



# ACLS Pharmacology

# Objectives

Review ACLS algorithms with specific focus on medications

Review pharmacodynamics of these medications

Discuss updated information and evidence cited by ILCOR/AHA

<b>I</b>	<b>Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.</b>
<b>II</b>	<b>Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.</b>
<i>Class IIa</i>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>
<i>Class IIb</i>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>
<b>III</b>	<b>Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.</b>

<b>LEVEL A</b>	
	<ul style="list-style-type: none"> <li>High-quality evidence‡ from more than 1 RCTs</li> <li>Meta-analyses of high-quality RCTs</li> <li>One or more RCTs corroborated by high-quality registry studies</li> </ul>
<b>LEVEL B-R</b>	<b>(Randomized)</b>
	<ul style="list-style-type: none"> <li>Moderate-quality evidence‡ from 1 or more RCTs</li> <li>Meta-analyses of moderate-quality RCTs</li> </ul>
<b>LEVEL B-NR</b>	<b>(Nonrandomized)</b>
	<ul style="list-style-type: none"> <li>Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies</li> <li>Meta-analyses of such studies</li> </ul>
<b>LEVEL C-LD</b>	<b>(Limited Data)</b>
	<ul style="list-style-type: none"> <li>Randomized or nonrandomized observational or registry studies with limitations of design or execution</li> <li>Meta-analyses of such studies</li> <li>Physiological or mechanistic studies in human subjects</li> </ul>
<b>LEVEL C-EO</b>	<b>(Expert Opinion)</b>
	Consensus of expert opinion based on clinical experience

# Cardiac Arrest

# Chain of Survival

Early Access and Cardiac Arrest Recognition

Early, High-Quality CPR

- Lay-rescuer should provide compression only CPR (I,C-LD)
- EMS may delay PPV in witnessed OHCA (IIb, C-LD)

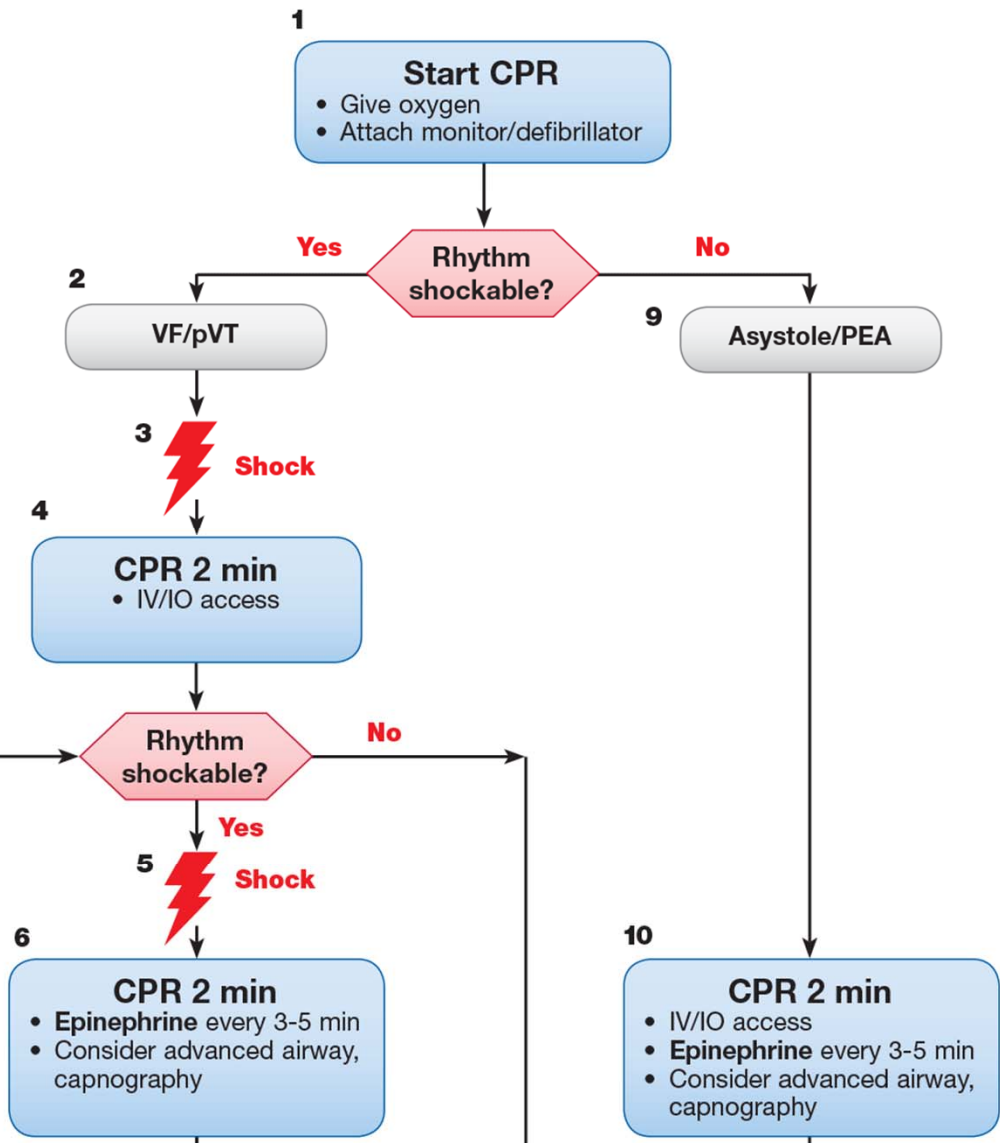
Early defibrillation

Advanced Life Support

Integrated postarrest care

When the links in the Chain of Survival are implemented in an effective way, survival can approach 50% in EMS-treated patients after witnessed out-of-hospital ventricular fibrillation arrest.”

