ACLS - The Pharmacology

A non-sanctioned, non-sponsored, non-official discussion of medications used in EMS delivery of Advanced Cardiac Life Support.

Background and Purpose

- The standardized approach of ACLS video supplemented classes reduced the ability to tailor information to the audience
- Students dealing with ACLS angst aren't the most receptive audience to anything else
- Memorization will get us through 16 hrs, but it has a tendency of failing at the fairly inopportune times

Objectives

- Refresh knowledge of ACLS medications
- Discuss some of the changes
- Increase awareness of available, less used medication
- Discuss some of the evidence

Common Sense Flow Chart

Cardiac Arrest Pharmacology

"The primary goal of pharmacologic therapy during cardiac arrest is to facilitate restoration and maintenance of a perfusing spontaneous rhythm"

Neumar et al. Part 8. *Circulation*. 2010: S743

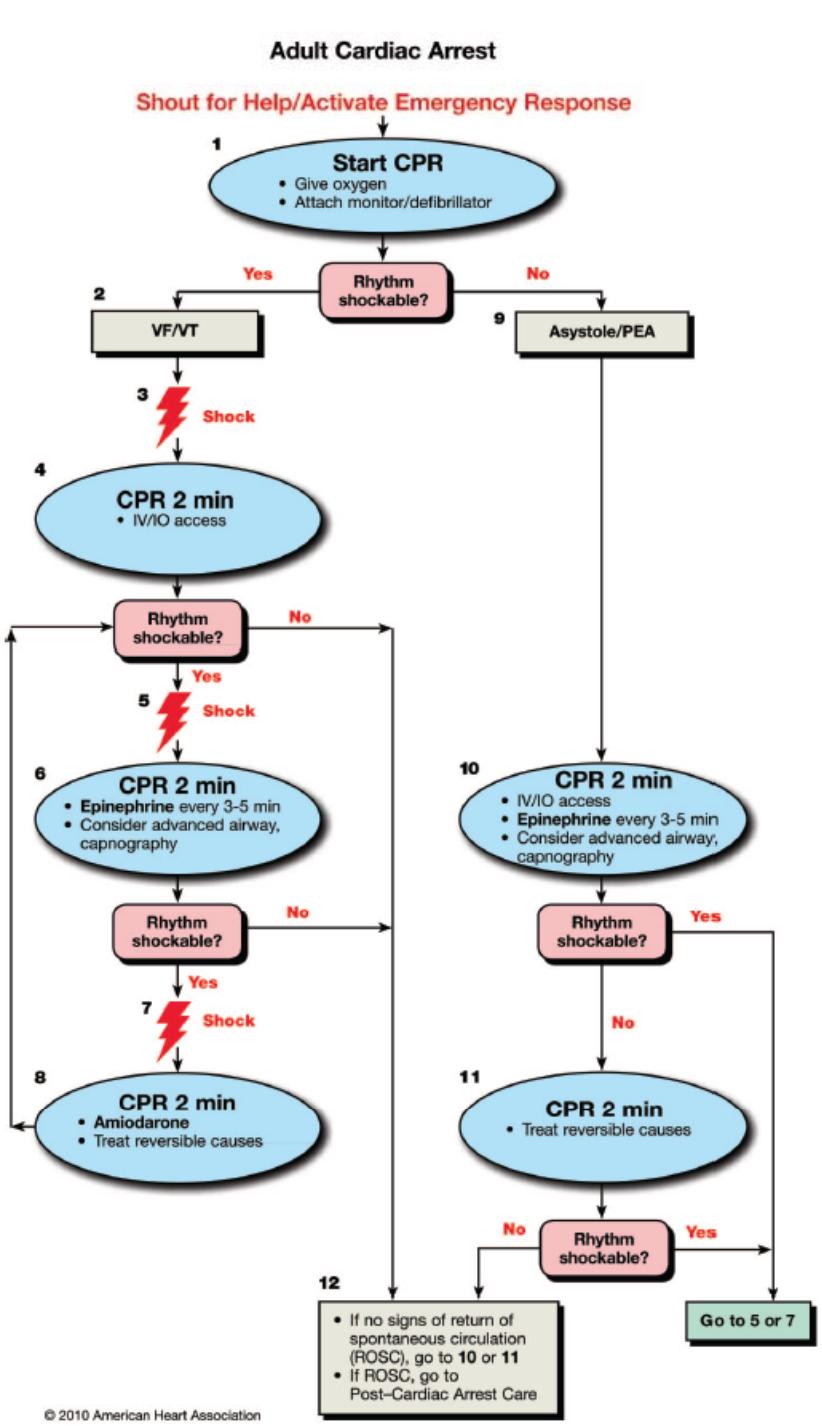
Chain of Survival

- Immediate recognition of cardiac arrest and activation of the emergency response system
- Early CPR that emphasizes chest compressions
- Rapid defibrillation if indicated
- Effective advanced life support
- Integrated post-cardiac arrest care

Berg RA et al. Part 5. *Circulation*. 2010;122(suppl 3):S685.

Effective implementation of the links of the chain can result in survival rates of witnessed out-of-hospital VF arrest approaching 50%

Rea TD et al. Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. *Circulation*. 2006; 114:2760-2765
(As cited in *Circulation.* 2010; 122(suppl 3): S685.)



CPR Quality
- Push hard (≥2 inches [5 cm]) and fast (≥100/min) and allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 minutes
- If no advanced airway, 30:2 compression-ventilation ratio
- Quantitative waveform capnography
  - If P_{ETCO_2} <10 mm Hg, attempt to improve CPR quality
- Intra-arterial pressure
  - If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CPR quality

Return of Spontaneous Circulation (ROSC)
- Pulse and blood pressure
- Abrupt sustained increase in P_{ETCO_2} (typically ≥40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

Shock Energy
- **Biphasic:** Manufacturer recommendation (eg, initial dose of 120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.
- **Monophasic:** 360 J

Drug Therapy
- **Epinephrine IV/IO Dose:** 1 mg every 3-5 minutes
- **Vasopressin IV/IO Dose:** 40 units can replace first or second dose of epinephrine
- **Amiodarone IV/IO Dose:** First dose: 300 mg bolus. Second dose: 150 mg.

Advanced Airway
- Supraglottic advanced airway or endotracheal intubation
- Waveform capnography to confirm and monitor ET tube placement
- 8-10 breaths per minute with continuous chest compressions

Reversible Causes
- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

Figure 1. ACLS Cardiac Arrest Algorithm.

Asytole/PEA

- Epinephrine – 1 mg
  - Repeat every 3-5 minutes
- Vasopressin – 40 Units
  - May replace 1st or 2nd dose of epi
- Remember when?
  - Sodium Bicarb
  - Atropine

Vasopressors

Vasopressors

Epinephrine

- What is it?
  - A) Catecholamine
  - B) Sympathomimetic
  - C) Adrenergic Receptor Agonist

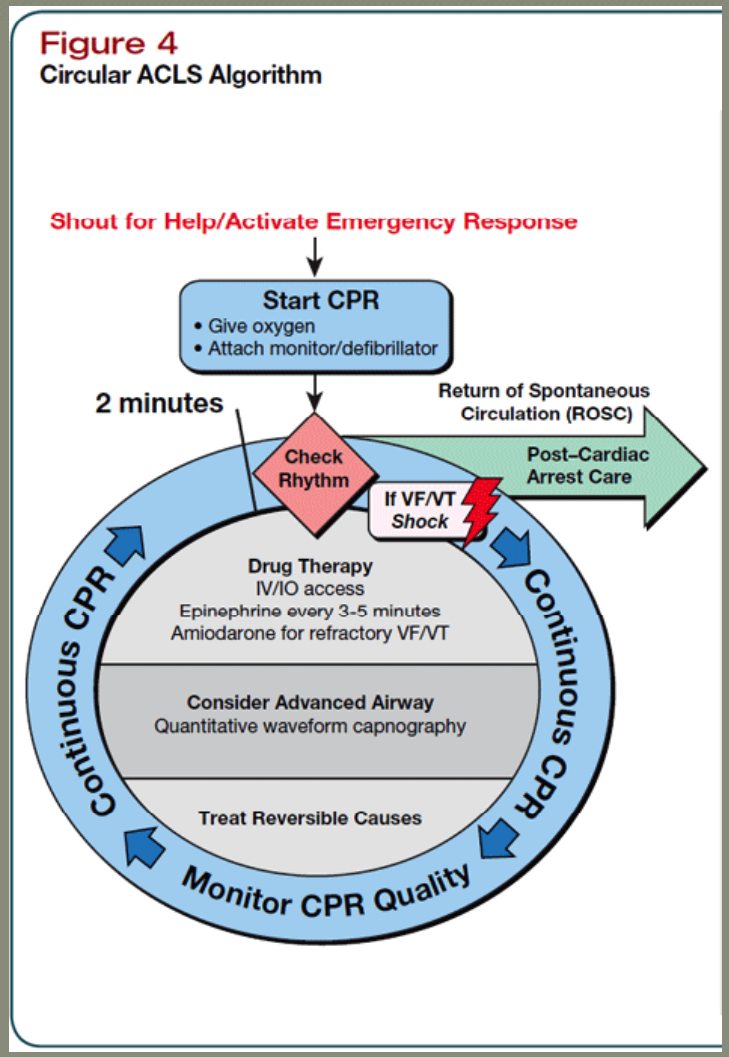
- Can you still name the receptors we are looking to activate in arrest? (bonus for the biologic effect they cause)

Vasopressors

Epinephrine

- So when are you giving the 1 mg?
  - Is this important?

Vasopressors



The 'circular algorithm' introduced to emphasize the importance of CPR

"There is insufficient evidence to recommend a specific timing or sequence of drug administration and advanced airway placement during cardiac arrest."

Neumar et al. Part 8. *Circulation*. 2010: S737

Vasopressors

Epinephrine

- So when are you giving the 1 mg?
  - Is this important?
- The half-life of catecholamines are measured are minutes (2ish)

Is timing important?

