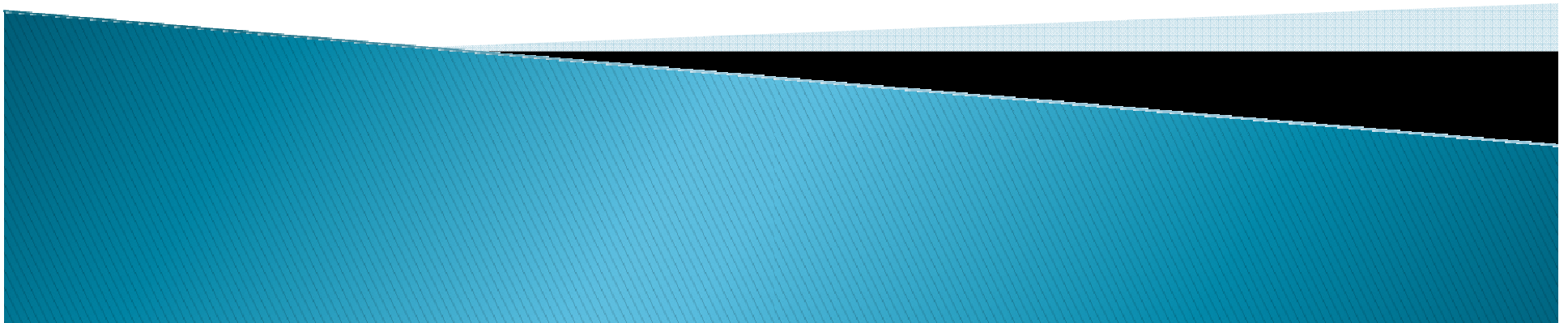


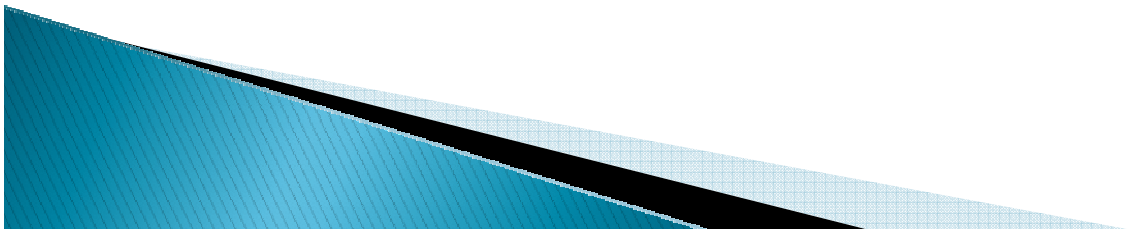
Post-Cardiac Arrest Management: Therapeutic Hypothermia

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Objectives

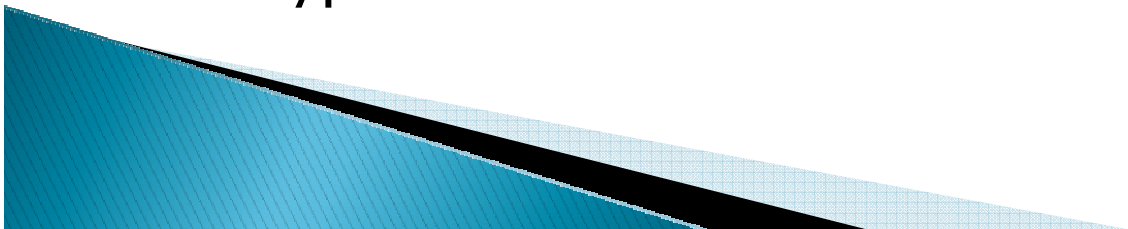
- ▶ Present a patient case and recognize indications for therapeutic hypothermia (TH) induction
- ▶ Review etiologies and goals of management in cardiac arrest
- ▶ Review the mechanisms of neuroprotection in TH
- ▶ Review inclusion/exclusion criteria for TH
- ▶ Understand the goals of the TH protocol
- ▶ Review TH adverse effects
- ▶ Review the effects on drug pharmacokinetics and pharmacodynamics