Linman ME, Brennan EE, Goldberger ZD, Swor RA, Terry M, Bobrow BJ, Gazmuri RP, Travers AH, Rea T. Part 5: adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015;132(suppl 2):S415.



# SDE good...?

Standard Dose Epinephrine (SDE)

- 1 mg IV/IO every 3-5 minutes

Vasopressin



# Epinephrine

# Epinephrine

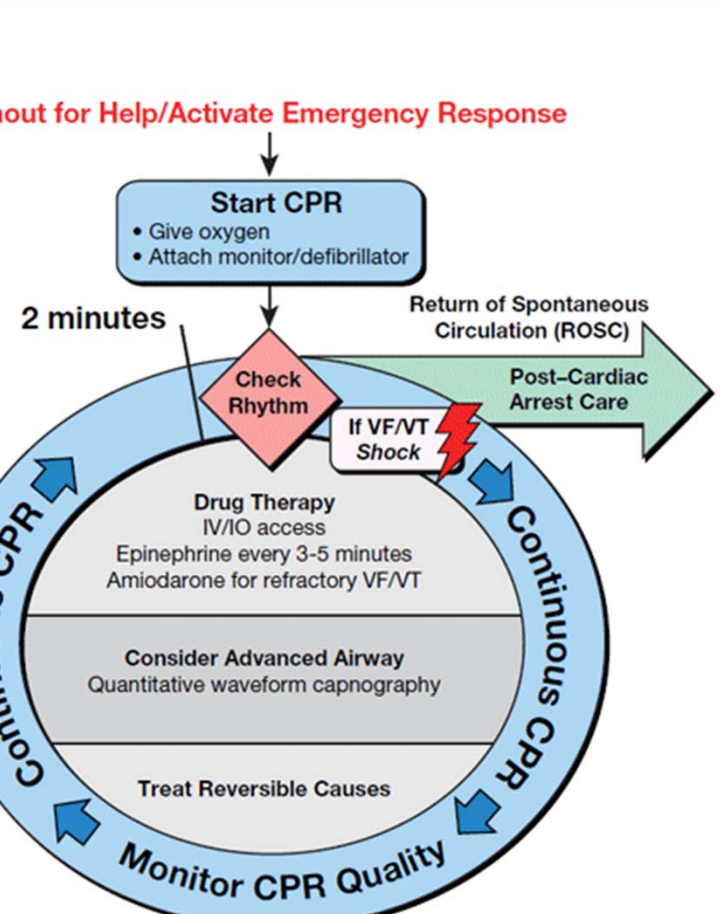
Classification

# Epinephrine

Classification

When?

# Epinephrine



The 'circular algorithm' introduced in 2010 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

# Epinephrine

Classification

When?

What is the significance of 3-5 minutes?

Time to administration

- < 9 min improved 1 month survival in non-shockable rhythms
- Dumas et al. – delayed administration associated with worse outcome

# Evidence

SDE (IIb, B-R)

- Jacobs et al. mentioned with explanation
- Observational Studies with conflicting results?
  - Hagihara et al.
  - Machida et al.

Dumas et al. (2014)

# Evidence

## Vasopressin (IIb, B-R)

- No benefit with Epi/vaso for survival to hospital admission or discharge

## Steroids, Vaso, Epi

- IHCA – SVE bundling significant improvement in survival to discharge vs. Epi and placebo
- Conclusion – IHCA may be considered, OHCA – uncertain benefit

# OHCA vs. IHCA

Why the distinctions? Do the data exist to make this legitimate?

## Targeted Temperature Management (I, B-R)

- Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest – NEJM
- Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia – Bernard et al.