- Maybe
- Part of why the endotracheal route was de-emphasized
  - Drug Concentration
  - Predictability of delivery and effect

Neumar et al. Part 8. *Circulation*. 2010: S743

Vasopressors

Vasopressin

- What is it?
  - A Peptide Hormone
  - Responsible for regulating water retention by controlling reabsorption in the tubules of the kidneys
  - Increases PVR
    - Causing B/P increase

Vasopressors

Vasopressin

- How is it different from Epinephrine?
  - Specificity
    - We know how Epi affects cardiac muscle
    - Desirable effects of increased PVR without acting on non-specific adrenergic receptors
  - Half life
- So why just consideration

N Sharman A & Low J. *Vasopressin and its role in critical care*.

VF/Pulseless VT

- Vasopressor
- Anti-Arrhythmic
  - Amiodarone 300 mg
    - Second dose of 150 mg

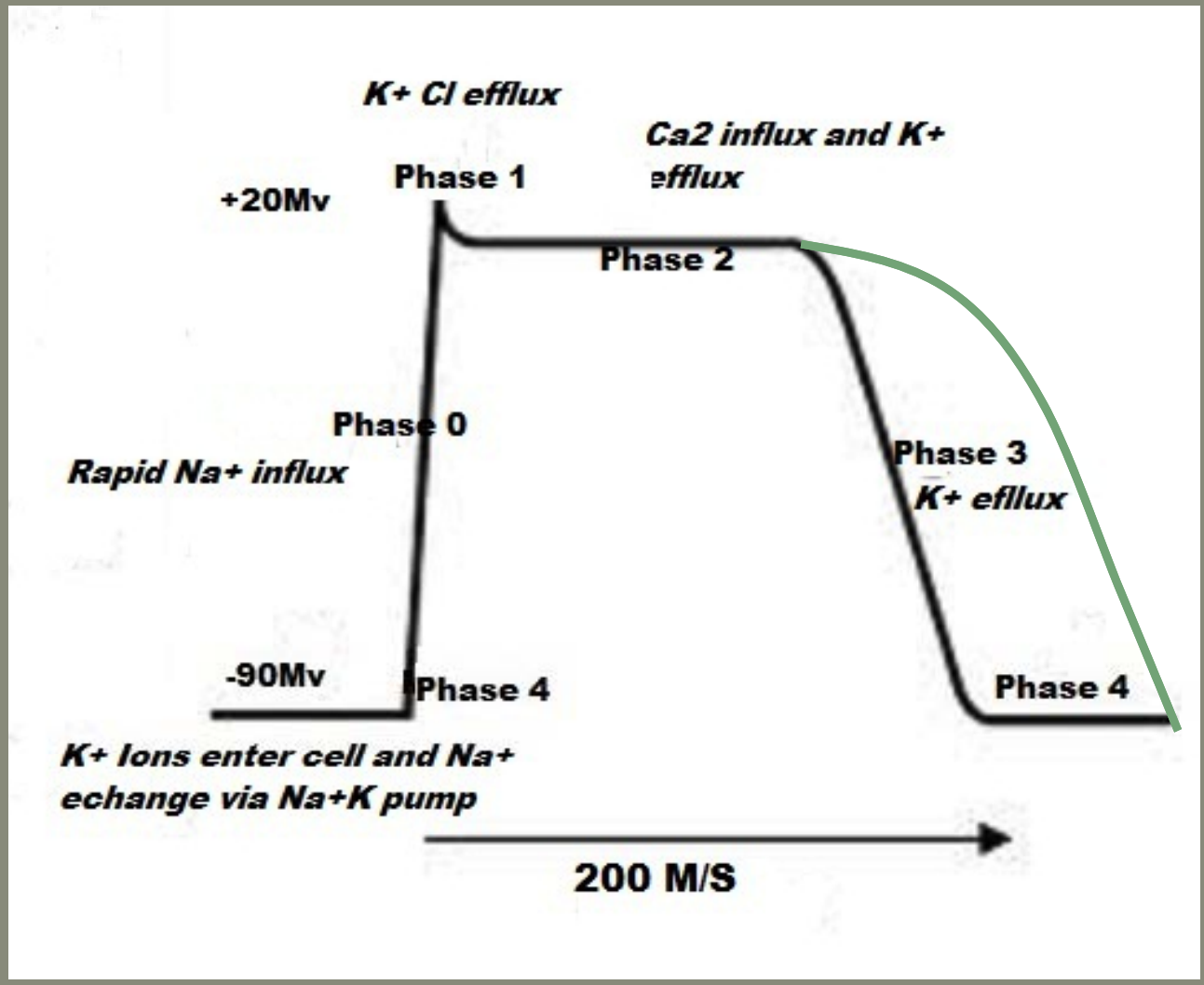
    Or
  - Lidocaine 1-1.5 mg/kg
    - Additional dosing 0.5 – 0.75 mg/kg every 5-10 min. to a max of 3 mg/kg

Antiarrhythmics

Amiodarone

- Class III antiarrhythmic agent
  - Prolongs phase 3 (repolarization) of the cardiac action potential

Remember this?



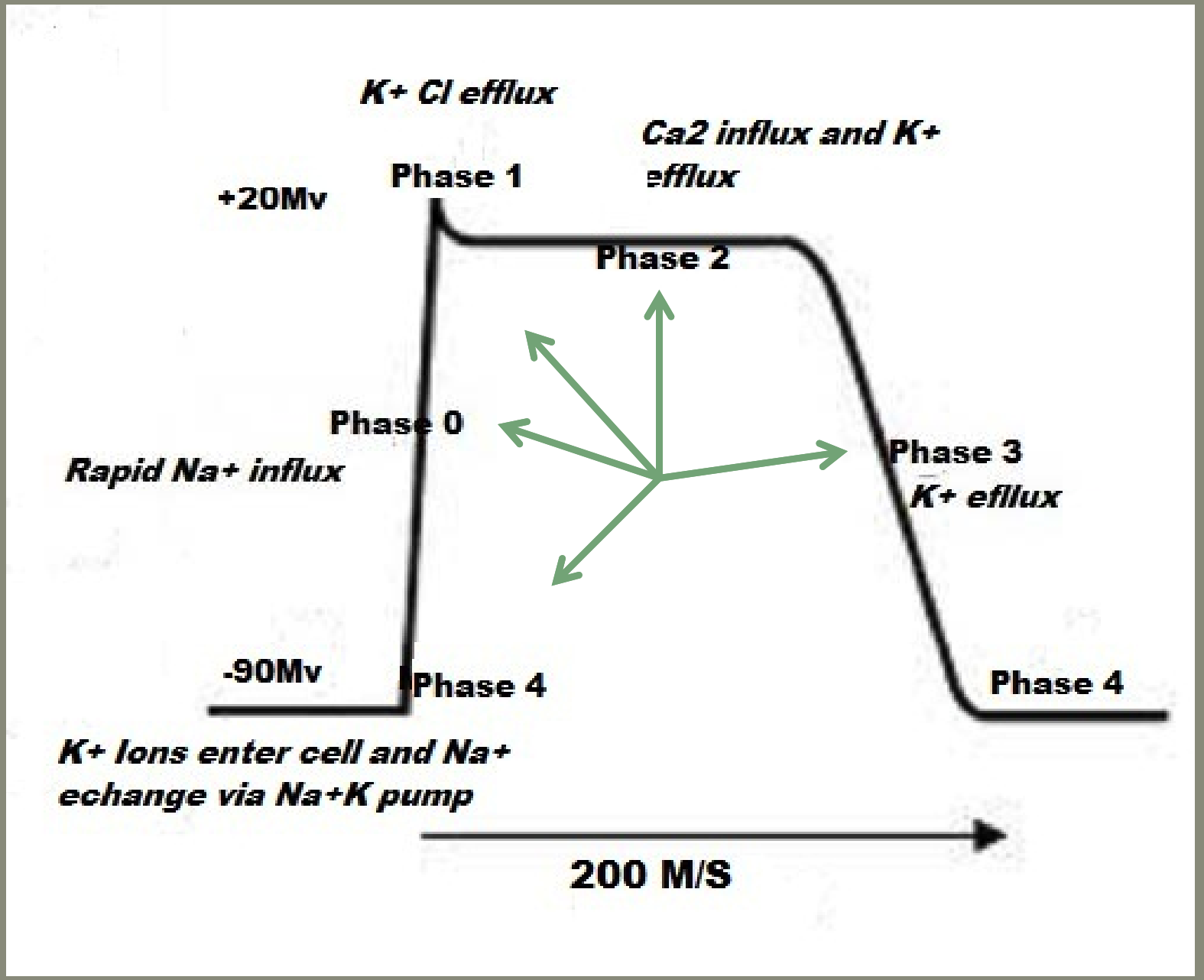
http://www.emergencymedicalparamedic.com/cardiac-action-potential/

Antiarrhythmics

Amiodarone

- Class III antiarrhythmic agent
  - Prolongs phase 3 (repolarization) of the cardiac action potential
  - Potassium Channel Blocker