Patient Case

▶ HPI

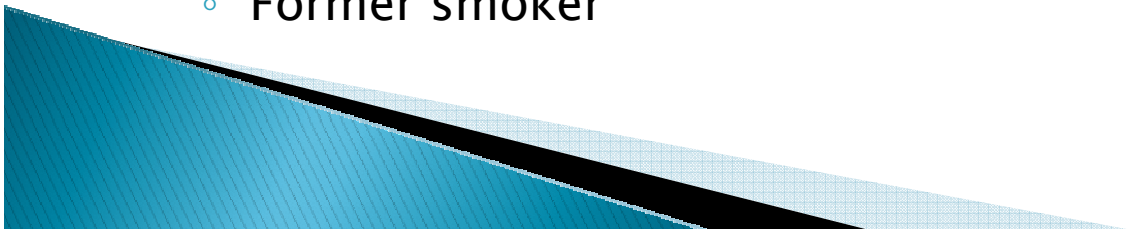
- 75 y/o female found at home down at home for at least 10 minutes on the evening of admission. Arrived at the ER and received 30 minutes of CPR. She was started on pressors before regaining a pulse. EKG showed subtle ST-segment elevation of the inferior leads. She underwent catheterization with no complications, which demonstrated 80% proximal right coronary artery stenosis and 50% eccentric left main. Post-cath she was unresponsive on no sedation and therapeutic hypothermia was then initiated.



Patient Case

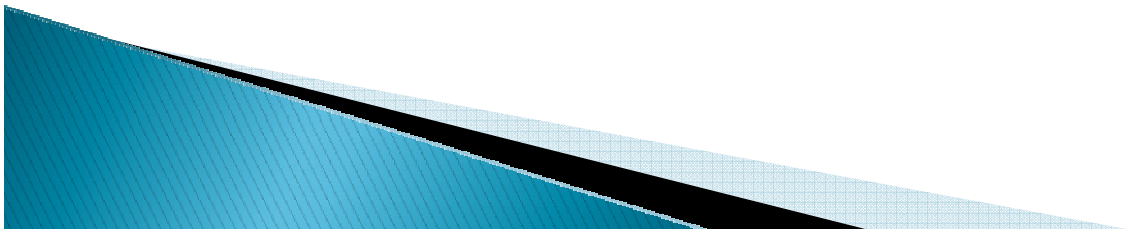
- ▶ Past Medical History
 - Paroxysmal A. Flutter s/p TEE cardioversion
 - H/O rheumatic hearts dz with moderate aortic stenosis & mild mitral stenosis
 - Hyperlipidemia
 - COPD
 - GERD
 - Esophageal Cancer s/p esophagectomy, XRT, and chemotherapy
- ▶ Family Hx
 - + coronary dz
- ▶ Social History
 - Former smoker

- Home Medications
 - Furosemide 20 mg M,W,F
 - Lipitor 40 mg daily
 - ASA 81 mg daily
 - Omeprazole 20 mg daily
 - Coumadin
 - Vit D
 - MVI



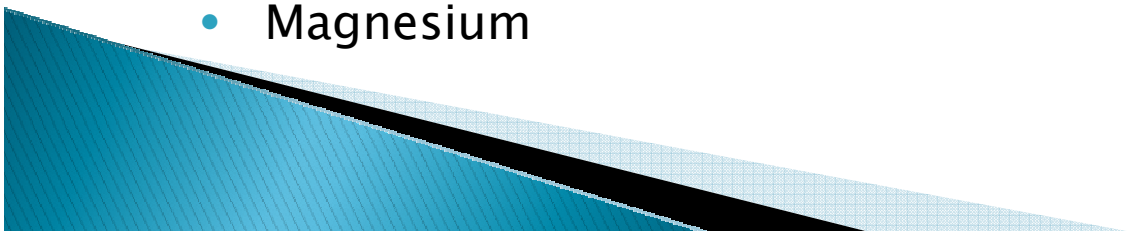
Cardiac Arrest

- ▶ Results in > 300,000 deaths in North America
 - Advancements in CPR and post-cardiac arrest care have improved outcomes
 - BLS and ACLS
- ▶ Management Goals
 - Determine and treat the cause of cardiac arrest
 - Performed concurrently with resuscitation efforts
 - Minimize brain injury
 - Most common cause of death in out-of-hospital cardiac arrest
 - Manage cardiovascular dysfunction
 - Most immediate threat to survival
 - Manage problems that may arise from global ischemia and reperfusion injury
 - Interventions to optimize blood pressure and maintain end-organ perfusion