# Antiarrhythmics

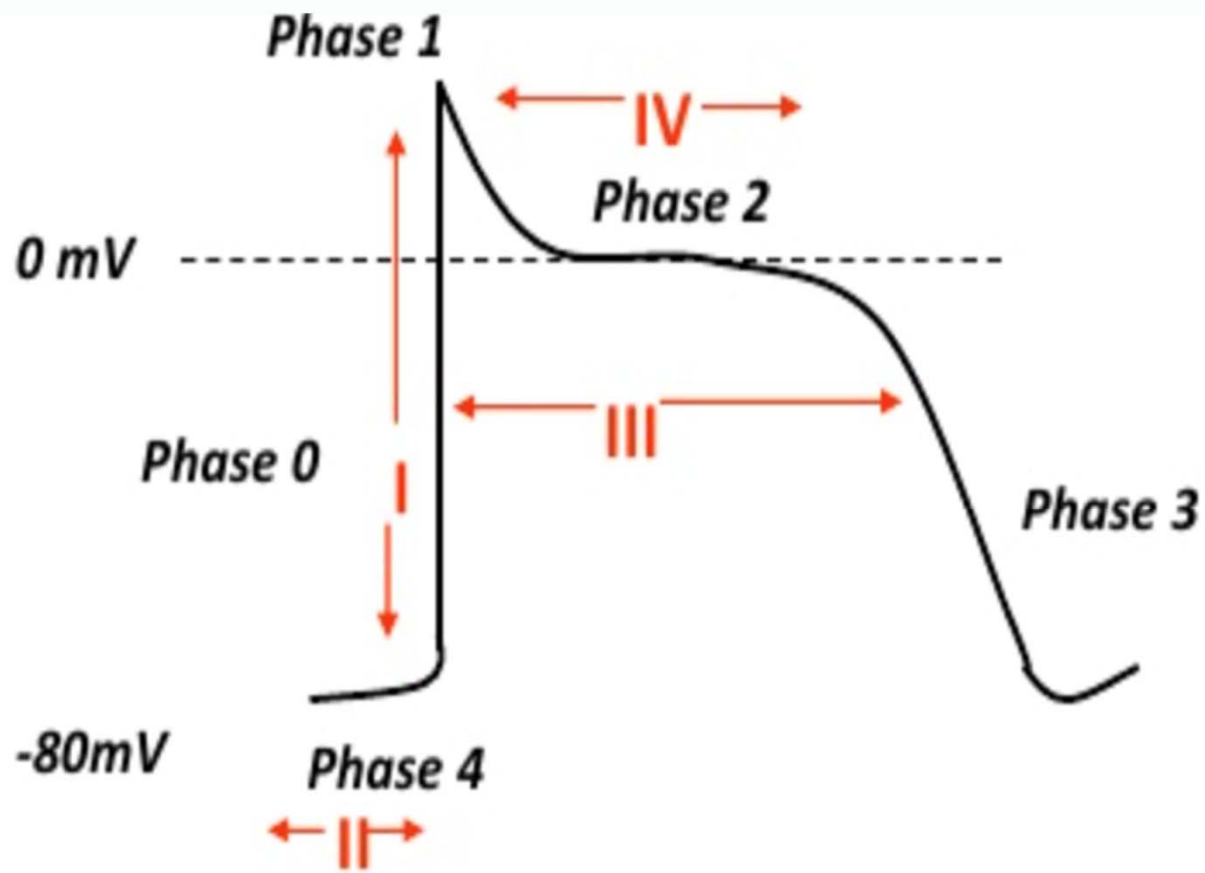
Amiodarone 300 mg

- 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

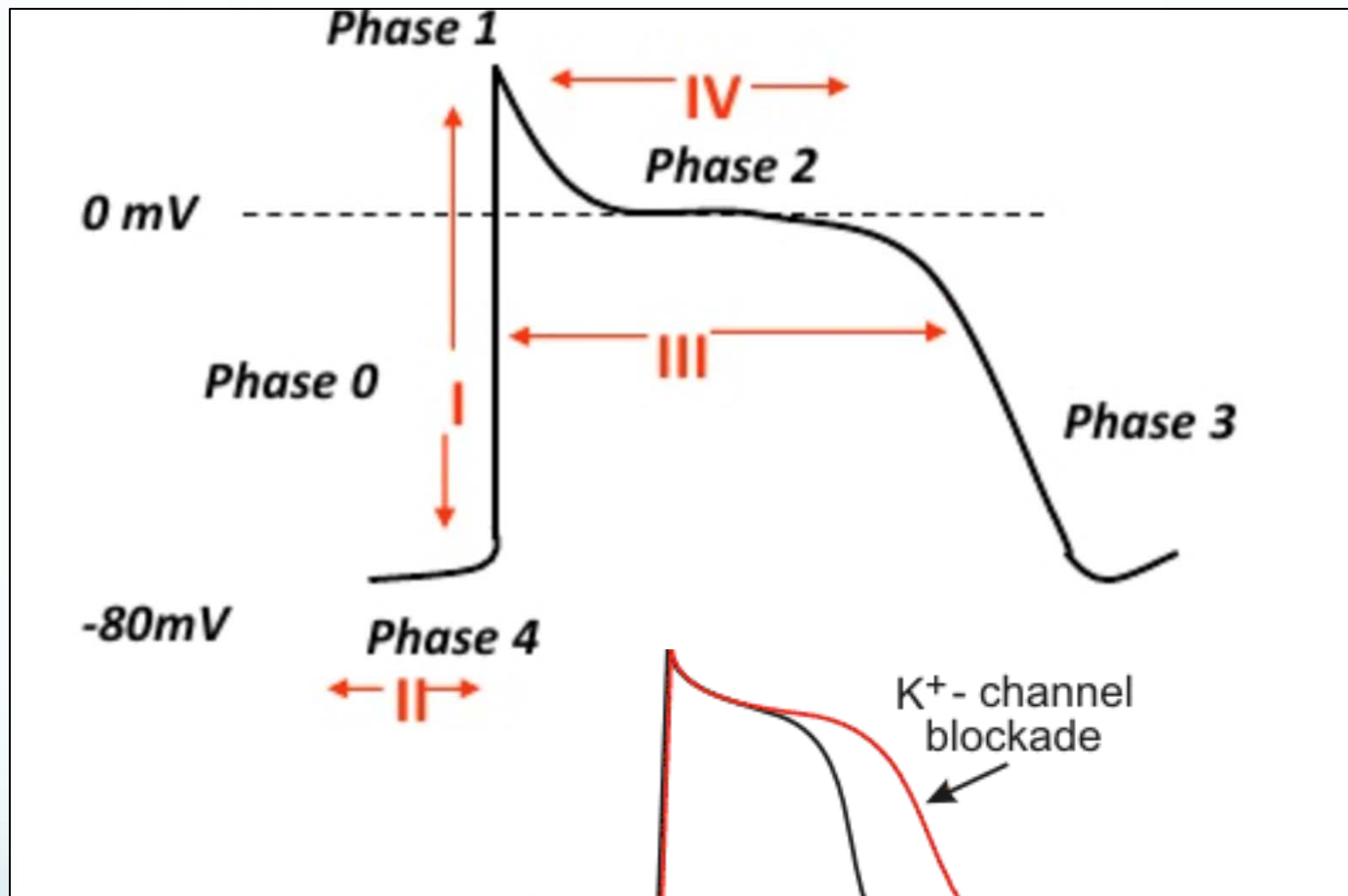


# Antiarrhythmics

miodarone

Class III antiarrhythmic agent

- Potassium Channel Blocker
  - Prolongs phase 3 (repolarization) of the cardiac action potential



