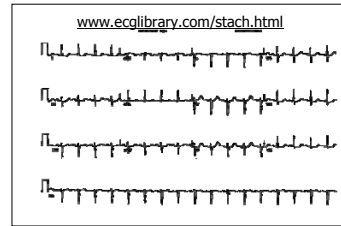


Toxic ACLS

Cynthia Aaron, MD
Wayne State University School of
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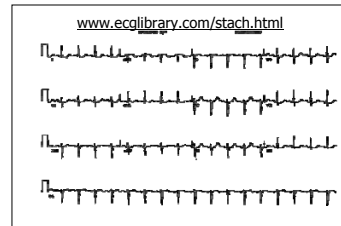


- 22 y/o m dropped at the ED unresponsive, cyanotic, pinpoint pupils, apneic, HR 110, BP 70 palpable
 - A. Start CPR
 - B. Bag patient –intubate
 - C. Bag patient-give IV naloxone
 - D. Give naloxone IV

Patient 1

- Opioid overdose with respiratory arrest
 - Acute withdrawal with hypercapnia → surge catecholamines 30x normal
 - CI ↑74% due to ↑HR and SV
 - Ventilate with BVM then administer naloxone
 - How much?
 - End-point
 - Who's at risk

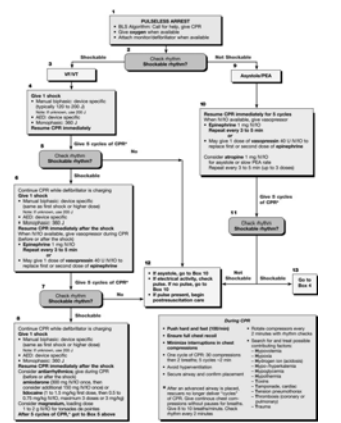
Ann Emerg Med 2001;37:S78

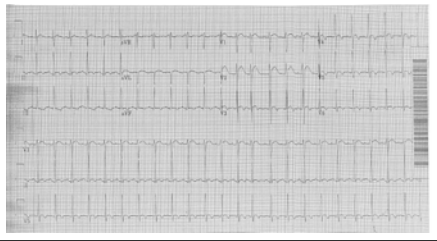


- 22 y/o m dropped at the ED unresponsive, cyanotic, pinpoint pupils, apneic, no palpable pulse or BP
 - A. Start CPR
 - B. Bag patient –intubate
 - C. Bag patient-give IV naloxone
 - D. Give naloxone IV

Patient 1 PEA

- No good evidence that naloxone improves outcome in patient with opioid-induced cardiac arrest
- Follow protocol
 - Ventilate
 - Intubate
 - 6H and 6 T
 - Hypoxia, hypoK, hyperK, hydrogen, hypothermia, hypovolemia
 - Trauma, toxicology, tension, tamponade, thrombosis cardiac/pulm
 - Consider naloxone
 - Circulation 2005;112:IV-126-IV.132
 - 2006 ACLS Provider Manual





- 42 y/o M drinking and snorting a line of cocaine
- SSCP radiating to left arm, BP 240/160
 - A. Nitroglycerin 0.4 mg SL titrate
 - B. Diazepam 10 mg IV
 - C. Metoprolol 5 mg IV
 - D. Labetalol 20 mg IV