    And…
  - It has effects similar to class Ia
  - II
  - IV



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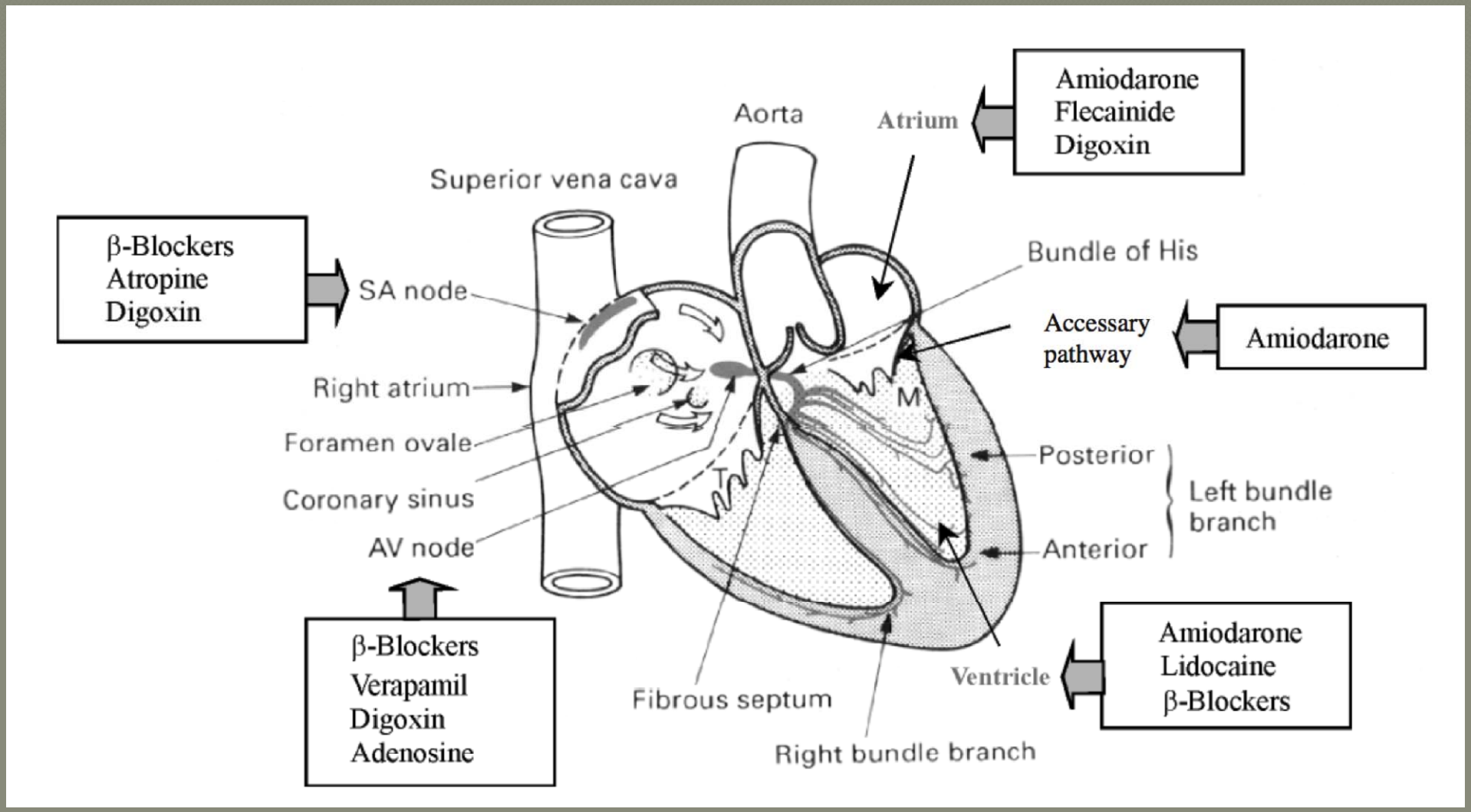
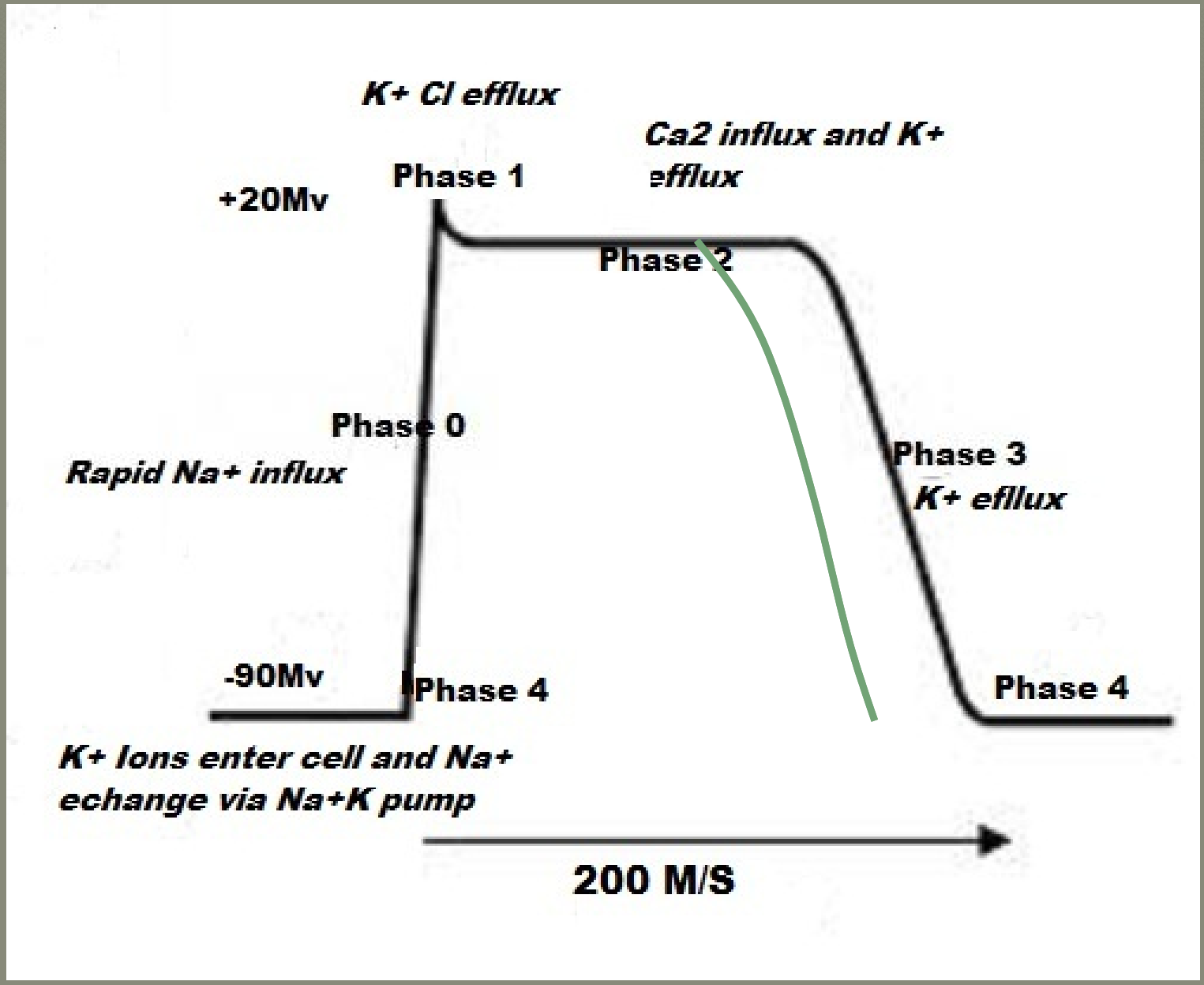


Sanghavi S & Rayner-Klein. Management of Peri-arrest Arrhythmia.

Antiarrhythmics

Lidocaine

- How does it ‘anti’ the arrhythmia?



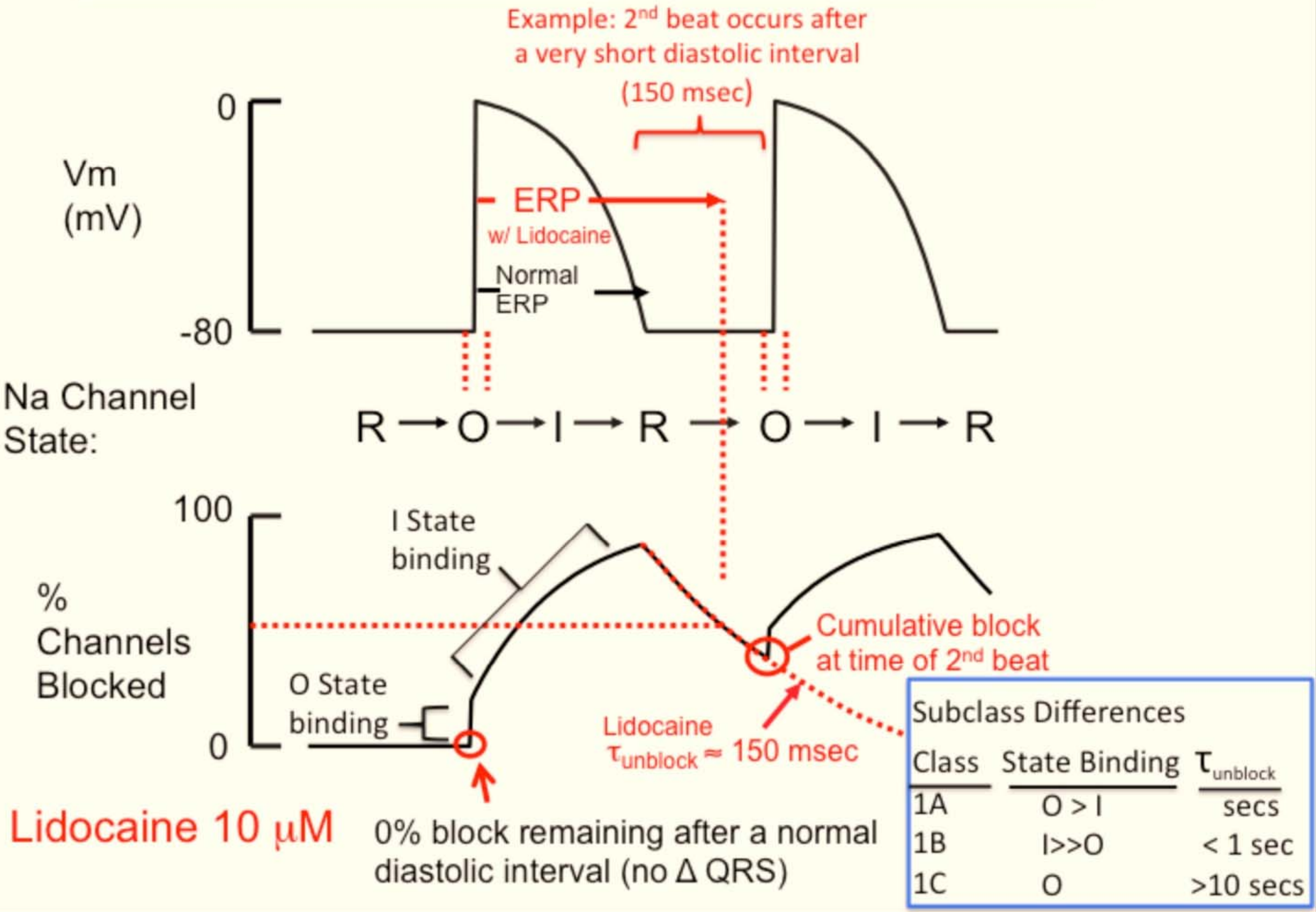
http://www.emergencymedicalparamedic.com/cardiac-action-potential/

Antiarrhythmics

Lidocaine

- How does it 'anti' the arrhythmia?
  - Class Ib
  - Na+ Channel Blocking
  - Ventricular arrhythmias only?