Ventricular Action Potential

# Antiarrhythmics

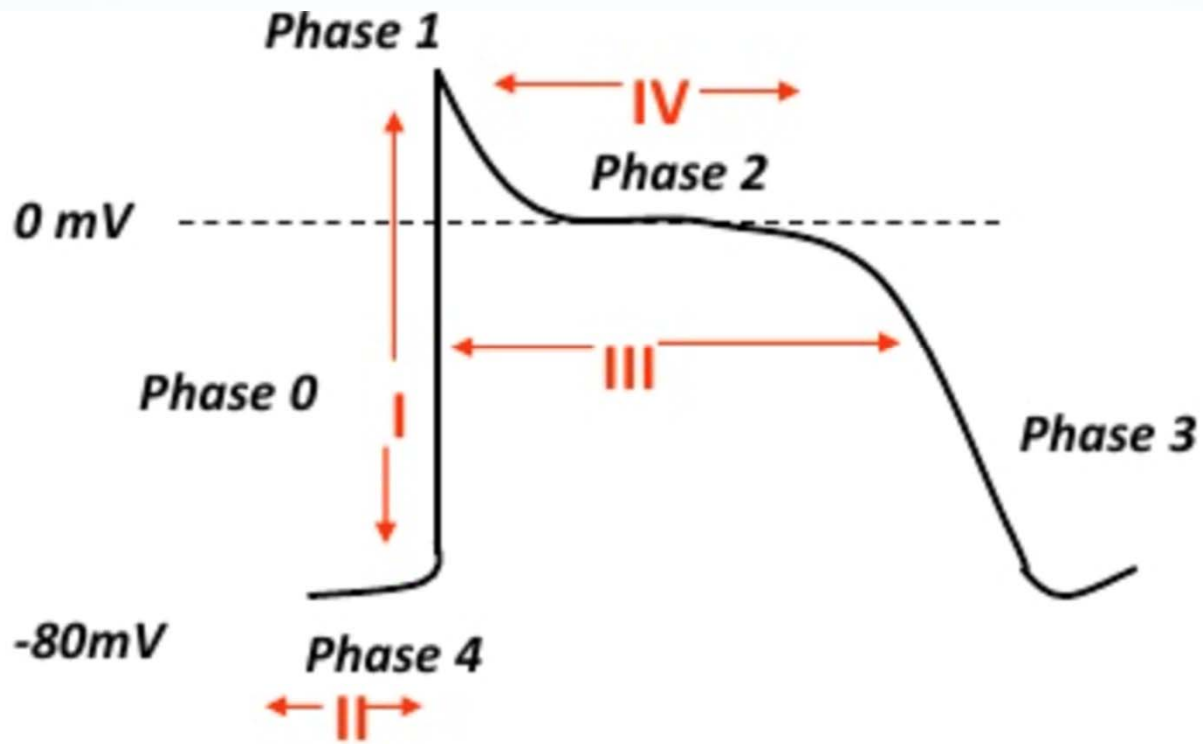
miodarone

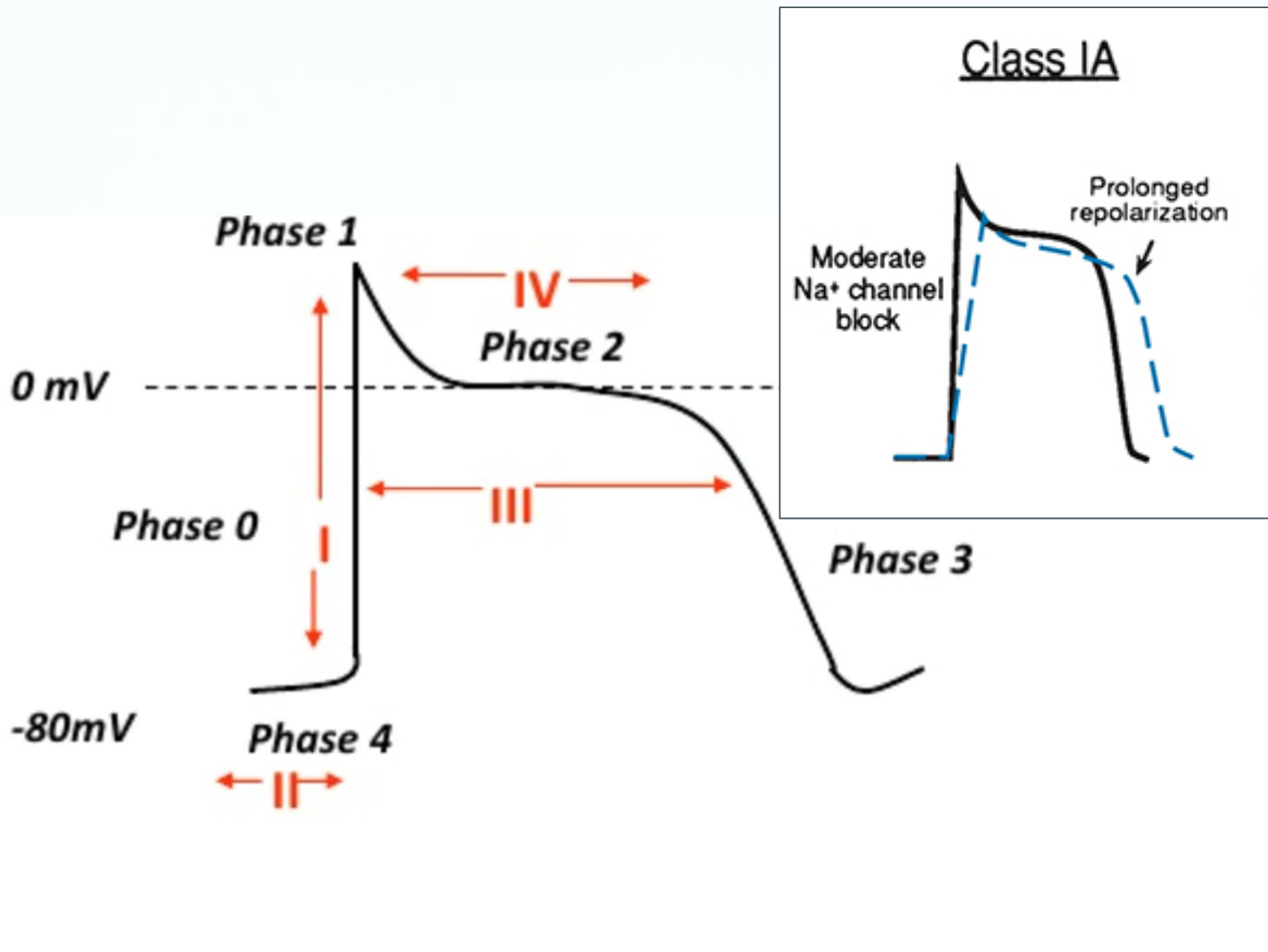
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