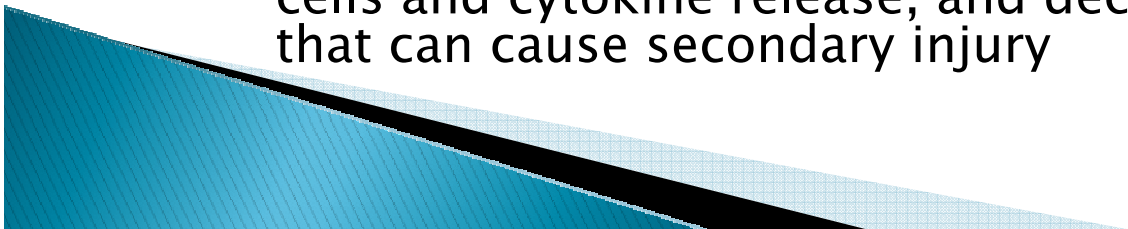
Cardiac Arrest Etiologies

- ▶ 4 H's and 4 T's
- ▶ Cardiac
 - ACS (most common)
 - Arrhythmia
 - Pericardial tamponade
- ▶ Respiratory
 - Airway Obstruction
 - Asthma/COPD exacerbation
 - PNA
 - PE
 - Tension pneumothorax
- ▶ Sepsis
- ▶ Electrolyte Disturbances
 - Potassium
 - Magnesium
- Hemorrhage and hypovolemia
 - Trauma
 - GI Bleeding
 - Abdominal aortic aneurysm rupture
 - Intracranial hemorrhage
 - Profound GI fluid loss
- Drugs and poisons
 - Opioids
 - Beta blockers
 - Calcium channel blockers
 - Benzodiazepines
 - Tricyclic antidepressants
 - Digoxin



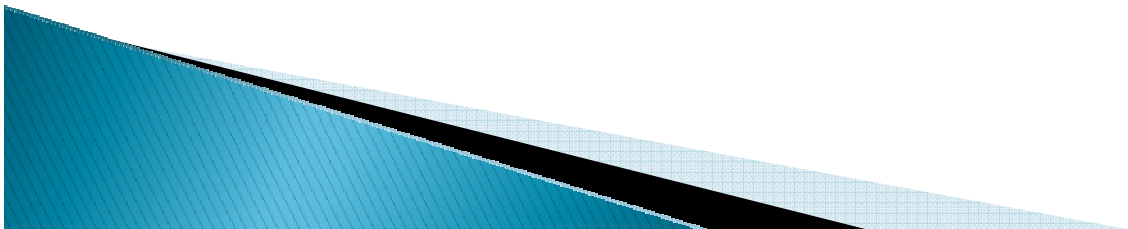
Therapeutic Hypothermia

- Indicated to prevent ischemic brain injury in post-cardiac arrest patients not following commands or showing purposeful movements following resuscitation
- Recently reported that only approximately 26% of U.S. physicians involved in resuscitating patients reported having performed it at least once
 - American Heart Association Class IIa recommendation
- Precise mechanisms of neuroprotection not well understood
 - Reduces cerebral metabolic rate and oxygen demand => decreases cerebral edema and intracranial pressure
 - May help prevent secondary ischemic injury due to impaired cerebral perfusion pressure
 - Preserves integrity of blood-brain barrier
 - Decreases glutamate release, thereby mitigating excitotoxicity
 - Decreases free radical reactions, suppresses inflammatory cells and cytokine release, and decreases enzymatic cascades that can cause secondary injury