Patient 2

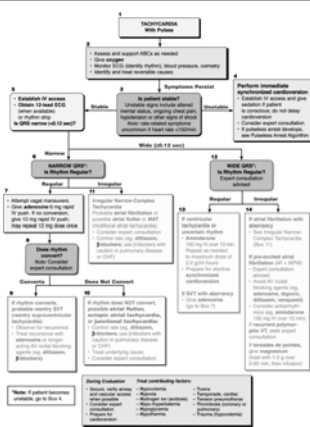
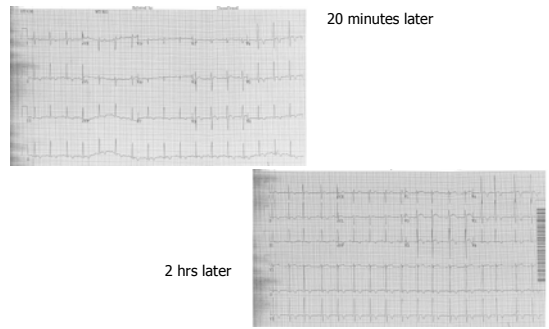
- Drug-induced HTN and ACS
 - Coronary artery vasoconstriction
 - Exacerbated by HTN and ↑HR associated with excess sympathetic stimulation
 - Benzodiazepines
 - Fibrinolytics higher risk-to-benefit ratio
 - Intracoronary fibrinolytics or vasodilators preferred
 - Nitroglycerin + phentolamine-cardiac cath data
 - Alternatives:
 - Labetalol: no significant effect (blks peripheral sympathomimetic excess without affecting CNS)
 - Metoprolol may induce hypotension

Patient 2

- Benzodiazepine first line
 - IV Nitroglycerin
 - IV Nitroprusside in refractory patients
- Phentolamine is second line
- Propranolol contraindicated
 - Metoprolol, esmolol, labetalol used with caution

Circulation 2005;112:IV-126-IV:132
 Circulation 2000;102:1-223

Patient 2



- 55 y/o female found moaning at home
- HR 32, BP 40/24, RR 12
- PMHx: HTN, afib, Type 2 diabetes, ↑cholesterol

Patient 3

- Differential diagnosis
 - Hypotensive, bradycardic, confused
 - A: α_2 (central) agonists and imidazolines/ peripheral α_1 antagonist (reflex)
 - B: beta blockers
 - C: calcium channel blockers/cholinergics
 - D: digoxin
 - E: extra: terminal event/ SA-AV node suppression

Patient 3

- How can you make the diagnosis?

Beta blocker	Calcium channel blocker
Hypoglycemia	Hyperglycemia
Cold, clamped extremities	Warm, pink extremities
↑ SVR	↓ SVR

- Alpha agonists
 - Pinpoint pupils



- CNS depression
- Response to simple measures
 - Fluids
 - Stimulation
 - Low dose catechols

- Alpha antagonist
 - Tachycardic

- Digoxin

- ↑ K
- Dysrhythmias

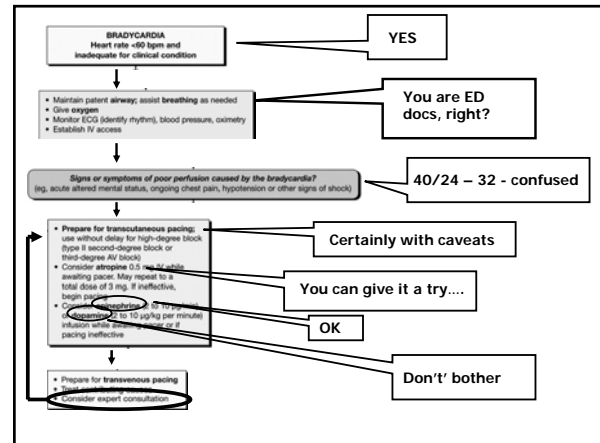


- Classic ECG changes



- Cholinergics

- "Wet and goopy"



Bradycardia/Hypotension

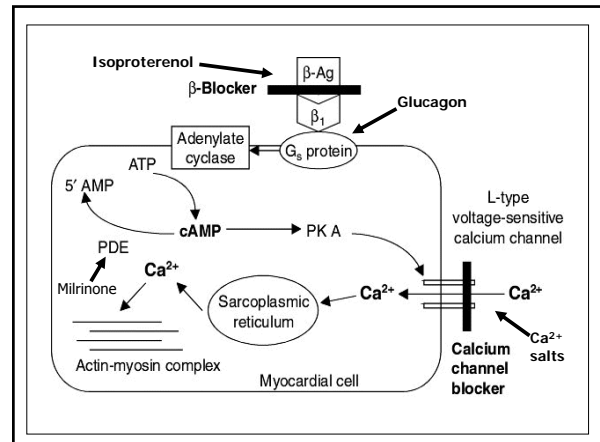
- Atropine
 - May be effective in mild cases CCB and BB
 - 3 mg either x 1 or in divided doses IV
 - Large doses in cholinergics
 - Average initial amt needed in OP 75 mg
- Isoproterenol
 - Pure beta agonist (β_1 β_2)
 - ↑ rate by mass effect at β receptor
 - Vasodilation