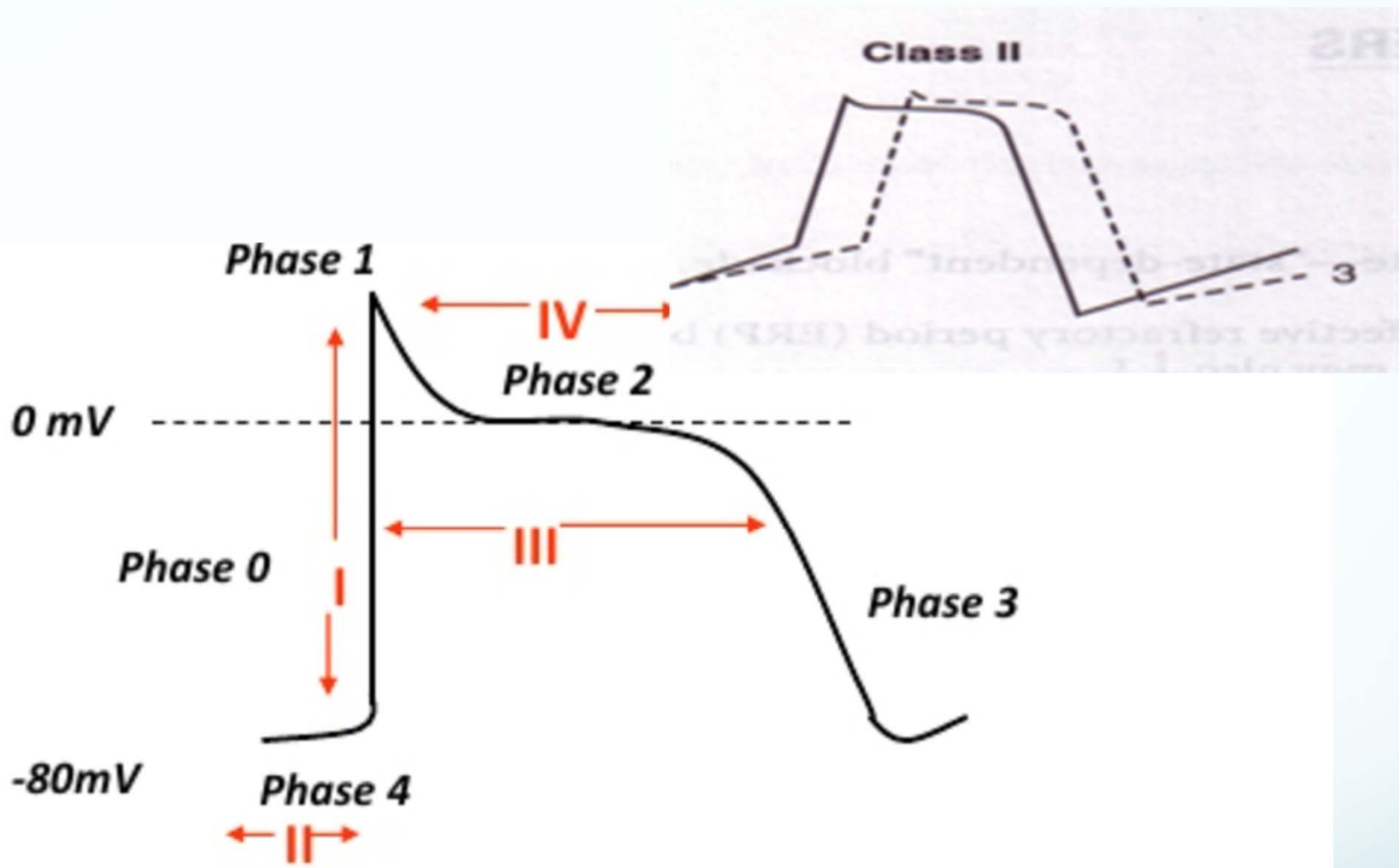
- Potassium Channel Blocker
  - Prolongs phase 3 (repolarization) of the cardiac action potential

And...

