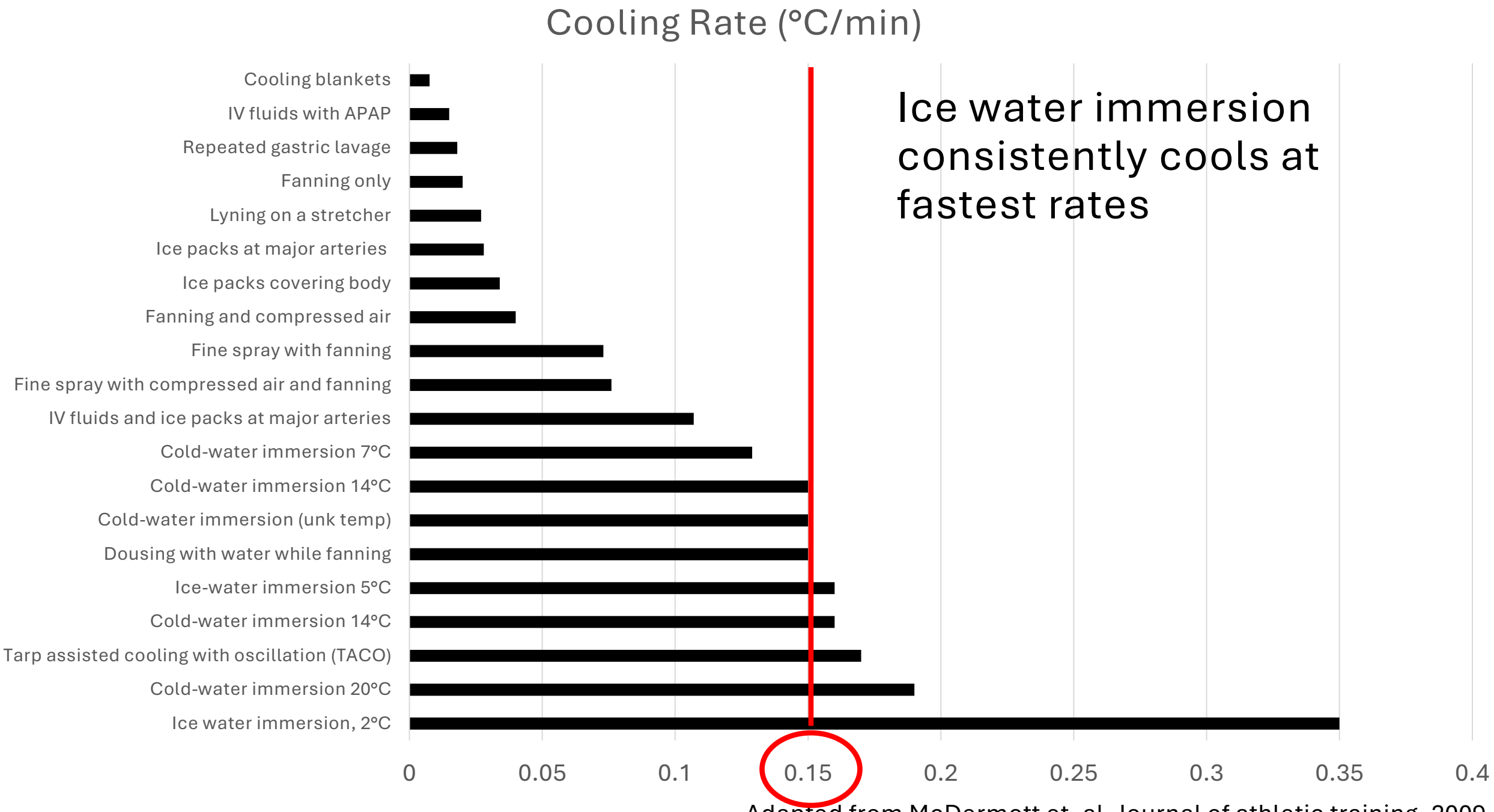
Casa DJ, et. al. Med Sci Sports Exerc. 2010 PMID:20559063.

Hyperthermia – Management

- Target = 39°C (102.2°F)
- Within 30 minutes
- Ideally within 15 minutes!!
- 0.15 °C/min