Class I - State Dependent Block & the ERP



Subclass Differences

Class	State Binding	$\tau_{unblock}$
1A	O > I	secs
1B	I>>O	< 1 sec
1C	O	>10 secs

Antiarrhythmics

- Amio vs. Lido
  - Is anyone using Lidocaine?
  - What the Amiodarone studies say
  - What the Lidocaine studies say

What did we miss in CA?

Magnesium Sulfate

- Electrolyte
- Indications
  - TdP
- Mechanism of Action
- Evidence?

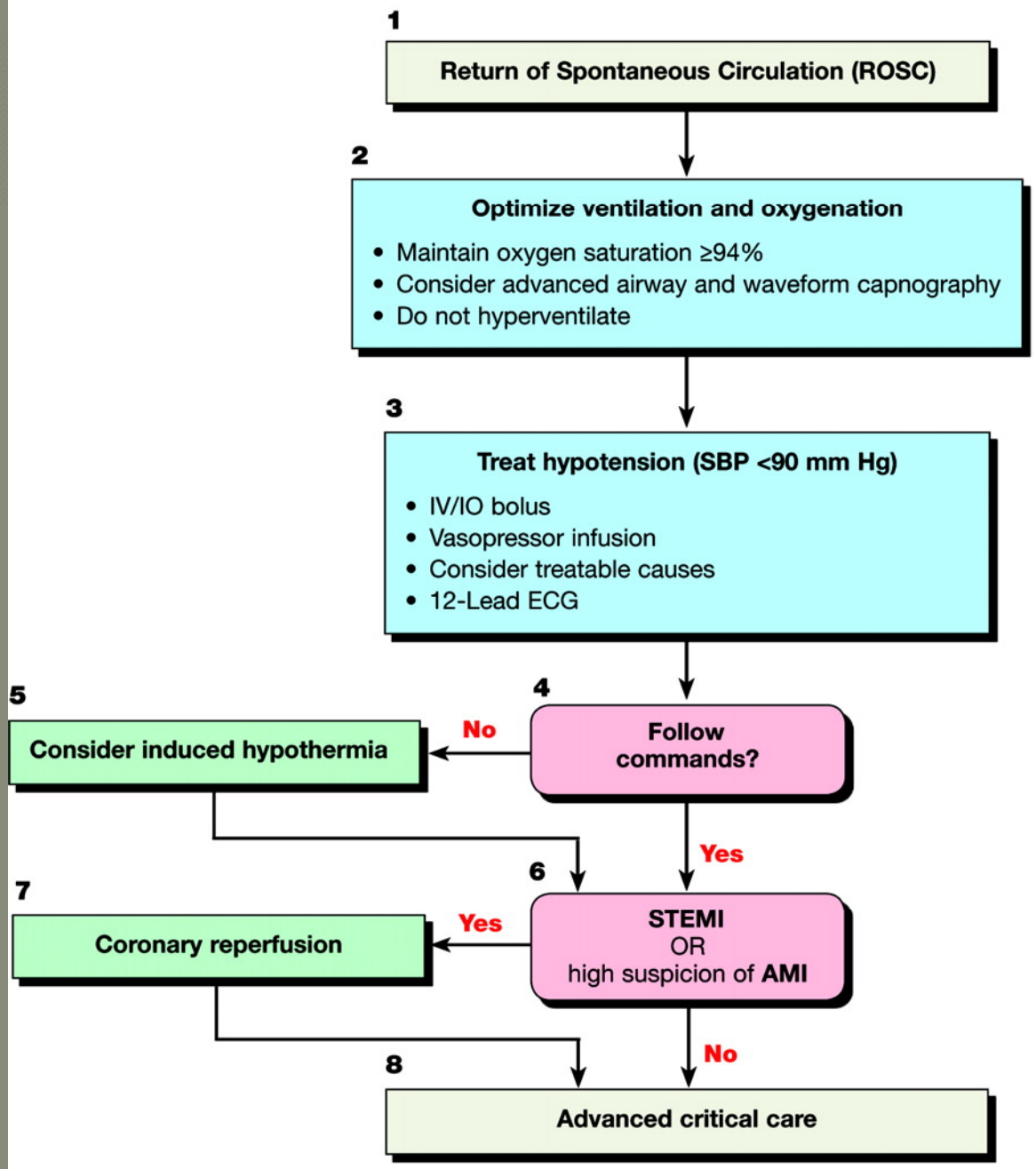
What (else) did we miss in CA?

- What to do with the patient that comes back to life

Pharmacology in the presence of a pulse

Mistakes may be more readily evident…

Adult Immediate Post–Cardiac Arrest Care



Doses/Details

Ventilation/Oxygenation
Avoid excessive ventilation. Start at 10-12 breaths/min and titrate to target P_{ETCO_2} of 35-40 mm Hg.
When feasible, titrate F_{IO_2} to minimum necessary to achieve Sp_{O_2} ≥94%.

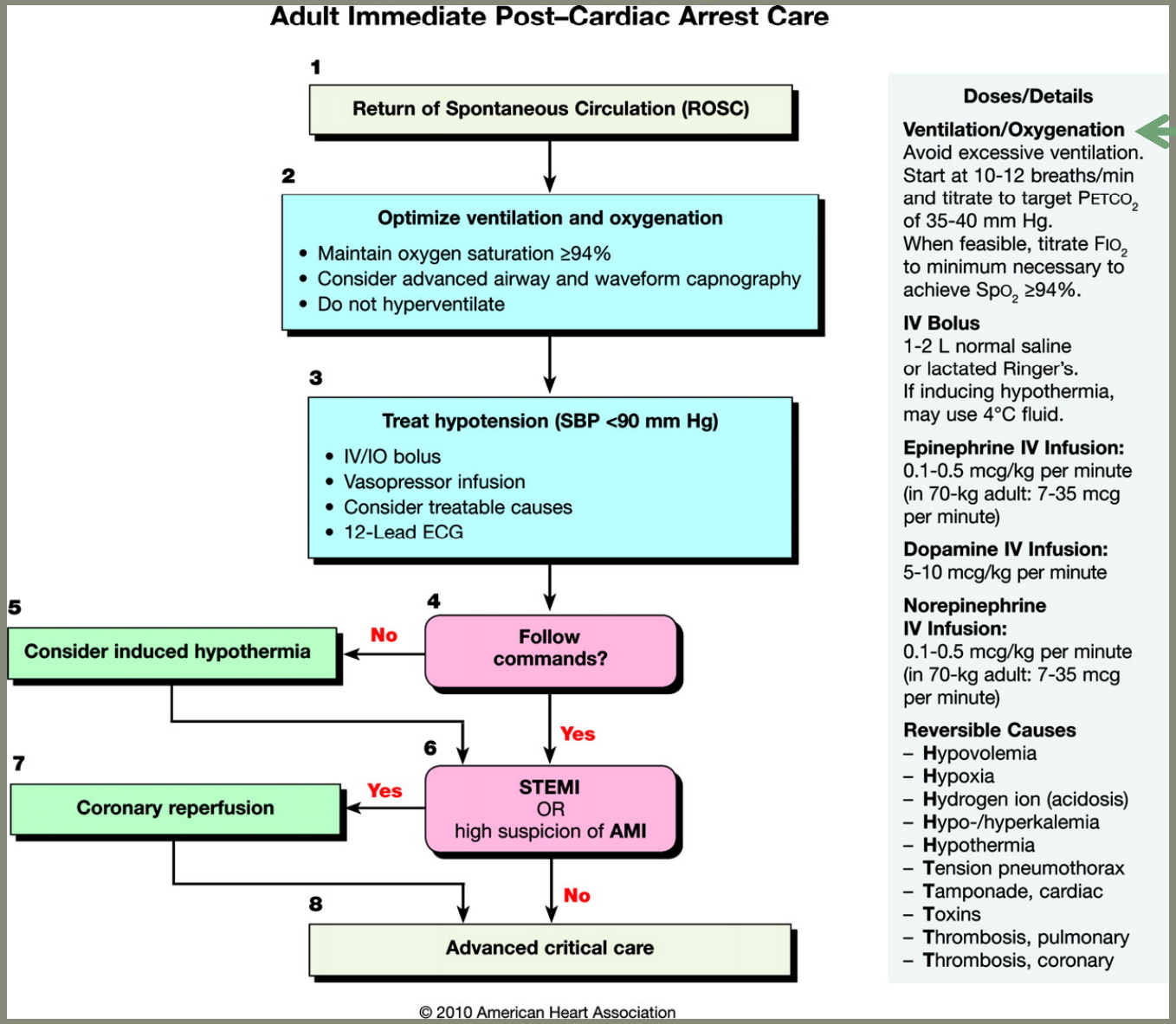
IV Bolus
1-2 L normal saline or lactated Ringer's.
If inducing hypothermia, may use 4°C fluid.