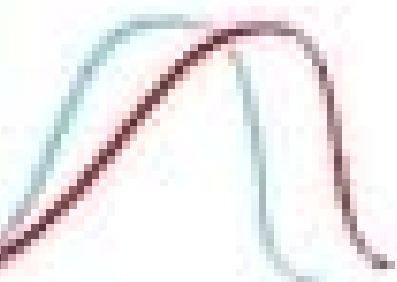
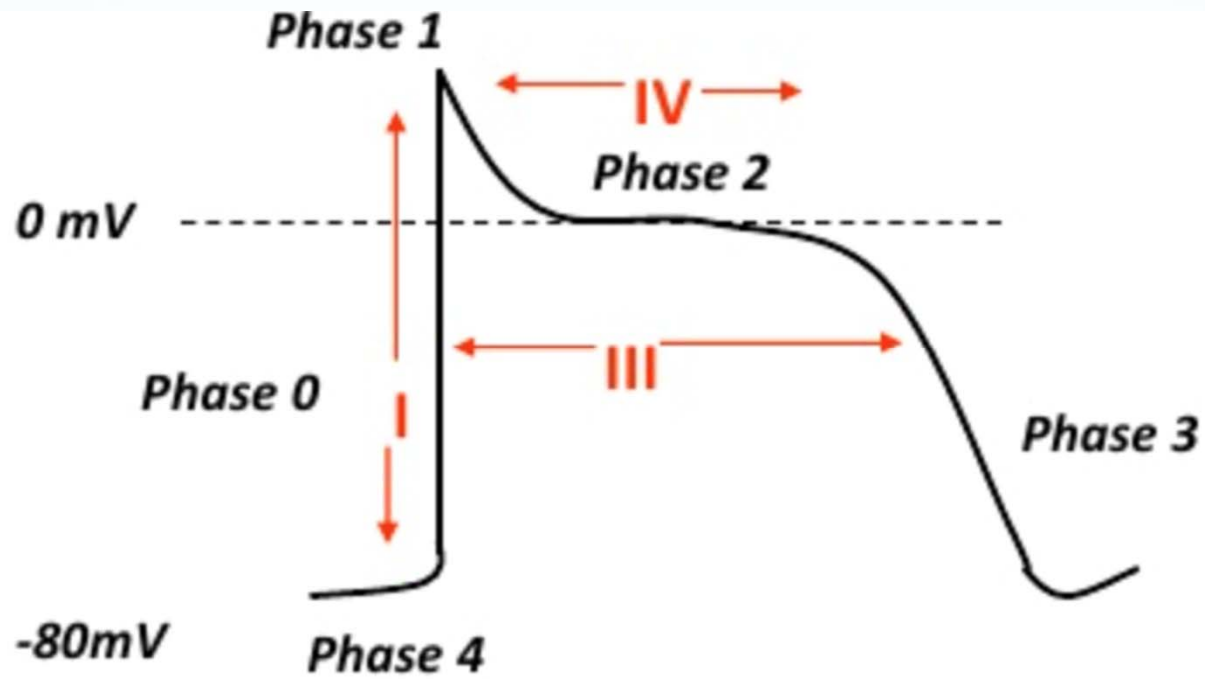
- It has effects similar to class Ia
- II
- IV