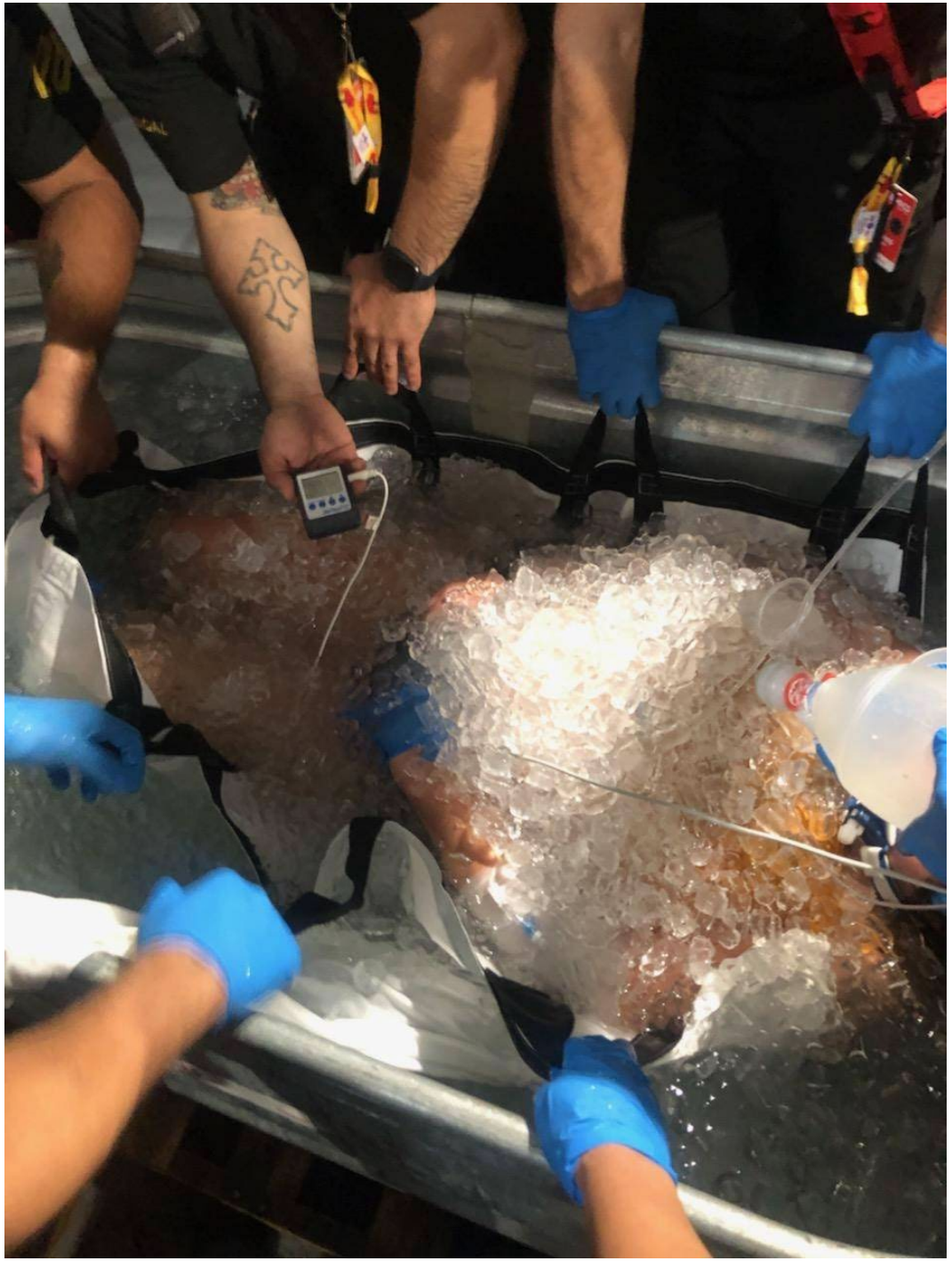


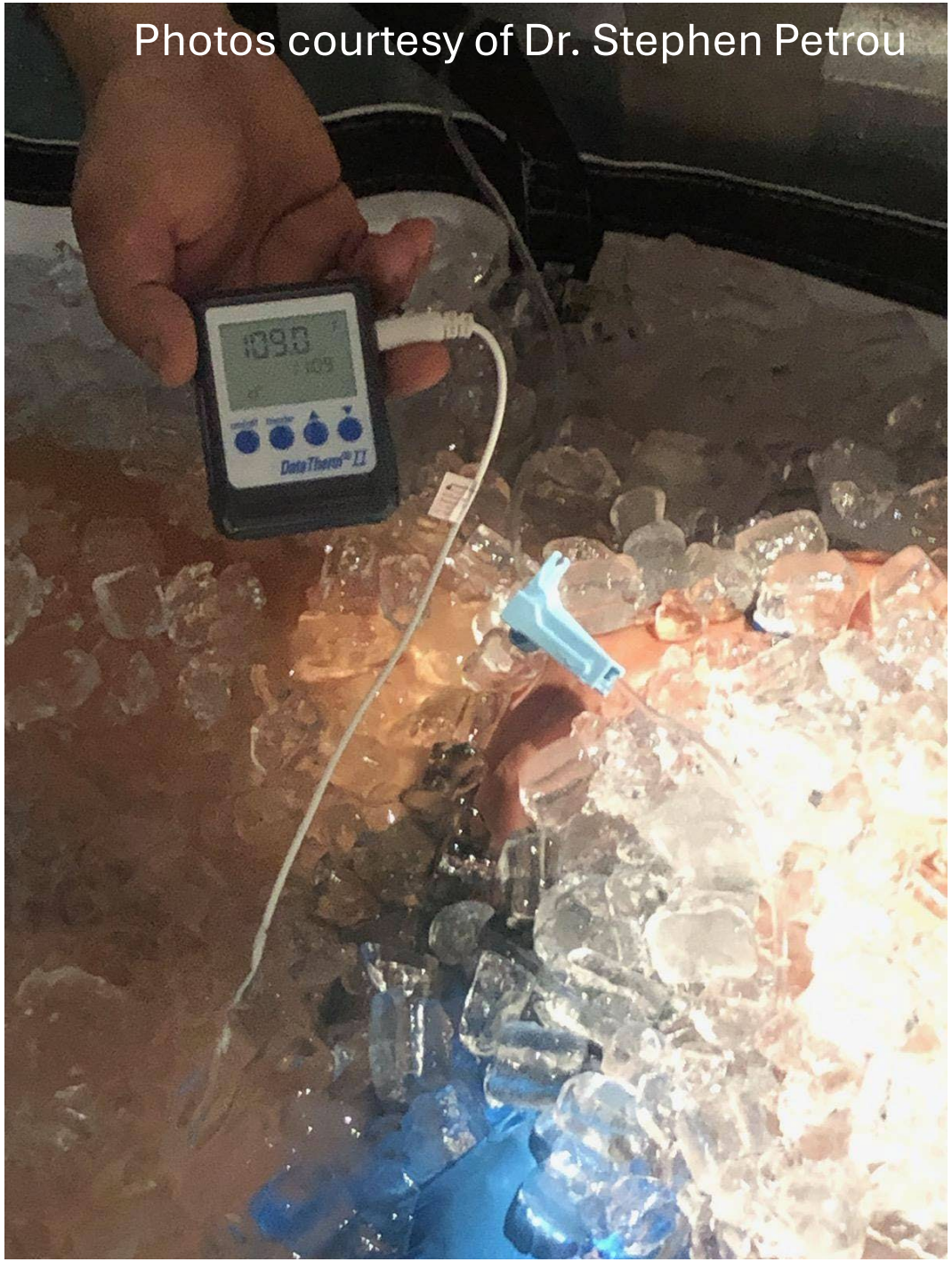
Adapted from McDermott et. al, Journal of athletic training, 2009