Bradycardia and Hypotension

- Calcium salts
 - Calcium chloride preferred to calcium gluconate
 - 3:1 difference between calcium availability
 - Maximum dose
- Glucagon
 - Bypasses beta receptor
 - Second messenger effect
 - Bolus plus drip
 - Very rapid metabolism
 - Vomiting
 - LIMITED SUPPLY

Bradycardia and Hypotension

- Phosphodiesterase inhibitors
 - Milrinone
 - Inhibits break down of cAMP
 - Increase in phosphokinase A
 - Calcium flux
 - Calcium mediated calcium release
 - Vasodilator



Hypotension and Bradycardia

- Cardiac myocytes
 - Unstressed aerobic environment
 - Oxidize free fatty acids for energy
 - Stress and decreased O₂ delivery
 - Switch to glucose
 - Readily available
 - Less energy requirements

CCB and BB

- L type calcium channels
 - Myocytes, vascular endothelium, pancreatic islets, gut mucosa
 - Block release Ca²⁺ into cell → calcium mediated cellular contraction is blocked
 - Hyperglycemia (no release insulin)
 - Decreased inotropy (decreased energy transfer across mitochondria)
 - Decreased chronotropy (blocked Ca²⁺ influx into pacemaker cells)
 - Vasodilation (vascular smooth muscle relaxation)
 - BB → unopposed alpha stimulation
 - Ileus (intestinal atony)

CCB and BB

- Hypoinsulinemia and acquired insulin resistance
- Hypoinsulinemia prevents myocyte glucose uptake
- Loss of inotropy and decreased SVR
- Hypoperfusion → ↓ glucose
- Lactic acidosis may be secondary to mitochondrial dehydrogenase inhibition during shock
 - Anaerobic metabolism in muscles

CCB and BB

- Calcium is major intracellular signaler for mitochondrial dehydrogenase activation *in vivo*
- L channels blocked on mitochondrial membrane
 - Prevents calcium release from SR and mitochondrial membrane
 - Decreases pyruvate dehydrogenase activity
- Pyruvate cannot enter TCA cycle → lactate accumulates

HIET

- Hyperinsulin-euglycemia therapy
 - Provide pharmacologic doses of insulin
 - Enhance glucose metabolism by myocytes
 - Insulin increases lactate oxidation and eliminates free fatty acid oxidation
 - Net result:
 - Increased LVEDP, coronary blood flow
 - Increased ratio of myocardial O₂ delivery/myocardial work
 - Enhanced contractility and blood pressure
 - Does not affect heart rate

HIET

- If FSBS < 200 mg/dL, bolus 50 ml D₅₀W
- Regular insulin 1 unit/kg IV bolus
- Immediately start insulin infusion 1 unit/kg/hr
- Start D₁₀W infusion at 100-200 ml/hr
 - FSBS q15 -30 mins until stable
 - Titrate to mean arterial BP ≥ 60 mmHg by 0.5 units/kg/30 minutes

HIET caveats

- Keep K⁺ between 3.0-4.0 mEq/L
- If patient becomes hypoglycemic
 - DO NOT decrease insulin
 - Increase glucose infusion
 - May need to switch to D₂₅W by central line
- Invasive or noninvasive monitoring of SVR and cardiac output
 - This is NOT SEPSIS
- Pacemaker

HIET therapy

- Once patient hemodynamically stable
 - Mean arterial BP ≥ 60 mm Hg
 - Lactate dropping
 - Urinary output improving
 - Improved perfusion
- Wean off all pressors
 - Then wean down insulin
 - May require glucose supplementation for 24 additional hours