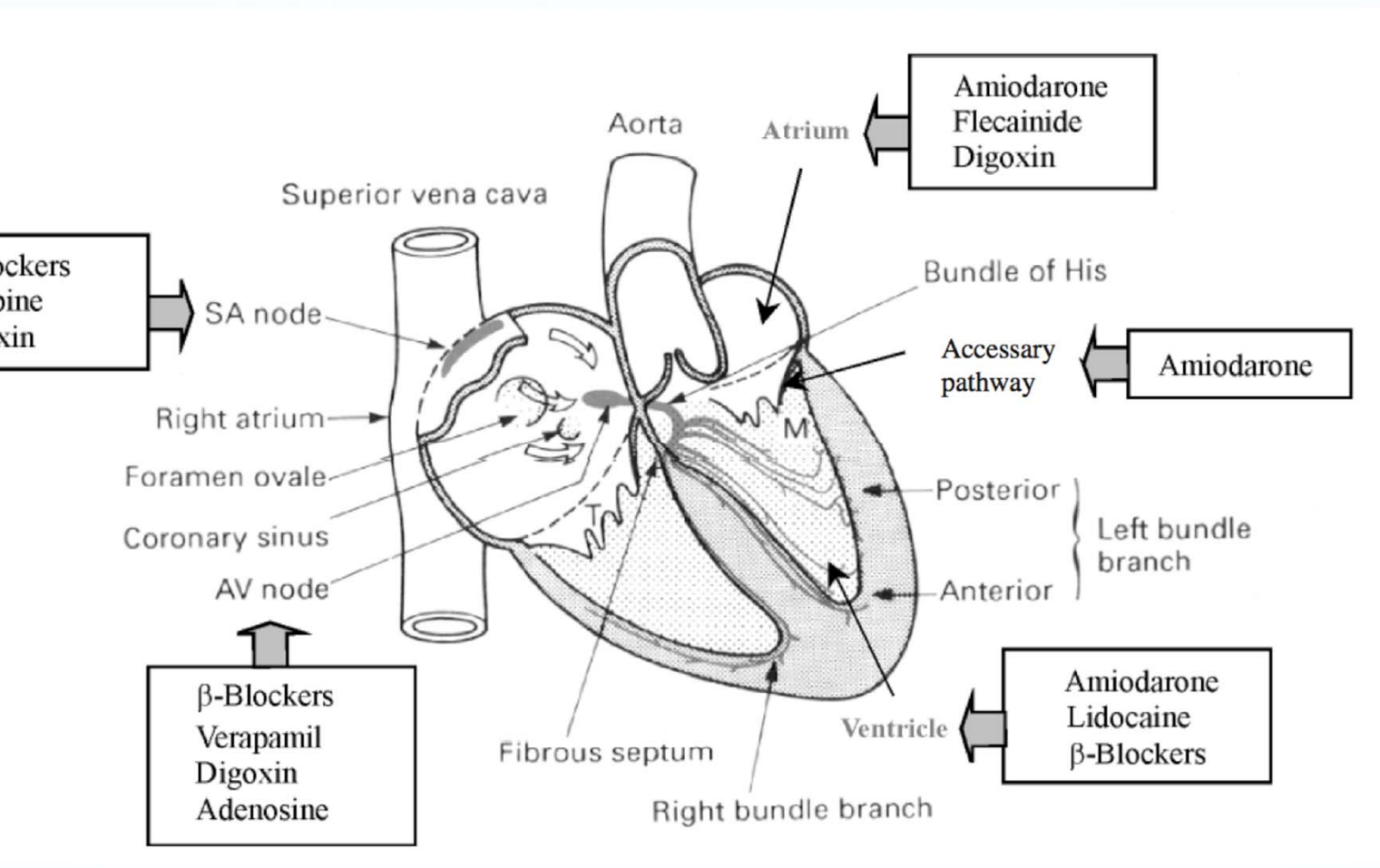








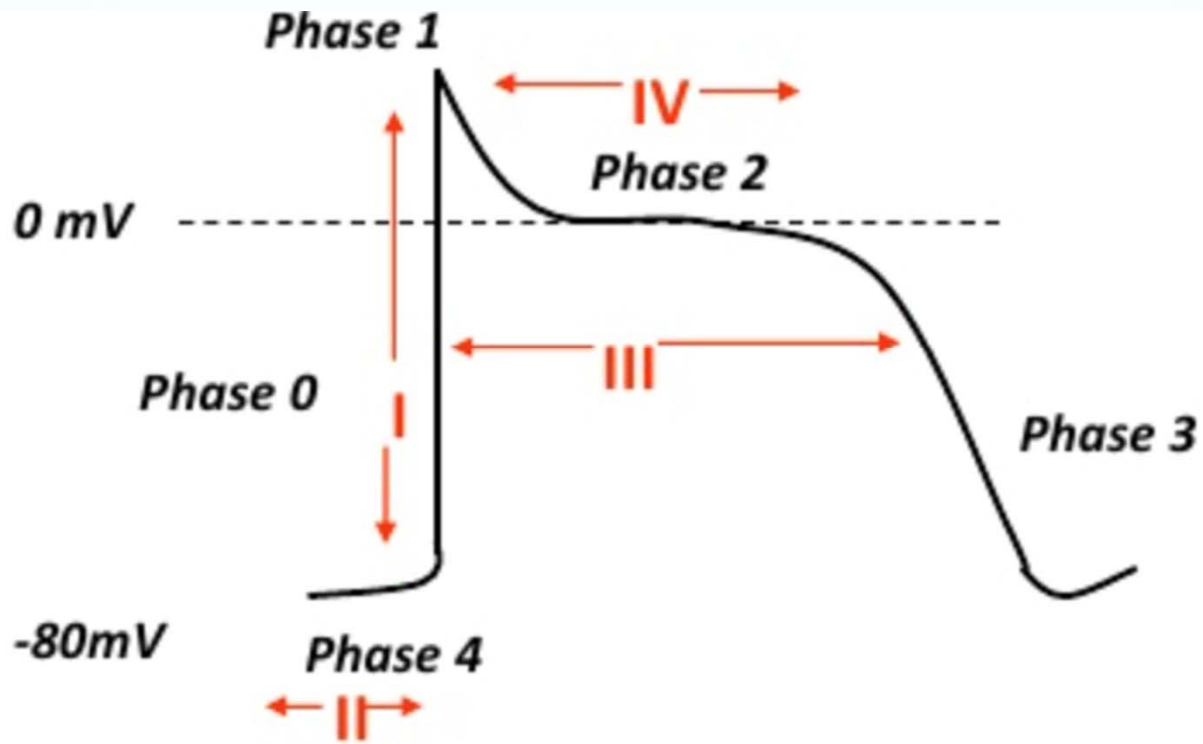
Class IV drugs (verapamil, diltiazem)



# Antiarrhythmics

procainamide

How does it 'anti' the arrhythmia?



# Antiarrhythmics

procainamide

How does it 'anti' the arrhythmia?

- Class Ib
- Na<sup>+</sup> Channel Blocking
- Ventricular arrhythmias

# Antiarrhythmics

Amio vs. Lido

- Is anyone using Lidocaine?
- Evidence of a superior choice?