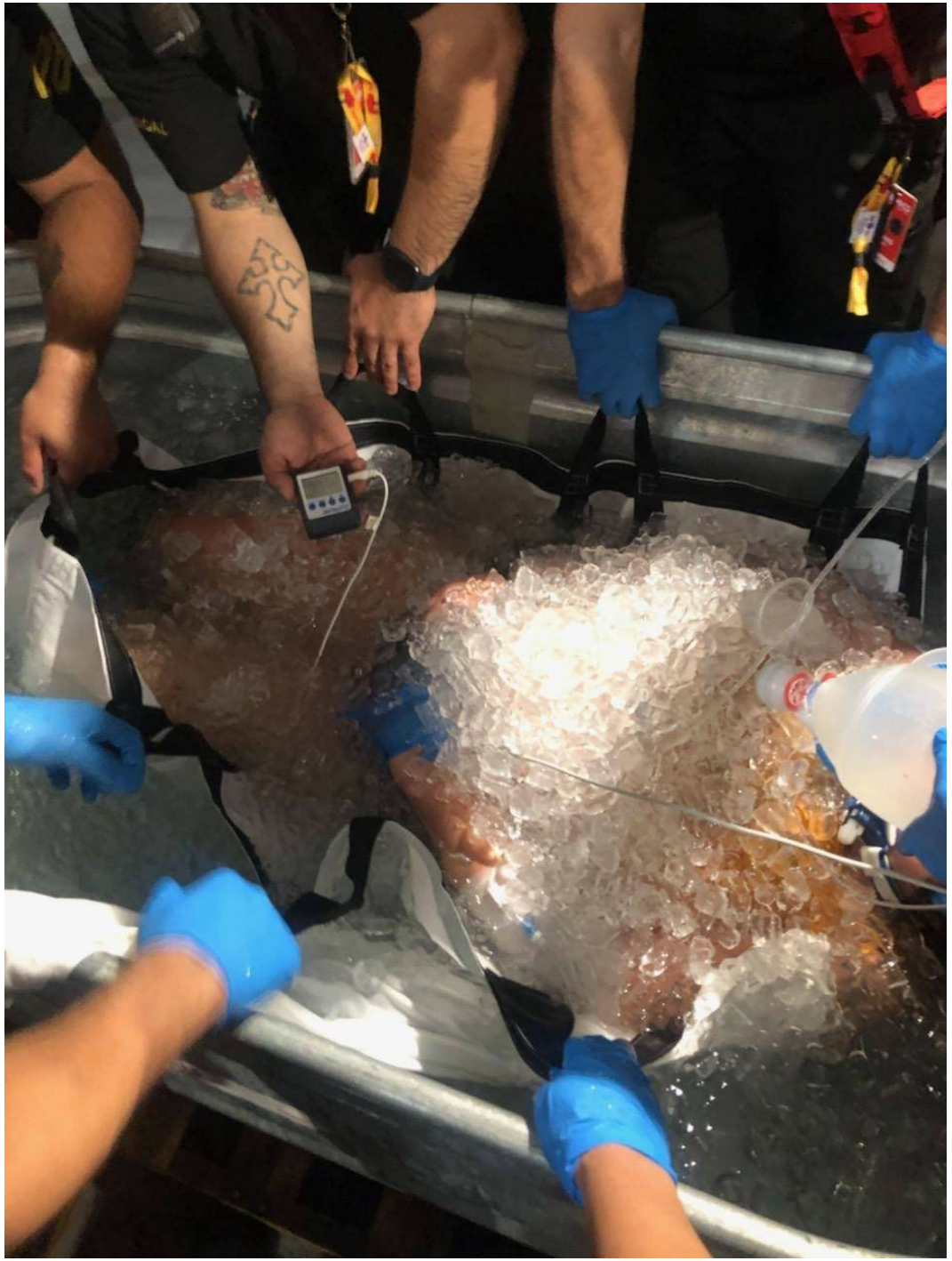


Adapted from McDermott et. al, Journal of athletic training, 2009


Photos courtesy of Dr. Stephen Petrou




Photos courtesy of Dr. Stephen Petrou




Photos courtesy of Dr. Stephen Petrou
1095
DataTherm II

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)

Malignant Hyperthermia

- Pharmacogenetic disorder (ryanodine receptor)
- Exposure to inhalation agents (halothane, isoflurane, sevoflurane etc.)
- And…succinylcholine (depolarizing neuromuscular blockers)
- Key clinical features: elevation of ETCO2, muscle rigidity, rhabdomyolysis, hyperthermia, tachycardia, acidosis and hyperkalemia.
- Mortality of 80% without treatment → Give Dantrolene!

Toxin Induced Life Threatening Hyperthermia Pearls

- Supportive Care
- Benzodiazepines for agitation
- Intubation and paralysis
- Cold water/ice water emersion
- Temperature goal 39 °C within 15-30 minutes

Case #2: Profound Acidosis

- 36-year-old female was found in a hotel room with acute intoxication.
- Initial Vital Signs: HR 95 bpm, BP 131/77, RR 27, O2 Sat 100% Temp 97.5.
- Physical Exam: GCS 8, Lungs clear, Heart normal
- VBG: pH 7.02, pCO2 20

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Case #2: What would you do?

- A) Immediate intubation (“GCS 8 intubate”)
- B) Start sodium bicarbonate drip (”Base neutralizes acid”)
- C) Start broad spectrum antibiotics and call the ICU
- D) Send every laboratory test you can think of
- E) All of the above

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- Physical Exam: GCS 8, Lungs clear, Heart normal
- VBG: pH 7.02, pCO2 20
- Labs: Na 142, K 4.3, Cl 113, HCO3 6, BUN9, Cr 1.04, Gluc 120, AG = 27

The "KULTO" of Anion Gap Acidosis

Ketones	Uremia	Lactate	Toxic Alcohol	Organic Acids
Alcoholic Ketoacidosis Diabetic Ketoacidosis Starvation Ketosis Salicylates Isopropyl alcohol	Renal Failure	Metformin Isoniazid Cyanide Carbon Monoxide Beta Agonists Un-couplers Dinitrophenol Salicylates NRTIs Non-tox: Sepsis hypoperfusion Others	Ethylene Glycol Methanol Rare alcohols (glycols)	Pyroglutamic Acid (APAP) Inborn errors of metabolism
SEND KETONES	CHECK RENAL FUNCTION	CHECK LACTATE	SUROGATE MARKERS SEND LEVELS	THINK ABOUT IT SEND APAP