Epinephrine IV Infusion:
0.1-0.5 mcg/kg per minute (in 70-kg adult: 7-35 mcg per minute)

Dopamine IV Infusion:
5-10 mcg/kg per minute

Norepinephrine IV Infusion:
0.1-0.5 mcg/kg per minute (in 70-kg adult: 7-35 mcg per minute)

Reversible Causes
- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary



We do this perfectly.

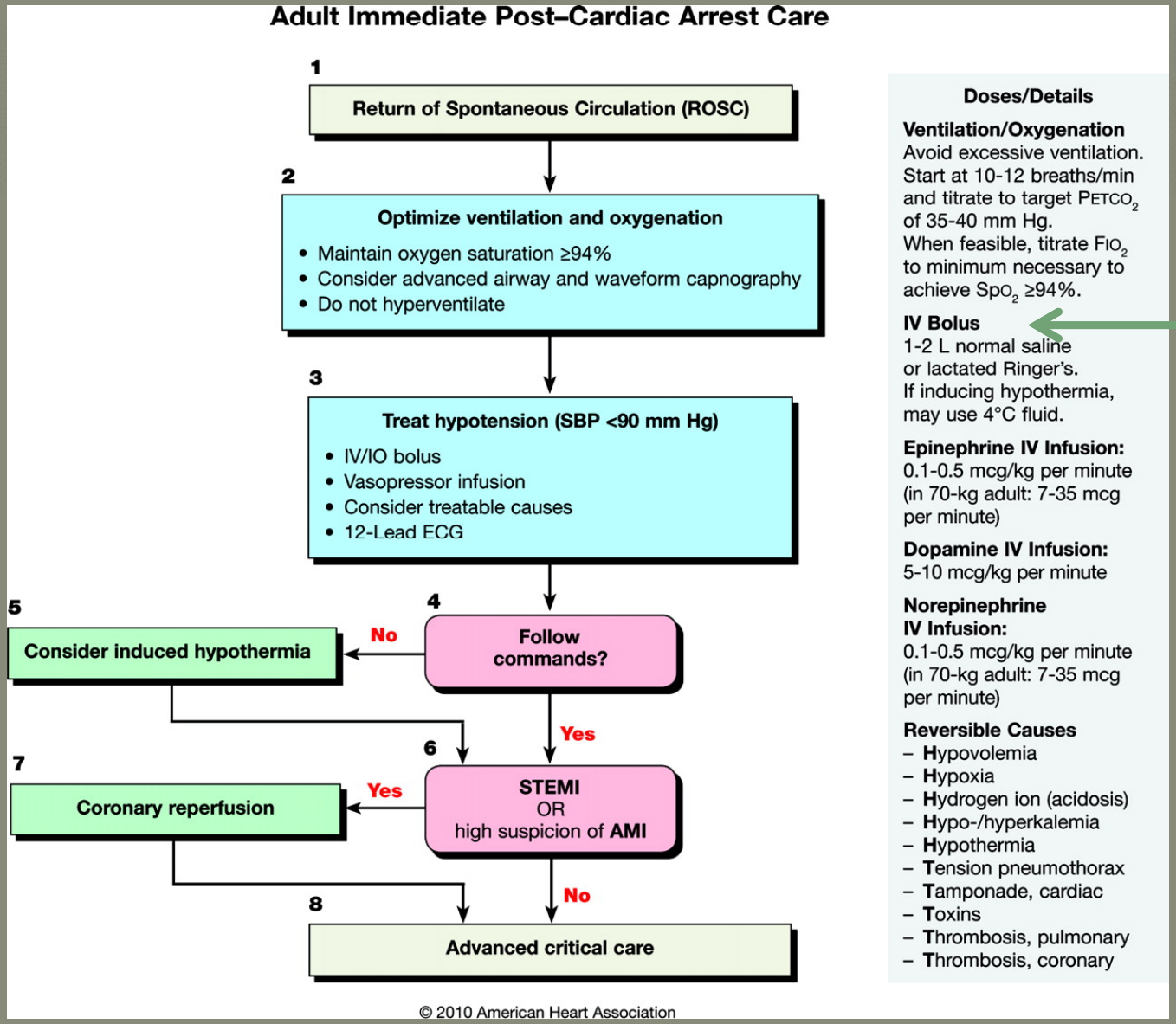
Always.

.

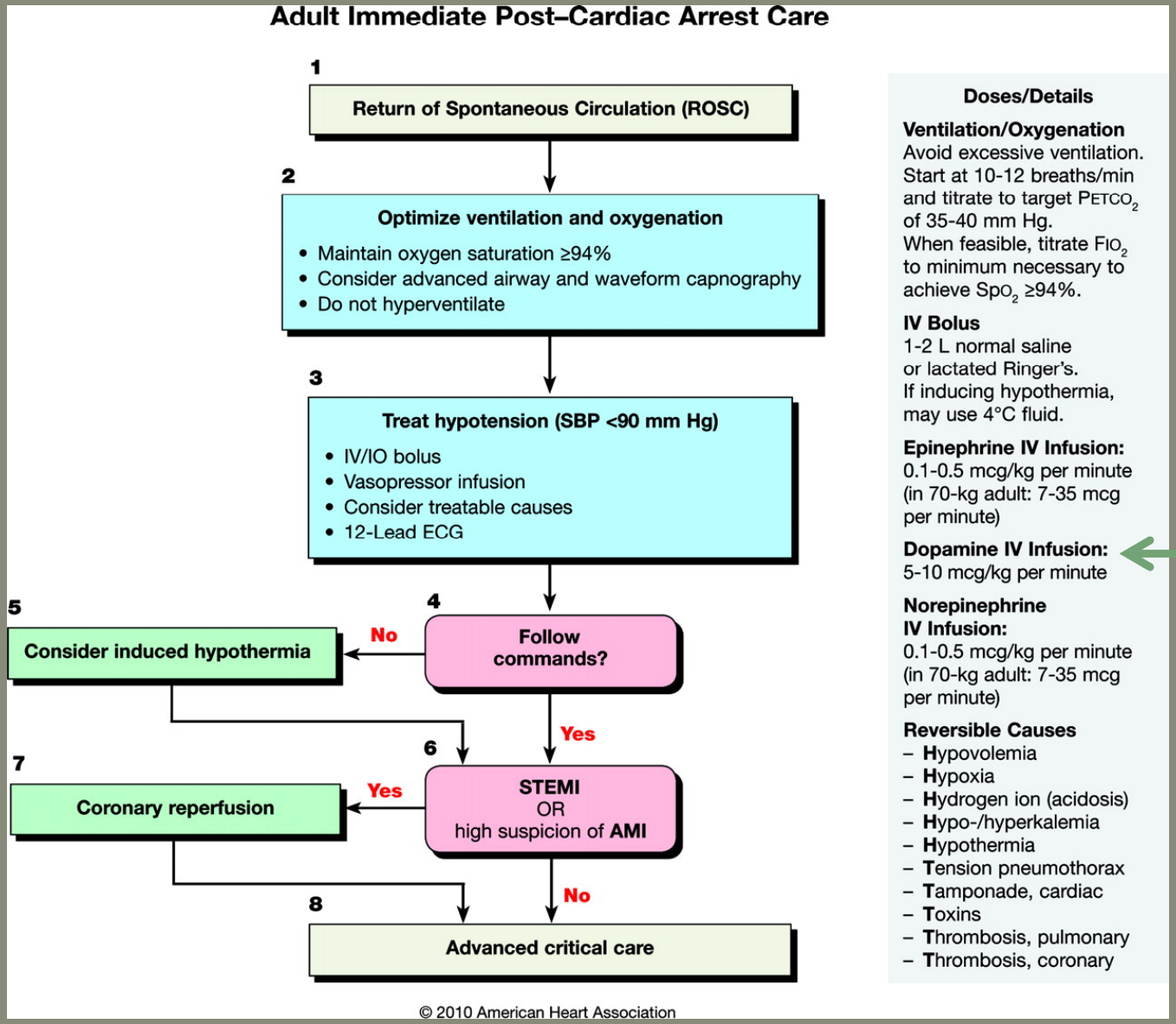
.

.