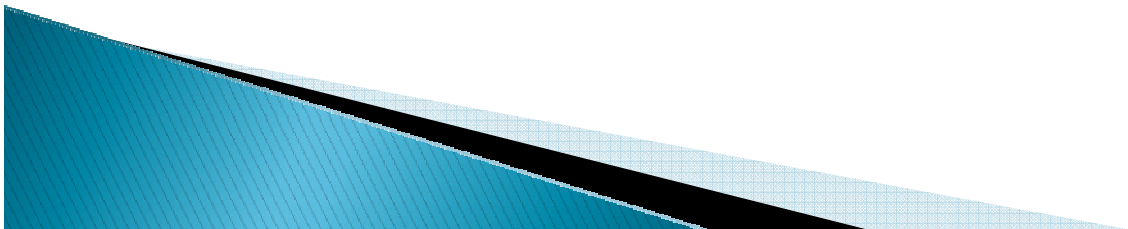
Inclusion criteria

- ▶ Witnessed primary cardiac arrest/non-traumatic cardiac arrest
- Downtime less than 15 minutes
- Comatose patients (GCS<9)
- No definite age limit (recommended ages: 18–75 y/o)
 - Pre-arrest quality of life is the important factor
- SBP > 90 with IVF or vasopressor support
- Can be used during coronary catheterization and with use of thrombolytics
 - Increased risk of bleeding



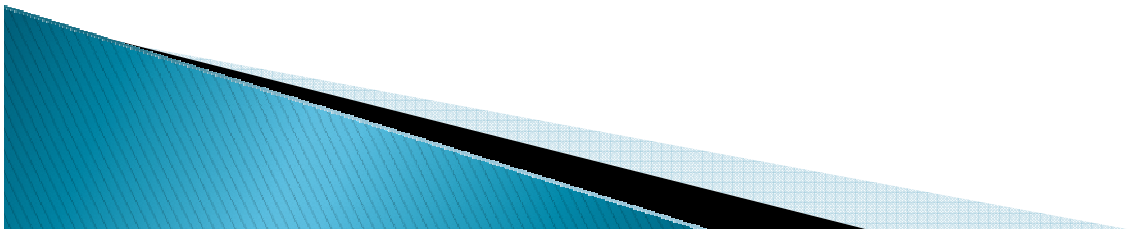
Exclusion Criteria

- ▶ Un-witnessed asystolic or un-witnessed PEA cardiac arrest
- ▶ CPR > 60 minutes from collapse to restoration of spontaneous circulation
- ▶ Refractory cardiogenic or septic shock in spite of IVF and vasopressors
- ▶ Recurrent VF or refractory VT in spite of appropriate therapy
- ▶ Severe coagulopathy with clinical evidence of bleeding
- ▶ Cardiac coma secondary to overdose or status epilepticus
- ▶ Core body temperature < 30° on admission
- ▶ Pregnancy
- ▶ Response to verbal commands following ROSC
- ▶ Hypersensitivity to hyperthermia
 - Raynaud's disease, sickle cell disease



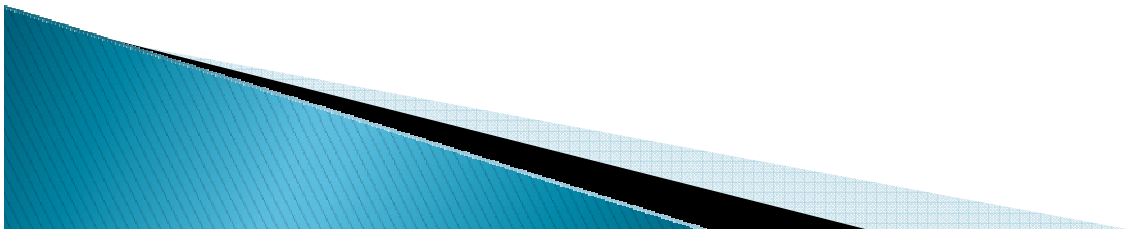
Therapeutic Hypothermia Induction

- ▶ Goal core temperature between 32 to 34°C
 - Optimal speed and ideal duration of treatment are unknown
 - Recommended to achieve goal core temperature within 6 hours and maintaining it for 12 to 24 hours
 - Memorial: achieve goal of 33° C within 3–6 hours
 - Memorial: < 30° C if unresponsive to drugs, pacers, or defibrillator