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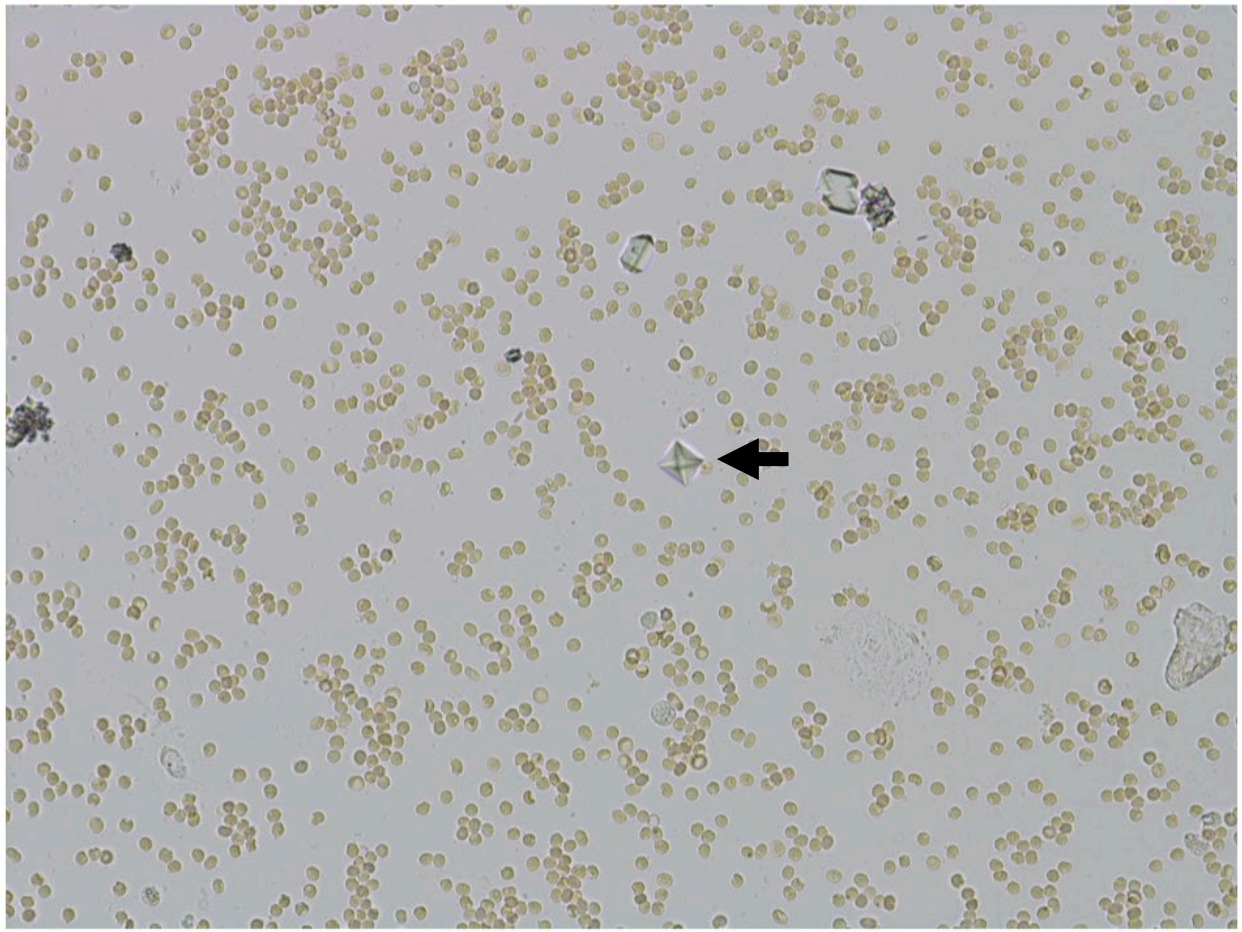
- VBG: pH 7.02, pCO2 20
- Labs: Na 142, K 4.3, Cl 113, HCO3 6, BUN9, Cr 1.04, Gluc 120, AG = 27
- Additional Labs:
  - Lactate - 5 mmol/L
  - Ketone – undetectable
  - Ethanol - negative
  - Serum Osm – 350
  - Measured Osm – 294

The “KULTO” of Anion Gap Acidosis

Ketones	Uremia	Lactate	Toxic Alcohol	Organic Acids
Alcoholic Ketoacidosis Diabetic Ketoacidosis Starvation Ketosis Salicylates Isopropyl alcohol	Renal Failure	Metformin Isoniazid Cyanide Carbon Monoxide Beta Agonists Un-couplers Dinitrophenol Salicylates NRTIs Non-tox: Sepsis hypoperfusion Others	Ethylene Glycol Methanol Rare alcohols (glycols)	Pyroglutamic Acid (APAP) Inborn errors of metabolism
SEND KETONES	CHECK RENAL FUNCTION	CHECK LACTATE	SUROGATE MARKERS SEND LEVELS	THINK ABOUT IT SEND APAP