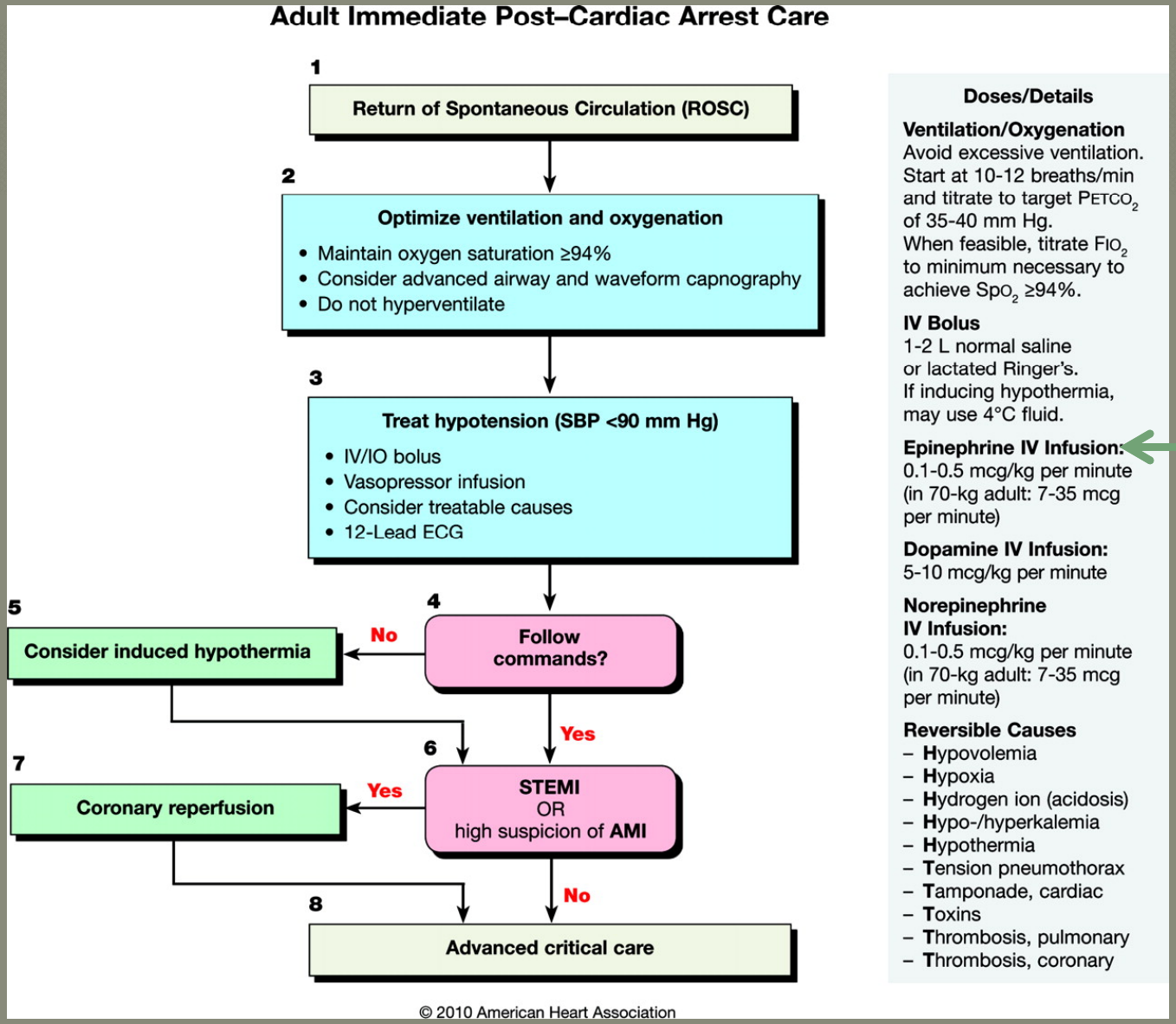
Right?



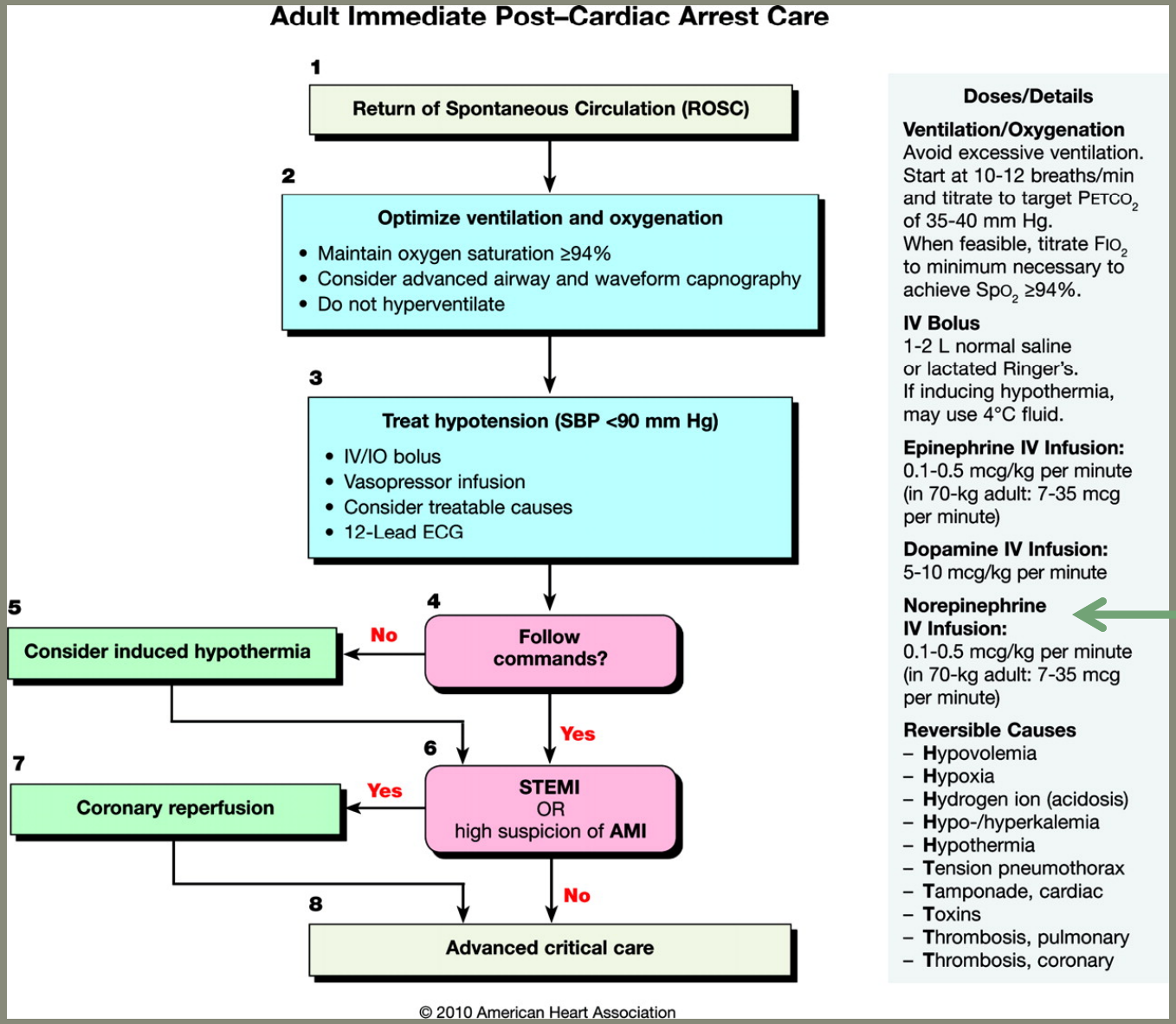
Increasing frequency in EMS



I remember this has something do with a clock



Familiar drug, but mcg/kg/min?



Norepi? There's a rhyme about that stuff.

Dopamine

- Natural catecholamine
- Positive chronotropic and inotropic effects

Ino…chrono…dromo…tropes

- Inotrope
  - in-ergy to get the job done
- Dromotrope
  - Driving = AVerage Velocity
- Chronotrope
  - Charging bulls run fast

Dopamine

- Natural catecholamine
- Positive chronotropic and inotropic effects
- Dose Specificity
  - 0.5 – 2.0 – Low (aka renal dosing)
  - 2.0-10.0 – Intermediate
  - 10.0-20.0 - High

Norepinephrine

- Alpha receptor agonist with inotropic tendency
  - Specificity can be a good thing
- Dose
  - 2-10 mcg/min
- May be seeing more of it shortly…
- Why the bad rep?

ACS

"Half of the patients who die of ACS do so before reaching the hospital"

O'Connor et al. Part 10. *Circulation*. 2010;122(suppl 3):S789.

"Changes" from 2010 update

- Return of the term *symptomatic*
- A nod to identifying the underlying issue
- Bradycardia
- Tachycardia

ACS

- Is Mona still greeting everyone?
  - She got cut back to part-time
- Oxygen
- ASA
- Nitrates
- Morphine (analgesia)