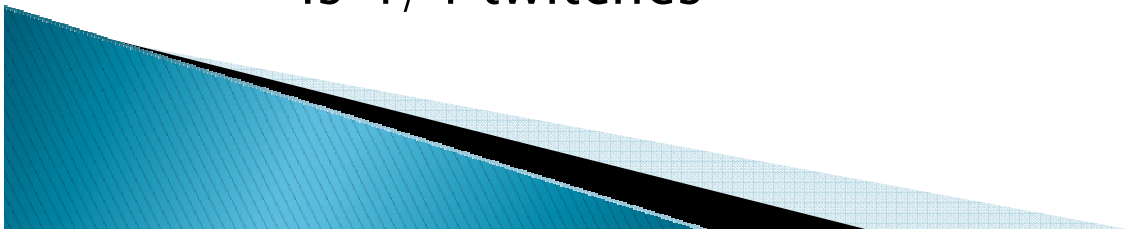
Therapeutic Hypothermia Rewarming

- ▶ Passive rewarming 12–24 hours after achieving targeted core temperature
 - No greater than 0.5 degrees per hour
 - Minimum of 8 hours
 - Maximum of 16 hours
- ▶ Maintain MAP goal
- ▶ Monitor for hyperkalemia



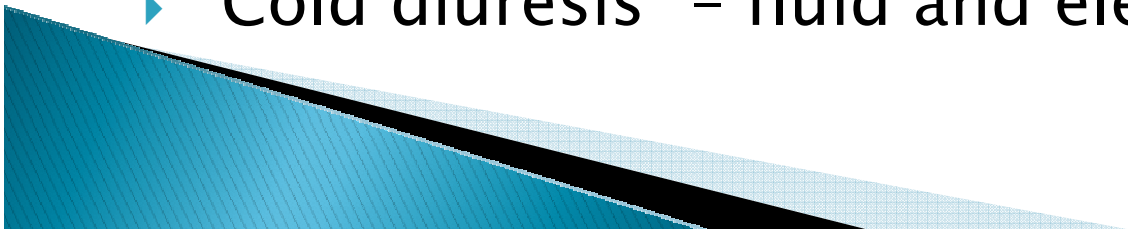
Therapeutic Hypothermia Procedure

- ▶ All IVF should be dextrose free during the cooling and rewarming phase
- ▶ Amiodarone can be mixed in D5W
- ▶ Hold all potassium 8 hours prior to rewarming
- ▶ Shivering – increases body temperature
 - Titrate sedation to shivering suppression
 - Memorial:
 - Fentanyl bolus plus titration up to 100 mcg/hr
 - Rocuronium drip titrated to maintain a goal of 1–2 twitches with Train of Four monitoring – baseline goal is 4/4 twitches



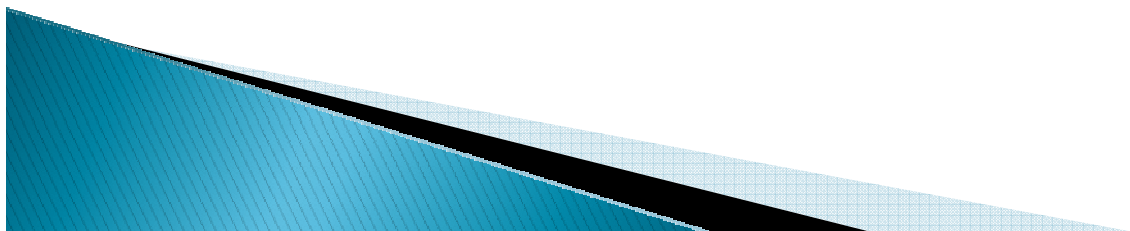
Therapeutic Hypothermia Adverse Effects

- ▶ Coagulation
 - At temperatures $< 35^{\circ}\text{C}$, clotting enzymes and platelets are impaired
 - Bleeding has been reported in up to 20% of patients
- ▶ Increased risk of infection
 - Impairs leukocyte function
 - Increased infection rates have been noted with 24 hours vs. 12 hours of TH but not associated with increased mortality
- ▶ Arrhythmias – slowed cardiac conduction
- ▶ Hyperglycemia – decrease in pancreatic release of insulin and insulin resistance
- ▶ “Cold diuresis” – fluid and electrolyte imbalances