Surrogate Markers



Surrogate Markers – Osmolar Gap

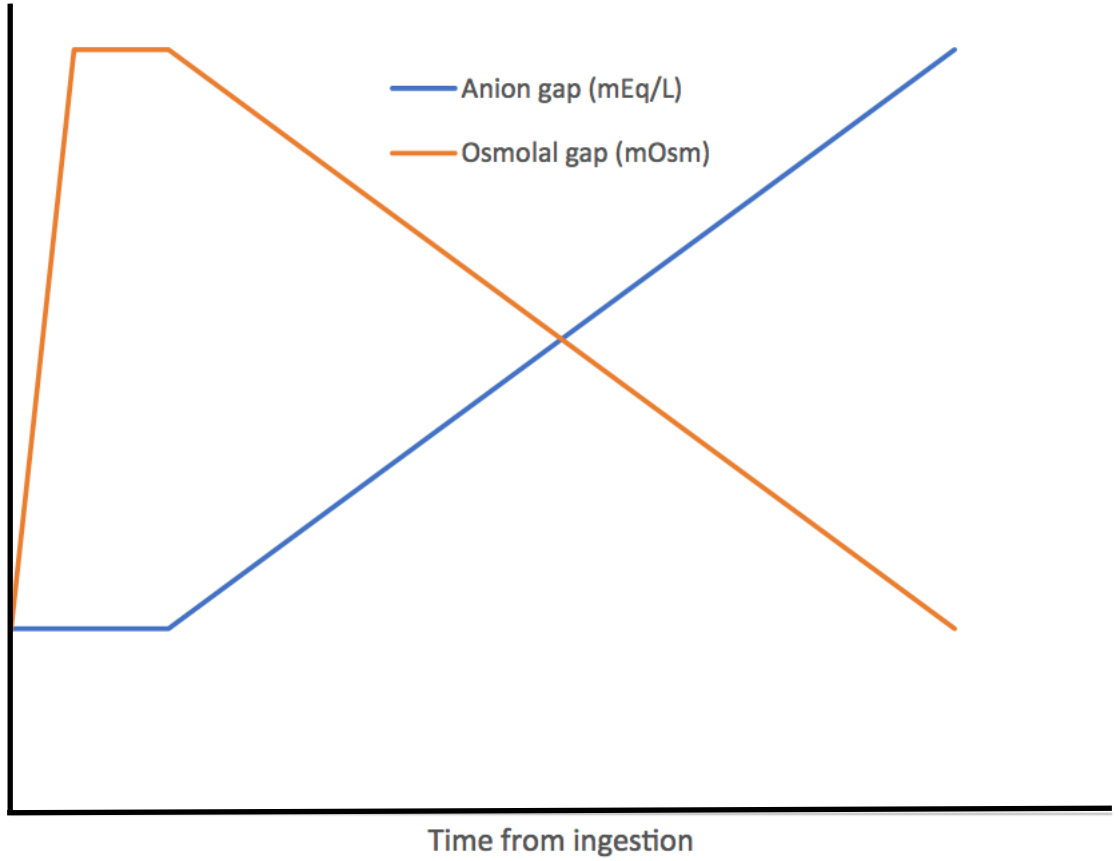


Fig. 3 Osmolal gap and anion gap in toxic alcohol poisoning

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- VBG: pH 7.02, pCO2 20
- Labs: Na 142, K 4.3, Cl 113, HCO3 6, BUN9, Cr 1.04, Gluc 120, AG = 27
- Additional Labs:
  - Lactate - 5 mmol/L
  - Ketone – undetectable
  - Ethanol - negative
  - Serum Osm – 350
  - Measured Osm – 294

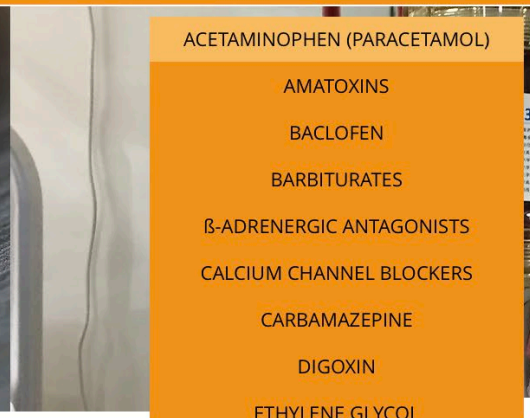
Management of toxic alcohols

- Supportive care
- Administer blocking agents
  - Fomepizole – Loading dose 15 mg/kg (up to 1.5 grams)
  - Ethanol
- Hemodialysis

EXTRIP

THE EXTRACORPOREAL TREATMENTS IN POISONING WORKGROUP

Blood Purification in Toxicology: *Reviewing the Evidence and Providing Recommendations*



- ACETAMINOPHEN (PARACETAMOL)
- AMATOXINS
- BACLOFEN
- BARBITURATES
- ß-ADRENERGIC ANTAGONISTS
- CALCIUM CHANNEL BLOCKERS
- CARBAMAZEPINE
- DIGOXIN
- ETHYLENE GLYCOL
- GABAPENTIN / PREGABALIN
- ISONIAZID
- LITHIUM
- METFORMIN
- METHANOL
- METHOTREXATE
- PHENYTOIN
- QUININE / CHLOROQUINE
- SALICYLATES
- THALLIUM
- THEOPHYLLINE
- TRICYCLIC ANTIDEPRESSANTS
- VALPROIC ACID

Newsflash: New EX olished!

202

20

2021: Baclofen, Isoniazid, ß-adr ntin / Pregabalin

2020: Calcium Chan quine

Pending

Posts from @ExtripWorkgroup

Nothing to see here - yet

When they post, their posts will show up here.

Profound Acidosis and Toxic Alcohols Pearls

- Calculate the anion gap
- Use “KULTO” to narrow the differential diagnosis
- Think toxic alcohols when ketones and lactate are normal in the setting of profound acidosis
- Treat with blocking agents and hemodialysis

Case #3: 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%

Case #3: 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%

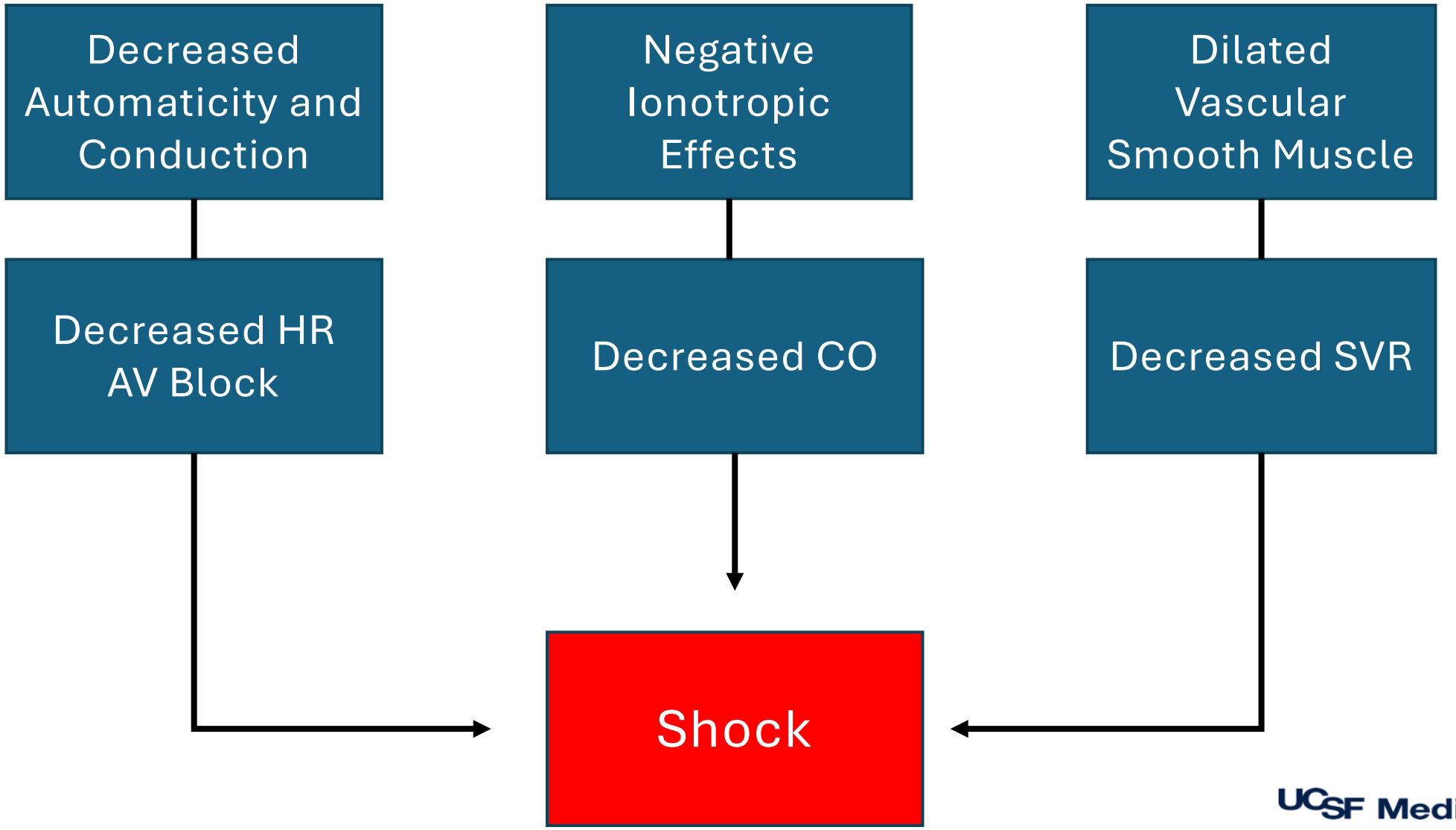
Toxicology DDx Hypotension and Bradycardia