Intravenous lipid emulsion

- Used by anesthesiologists for local anesthetic cardiotoxicity
 - Case reports
 - Lidocaine, bupivacaine, mepivacaine, ropivacaine, bupropion
- ILE: 20% Intralipid™
 - 20% soybean oil
 - 1.2% egg yolk
 - 2.5% glycerin
 - Remainder water

Intravenous Lipid Infusion

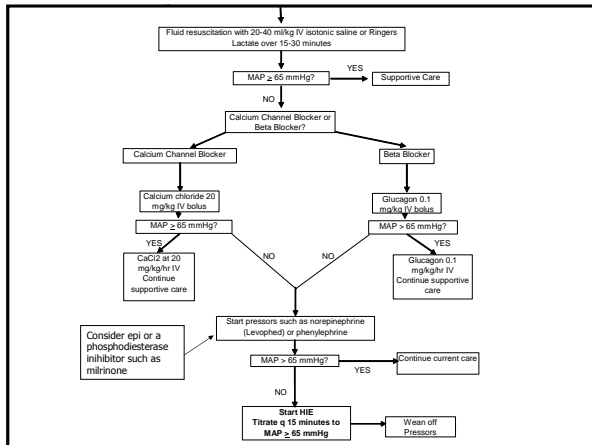
- Three theories
 - Cardiac myocyte: Free fatty acid normally provide ATP
 - Provision of additional FFA improves energy pool for myocardial substrates
 - Post CABG heart data
 - In voltage clamped cells: linoleic acid improves L type calcium channel function
 - Lipid sink: lipophilic medications dissolve into lipid pulling the xenobiotic off the receptors

ILE

- Off label use
 - No randomized controlled trials, no outcome studies-all case reports
 - Use with extreme caution
 - 1.5 ml/kg of a 20% solution over 1 minute
 - May rebolus 1-2 times q3-5 minutes
 - 0.25 ml/kg/min of a 20% solution over 30-60 mins
 - May increase infusion to 0.5 ml/kg/minutes
 - Maximum dose 8 ml/kg

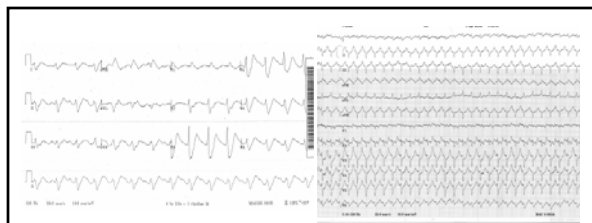
ILE

- Side effects
 - Hyperlipidemia
 - Allergic reactions (egg or peanut/soybean)
 - Fat emboli
 - Hypercoagulability
 - Metabolic acidosis
 - Dyspnea
- Propofol is NOT equivalent (10%)
 - Hypotension, AV blocks, metabolic acidosis