OANA isn't a good mnemonic…

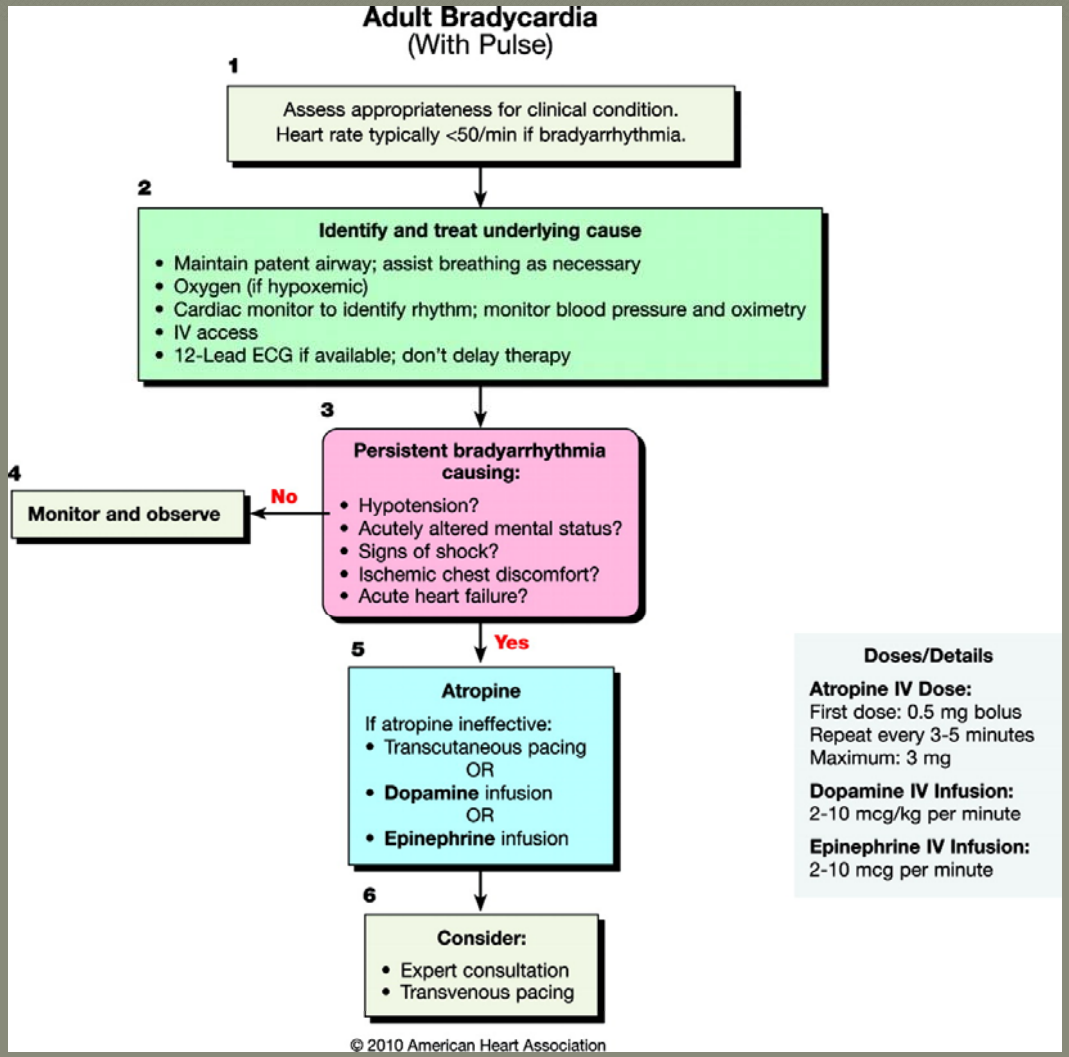
ACS Pharm

- Oxygen
- So why the change
  - Studies
  - Oxygen still there for the respiratory distress, heart failure, shock
- ASA
  - Why?
  - What if they took their own?

ACS Pharm

- Nitrates
  - Concerns?
- Pain management
  - With?
- Beta-Blockers

Bradycardia



Bradycardia

Identify and treat underlying cause

- Maintain patent airway; assist breathing as necessary
- Oxygen (if hypoxemic)
- Cardiac monitor to identify rhythm; monitor blood pressure and oximetry
- IV access
- 12-Lead ECG if available; don't delay therapy

Persistent bradyarrhythmia causing:

- Hypotension?
- Acutely altered mental status?
- Signs of shock?
- Ischemic chest discomfort?
- Acute heart failure?

Atropine

If atropine ineffective:

- Transcutaneous pacing

OR

- **Dopamine** infusion

OR

- **Epinephrine** infusion

Bradycardia

Doses/Details

Atropine IV Dose:
First dose: 0.5 mg bolus
Repeat every 3-5 minutes
Maximum: 3 mg

Dopamine IV Infusion:
2-10 mcg/kg per minute

Epinephrine IV Infusion:
2-10 mcg per minute

Bradycardia

Atropine

- Anticholinergic

OR

- Nonselective muscarinic acetylcholinergic antagonist

Bradycardia

Atropine

- Anticholinergic
- Nonselective muscarinic acetylcholinergic antagonist
  - Parasympathetic NS insurgence
    - Infiltration
    - Remove the command structure
    - Interruption of communications

Bradycardia

Atropine

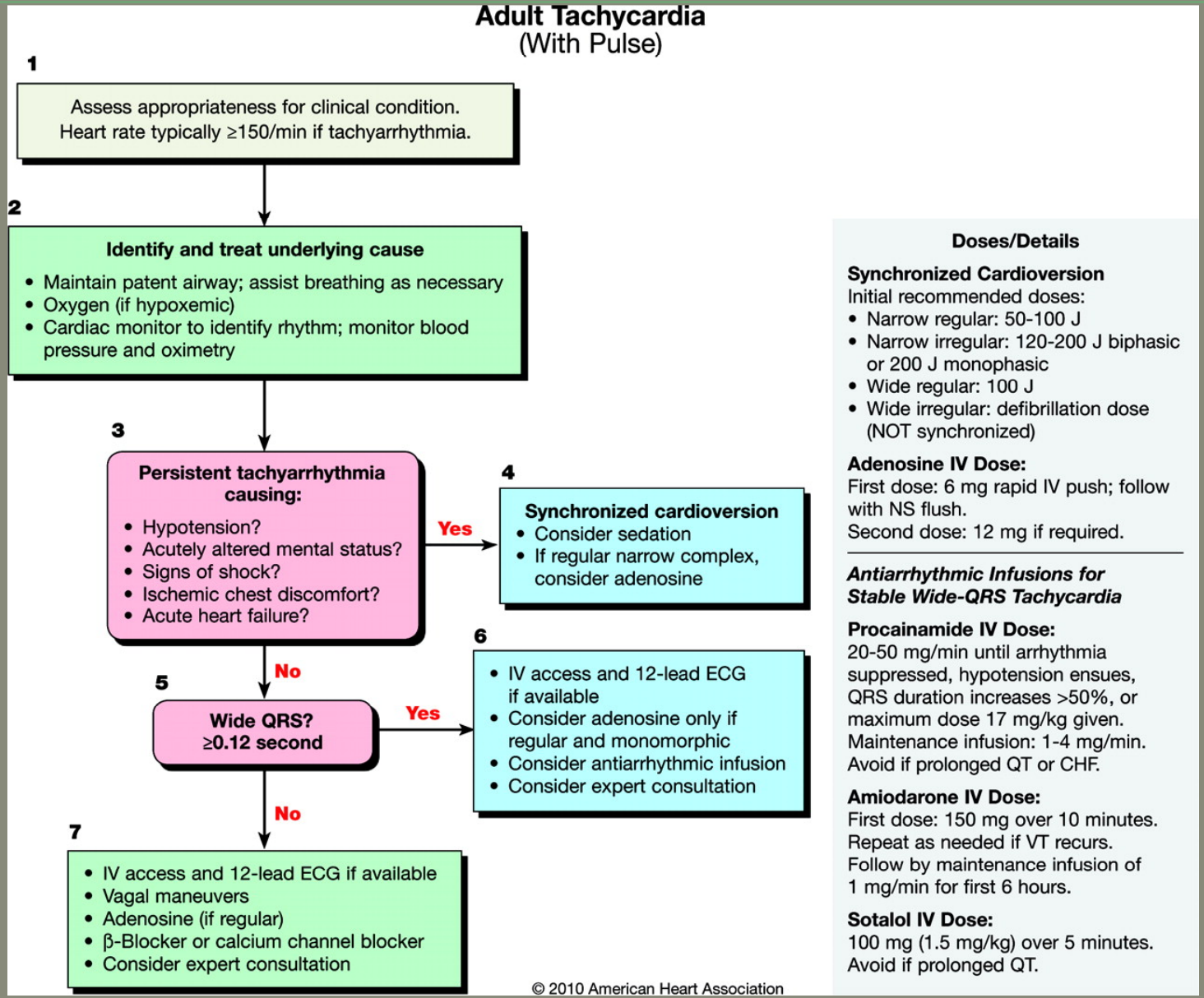
- Any considerations prior to counter-insurgency?

- And what about the ‘high blocks’?

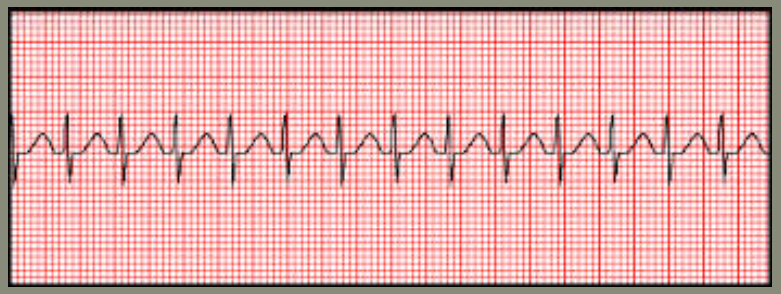
Bradycardia

- Our common pressors haven't changed
- We're still using those a couple of the "tropes"
  - Inotrope
    - Epi
  - Chronotrope
    - Dopamine (epi too)

Tachycardia



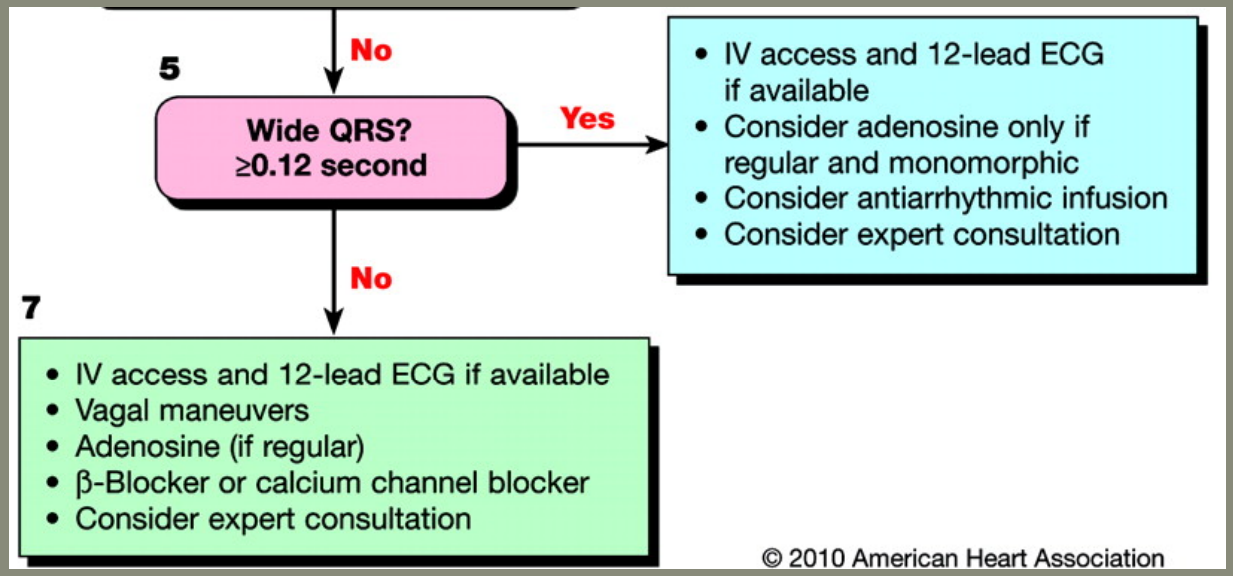
The Good



The Bad

The Ugly

Adenosine



Adenosine IV Dose:
First dose: 6 mg rapid IV push; follow with NS flush.
Second dose: 12 mg if required.