- 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.

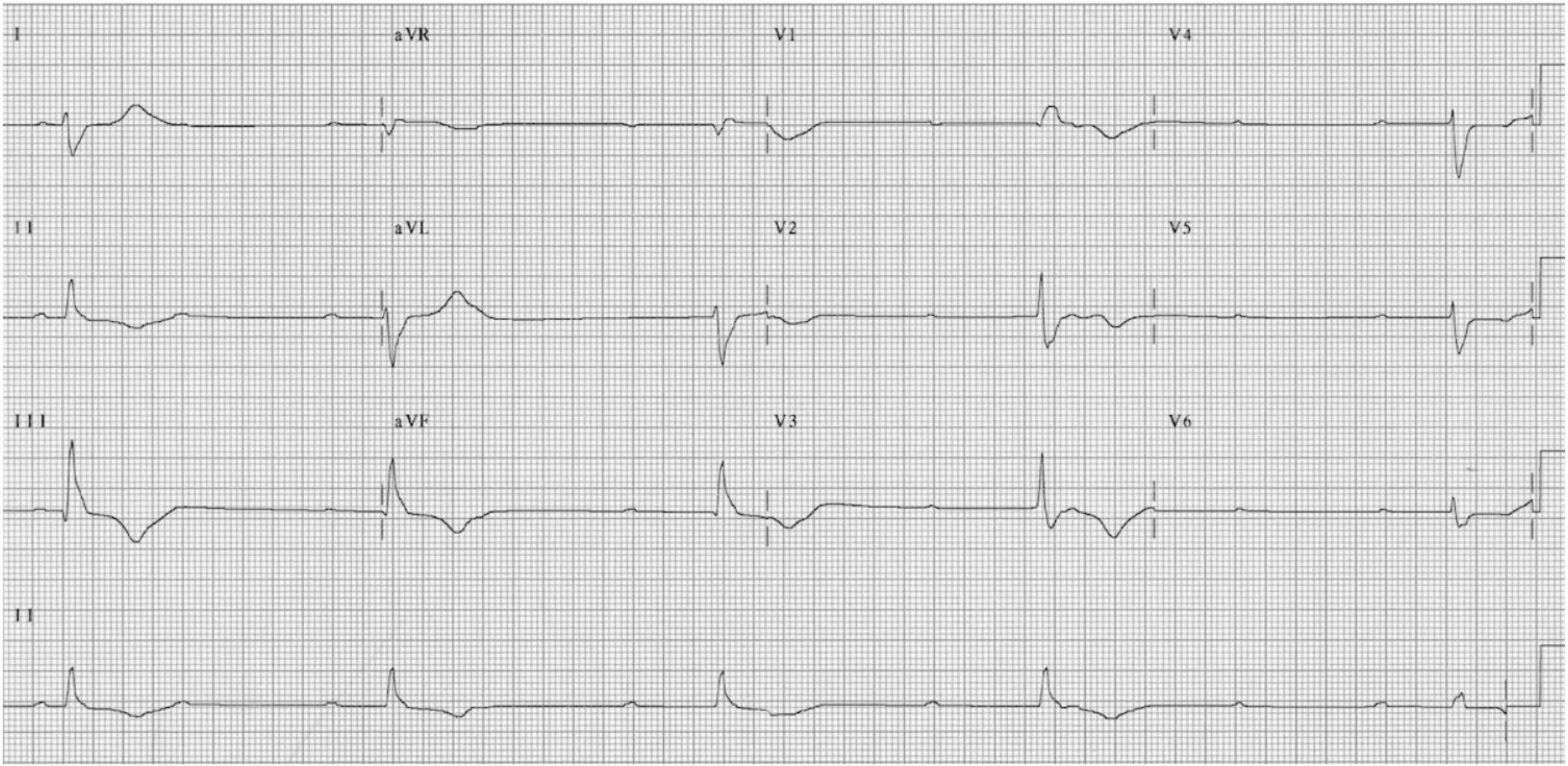
Calcium Channel Blocker Toxicity