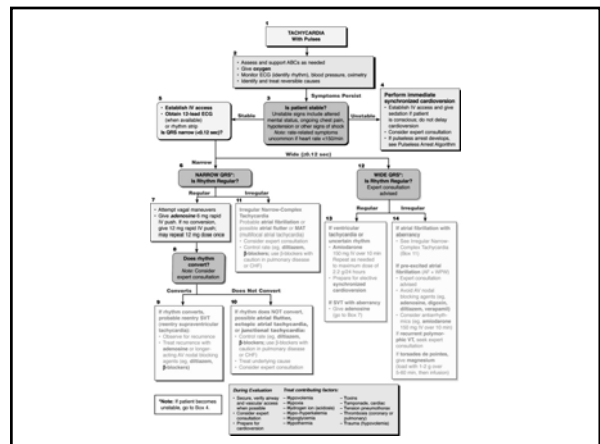


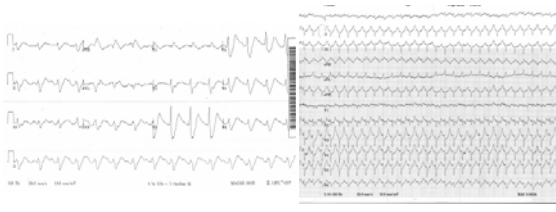
Hypotension and Bradycardia

- Fluids
- \pm Atropine
- Calcium chloride 20 mg/kg bolus then infusion
- Glucagon 0.1 mg/kg bolus then 0.1 mg/kg/hr
- Pacemaker
- HIET
 - Can start pressors (norepinephrine, epinephrine, vasopressin) to buy time while mixing insulin
- Wean off pressors
- Failure of all
 - ILE
 - Balloon pump
 - Partial bypass



- 67 y/o female presented unresponsive
- HR 160, BP 64/48, RR 8, Temp 38.9 C
- PMHx: hyperlipidemia, HTN, Type 2 DM





Choose your management

- A: Cardioversion
- B: Amiodarone
- C: Sotalol
- D: Lidocaine
- E: Adenosine
- F: Sodium bicarbonate
- G: Diltiazem

Wide complex tachycardia

- Cardioversion
 - Ongoing presence of drug make rhythm refractory
- Amiodarone
 - Has Na and Ca channel effects with alpha and beta blockade
 - Potentially additive toxicity
 - Worsening of hypotension

Wide complex tachycardia

- Sotalol
 - Beta blockade will worsen hypotension
 - Prolongs AP duration and refractoriness
 - Risk of torsades
- Lidocaine
 - Has been studied in animal models
 - Ib antiarrhythmic
 - Would consider it as a second or third line drug

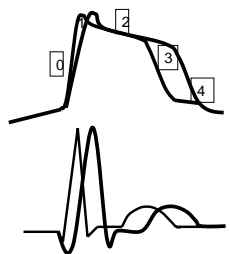
Wide complex tachycardia

- Adenosine
 - Briefly depresses AV and SA node
 - Unlikely to be effective
- Diltiazem
 - Slow conduction and increase AVN refractoriness
 - Worsen hypotension
 - Calcium effect additive to negative inotropy

Wide complex tachycardia

- Sodium bicarbonate
 - Increases the rate of rise in phase 0 of the action potential and narrows the QRS
 - Both pH and $[Na^+]$ dependent
 - Can use hypertonic saline
 - Aim for pH 7.50-7.55

Sodium Channel Blockade



Wide complex tachycardia

- 3 stages of sodium channels
- Faster HP = more channels are in the active and inactive states, therefore more blockade.
- Na⁺ channel blockade increases with ↓ pH
- Association originally described with TCA overdose.

The Terminal 40 msec

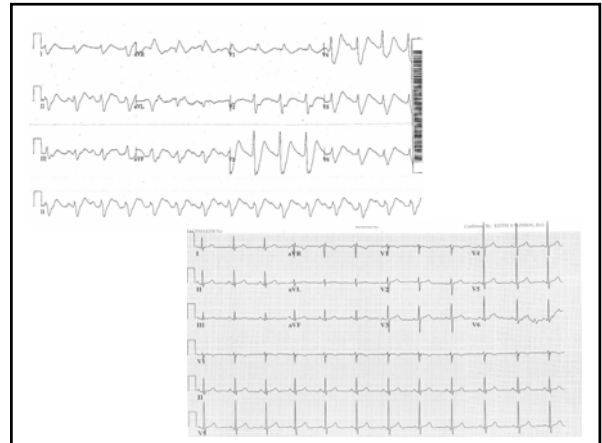
- The terminal 40 ms in aVR is sensitive, but not specific for sodium channel blockade.



Wolfe et al. *Ann Emerg Med* 1989; 348-351

Drugs With Na⁺ Channel Blocking Activity

- TCAs (cyclobenzaprine)
- Diphenhydramine (antihistamines)
- Carbamazepine
- Propranolol (β blockers)
- Cocaine
- Phenothiazines (thioridazine, compazine)
- Quinidine/Quinine
- Loxepine
- Type I antidysrhythmics



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