Antiarrhythmic Infusions for Stable Wide-QRS Tachycardia

Procainamide IV Dose:
20-50 mg/min until arrhythmia suppressed, hypotension ensues, QRS duration increases >50%, or maximum dose 17 mg/kg given.
Maintenance infusion: 1-4 mg/min.
Avoid if prolonged QT or CHF.

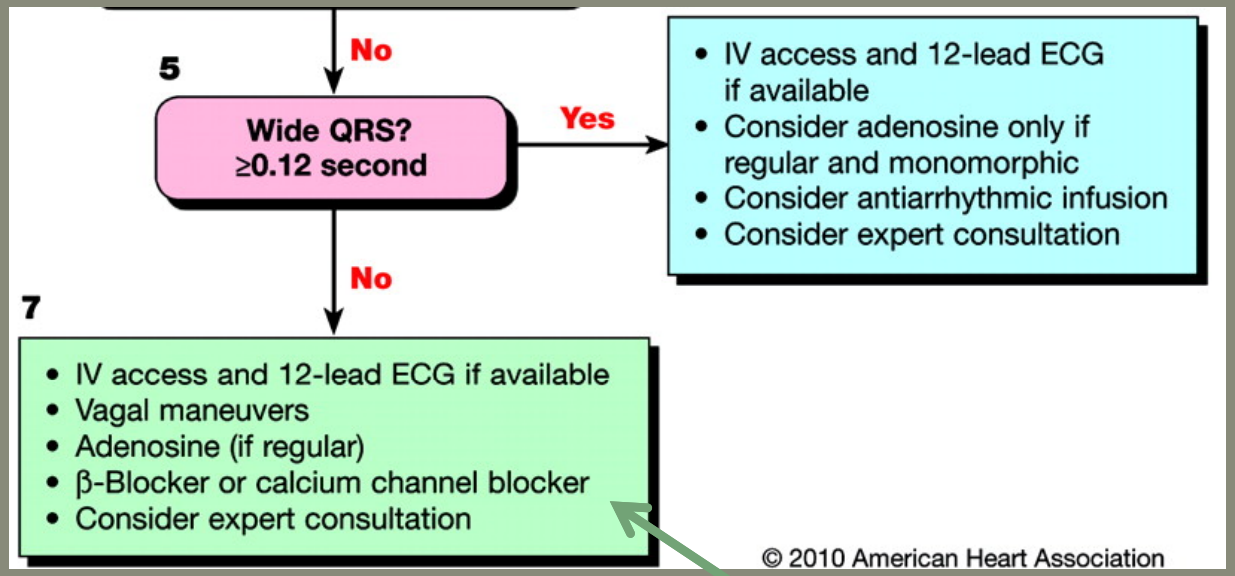
Amiodarone IV Dose:
First dose: 150 mg over 10 minutes.
Repeat as needed if VT recurs.
Follow by maintenance infusion of 1 mg/min for first 6 hours.

Sotalol IV Dose:
100 mg (1.5 mg/kg) over 5 minutes.
Avoid if prolonged QT.

Adenosine

- What is adenosine?
- MOA
- What limits its effect with atrial or ventricular dysrhythmias

Blocking Beta and Ca+ Channels



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Blocking Beta and Ca+ Channels

- Calcium Channels
  - Produce Action Potential Plateau and modulate contraction strength
  - In more depolarized regions (SA & AV) responsible for conduction and refraction
- Beta Receptor Antagonists
  - Reduction of response
  - Increased ERP

Meds we know

- What we are used to
  - Amiodarone
  - Metoprolol or Diltiazem
- Procainamide?

Procainamide

- Effects
  - ↑ Atrial effective refractory period
  - ↑↓ A-V node function
  - ↓ Myocardial excitability – from atria to ventricle
- Less desirable
  - ↓ Cardiac Output (undamaged)
  - ↓ CO (damaged)
- Class 1a

Procainamide

- ECG
  - Sinus Tach
  - Widened QRS
  - Lengthened QTI and PRI
  - Decreased amplitude of QRS and T wave

Antiarrhythmic Infusions for Stable Wide-QRS Tachycardia

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20-50 mg/min until arrhythmia suppressed, hypotension ensues, QRS duration increases >50%, or maximum dose 17 mg/kg given.
Maintenance infusion: 1-4 mg/min.
Avoid if prolonged QT or CHF.

How about that Evidence

"There are three kinds of lies: lies, damned lies, and stastistics"

- Mark Twain (attributed)

Interestingly

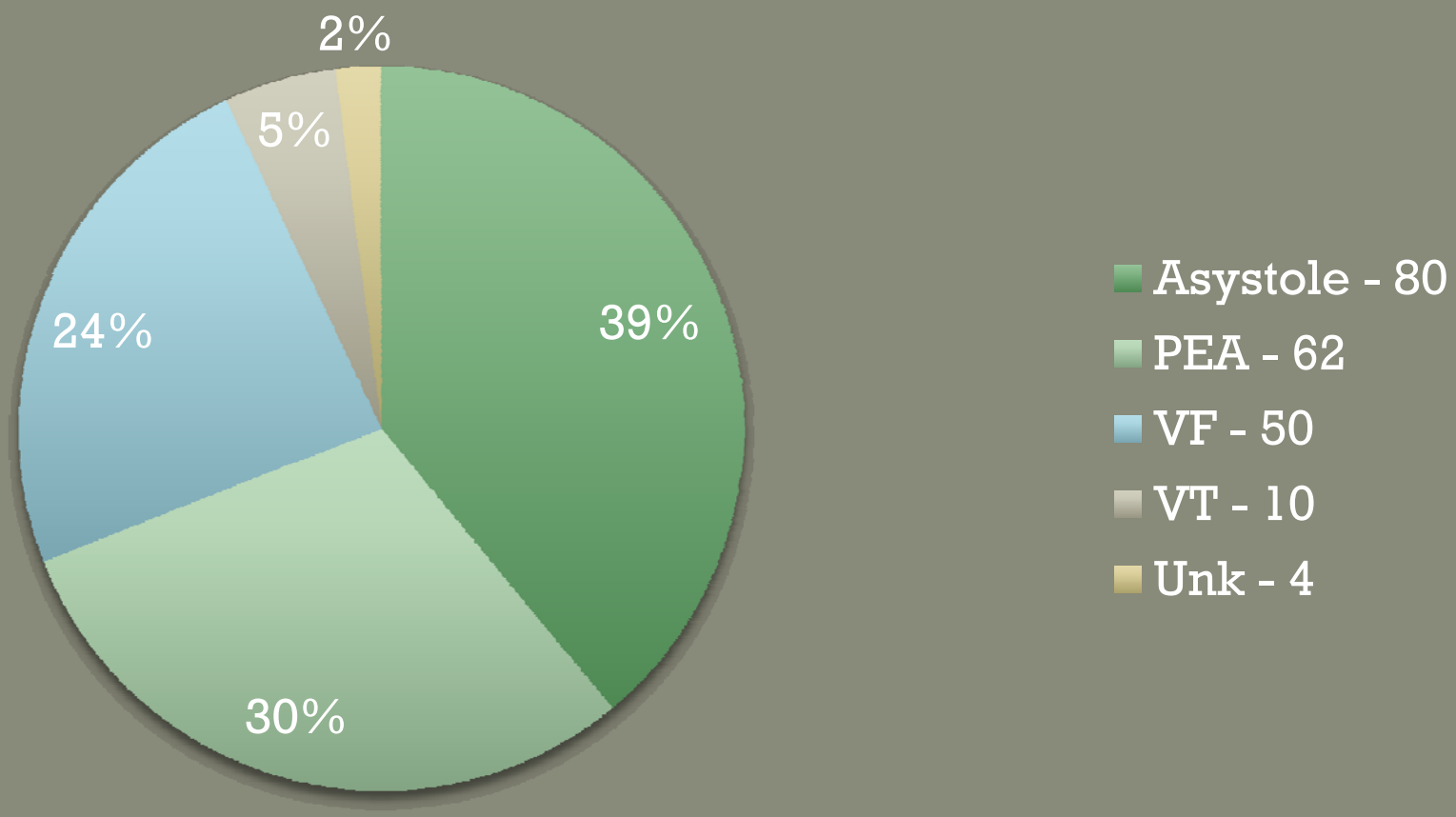
- Arrest protocols from Richmond Ambulance Authority differ

- 2009-2012
  - Out of Hospital Cardiac Arrests: 765 (40% unwitnessed)
  - ROSC at Hospital: 206
    - That's 27% of patients included
    - Bystander CPR in 24%
  - National ROSC without bystander CPR: 15%

Stats

- Autopulse Usage
  - 161 of the 206 with ROSC: 83% (failures excluded)
- Avg # of Epi doses per arrest – 1.6
- Avg # of Vaso doses per arrest – 1.5

Stats


Breakdown of ROSC by initial Rhythm
2%
5%
24%
39%
30%
Asystole - 80
PEA - 62
VF - 50
VT - 10
Unk - 4

What's different

- Autopulse CPR
- Vasopressin use
- Transport time
- Hypothermia starting in the field
  - In 2009, 52% of patients with ROSC and hypothermia started in the field survived to hospital discharge

Questions, Concerns, Discussion?

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Image from: Introduction to Arrhythmia Pharmacology
http://tmedweb.tulane.edu/pharmwiki/doku.php/intro_to_antiarrhythmics