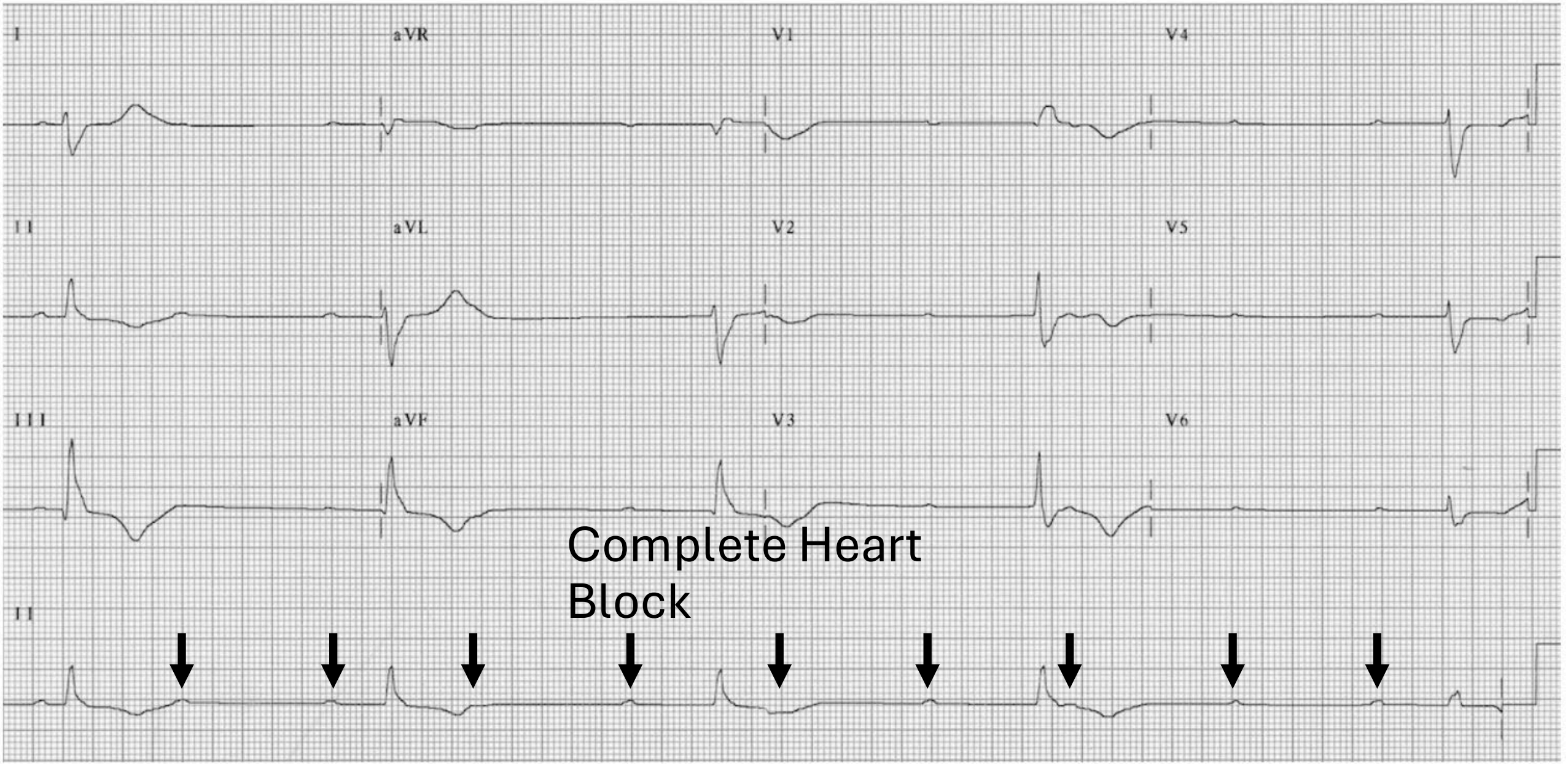


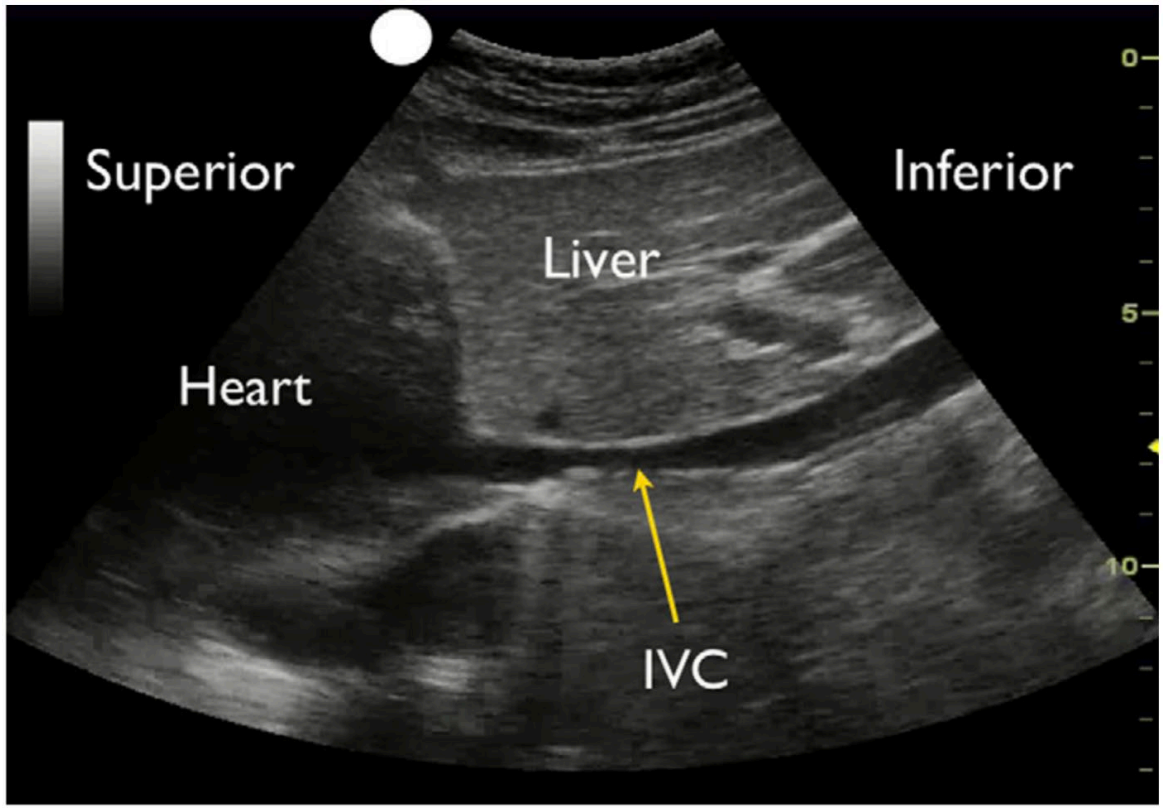
First Line Treatments and Desired Effects