Effects on Drug's Pharmacokinetics and Pharmacodynamics

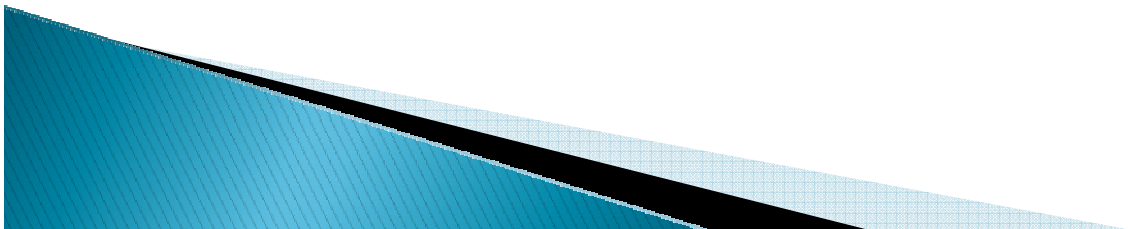
- ▶ Limited data exists on the effects of hypothermia on drug disposition
- ▶ Most enzyme-dependent processes are temperature dependent and will decrease with hypothermia
 - Decreased activity CYP450 elimination pathway
- ▶ Drugs with zero-order (saturable) kinetics may be more susceptible to the inhibitory effects of hypothermia
 - Phenytoin => AUC increased 180% and K_{el} decreased 50%



Effects on Drug's Pharmacokinetics and Pharmacodynamics

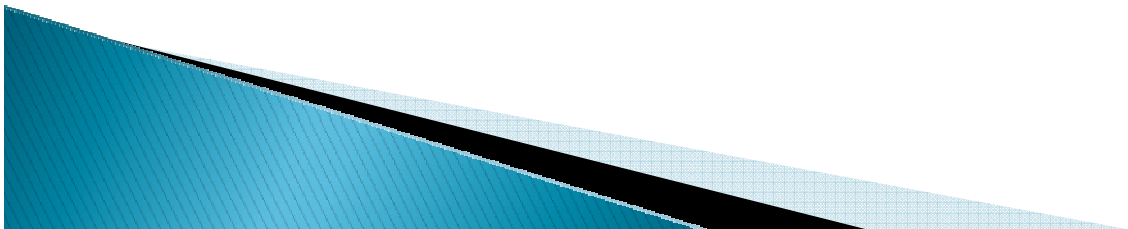
▶ Effects on selected drugs

- Aspirin – no augmentation of platelet inhibition
- Fentanyl – plasma concentrations increased by 25%
- Propofol – Decreased clearance, increased serum level by 28%
- Rocuronium – Decreased clearance by 50%, doubled the duration of action
- Vecuronium – Decreased clearance by 11% per °C, doubled the duration of action



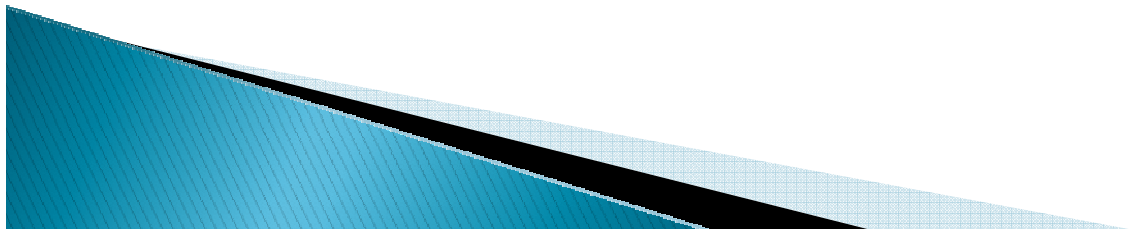
Back to the Patient Case

- ▶ High clinical suspicion of anoxic encephalopathy given at least 30 minutes of pulseless activity
- ▶ Following rewarming patient was in regular sinus rhythm but had no purposeful movements
- ▶ Family decided to w/d mechanical support
- ▶ Condition continued to decline and later passed





YOU A QUESTION



References

- ▶ Tortorici, MA, Kockanek, PM, and Poloyac, SM. “Effects of hypothermia on drug disposition, metabolism, and response: A focus of hypothermia-mediated alterations on the cytochrome p450 enzyme system.” *Crit Care Med.* 2007; 35–9.
- ▶ Arpino, Paul A. and Greer, David M. “Practical Pharmacologic Aspects of Therapeutic Hypothermia After Cardiac Arrest.” *Pharmacotherapy.* 2008; 28(1):102–111)
- ▶ UpToDate: Post-cardiac arrest management in adults