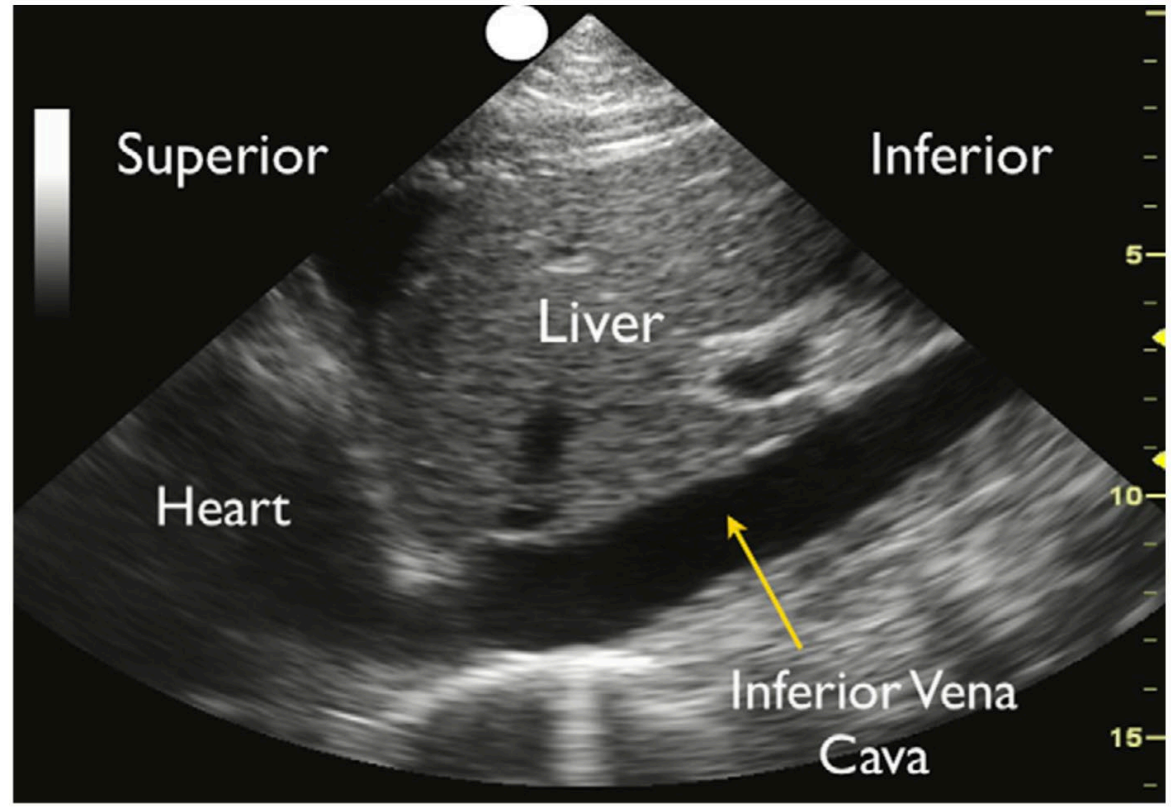
Treatment	Desired Effect
Intravenous Fluids	Intravascular volume repletion, increase blood pressure
Intravenous Calcium	Increase cardiac contractility, increase blood pressure
Vasopressors Norepinephrine Epinephrine Dobutamine	 Increase blood pressure Increase cardiac contractility, increase heart rate 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)

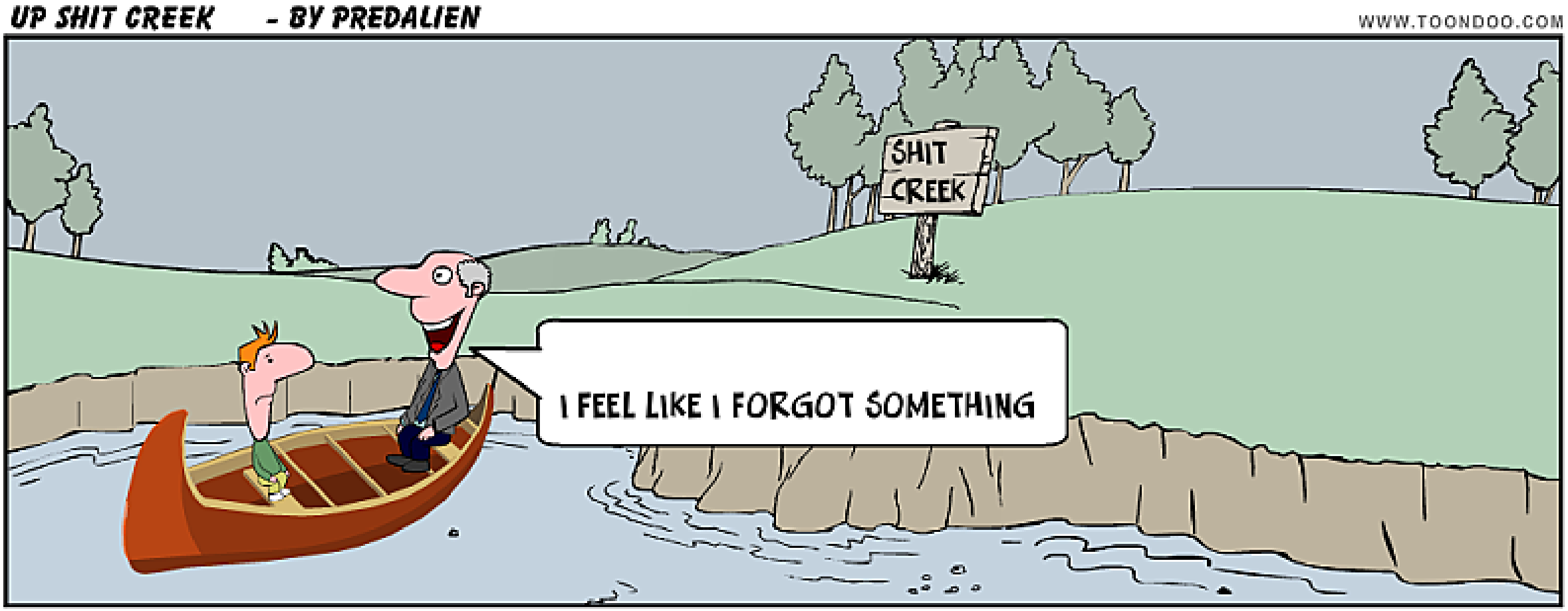
High Dose Insulin (HIE)

- 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 Pearls

- 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?