# More arrest pharm

Magnesium Sulfate

Electrolyte

Indications

Mechanism of Action

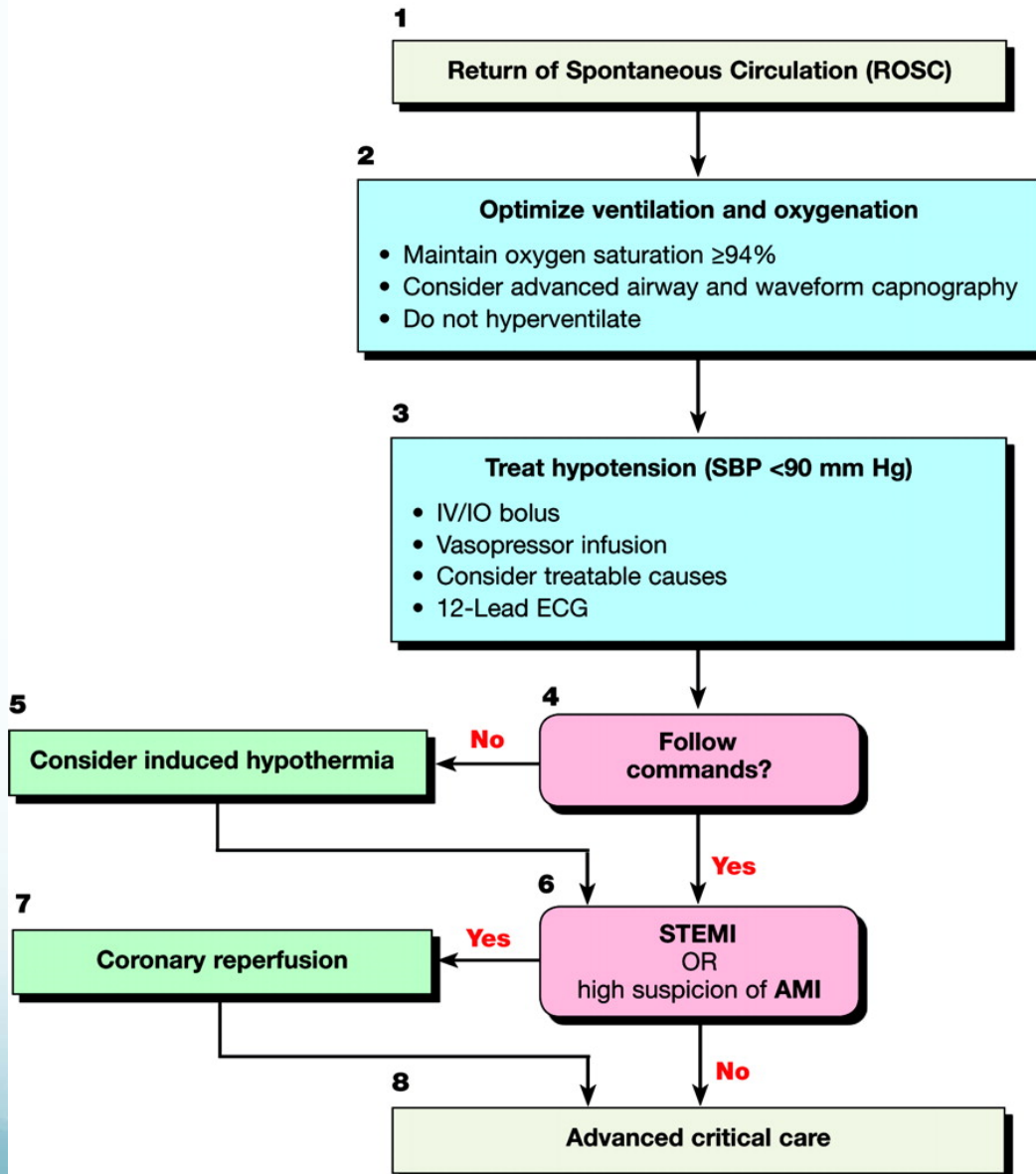
Evidence?

# Post-arrest

What to do with the patient that comes back to life



## Adult Immediate Post-Cardiac Arrest Care



### Doses/Details

#### Ventilation/Oxygenation

Avoid excessive ventilation. Start at 10-12 breaths/min and titrate to target PETCO<sub>2</sub> of 35-40 mm Hg. When feasible, titrate FIO<sub>2</sub> to minimum necessary to achieve SpO<sub>2</sub>  $\geq 94\%$ .

#### 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

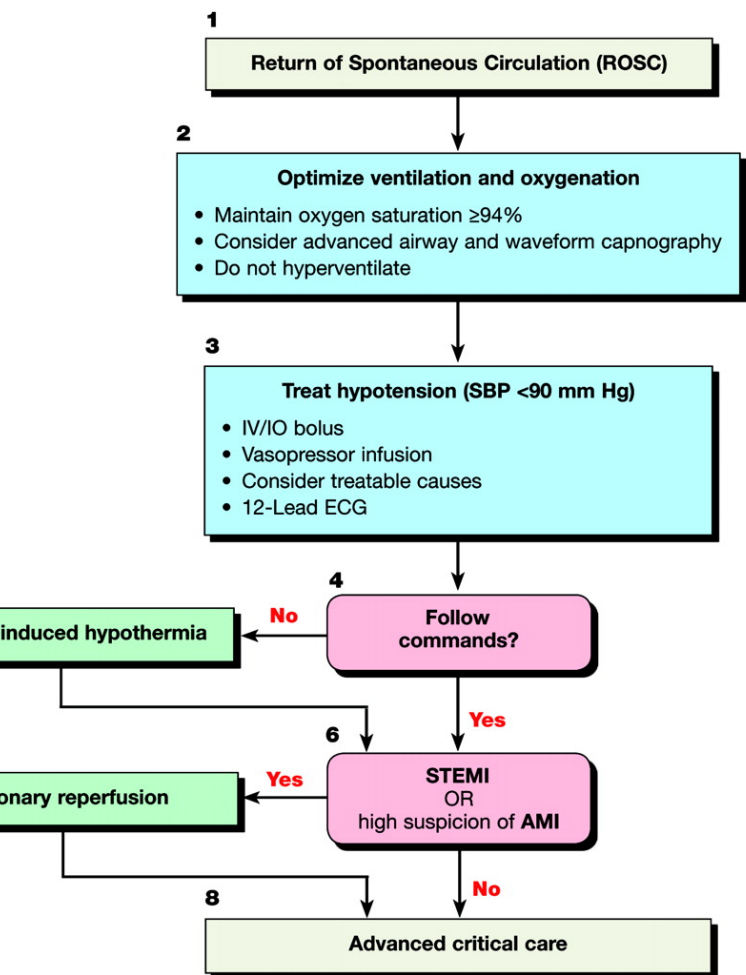
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#### Reversible Causes

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary

## Adult Immediate Post-Cardiac Arrest Care



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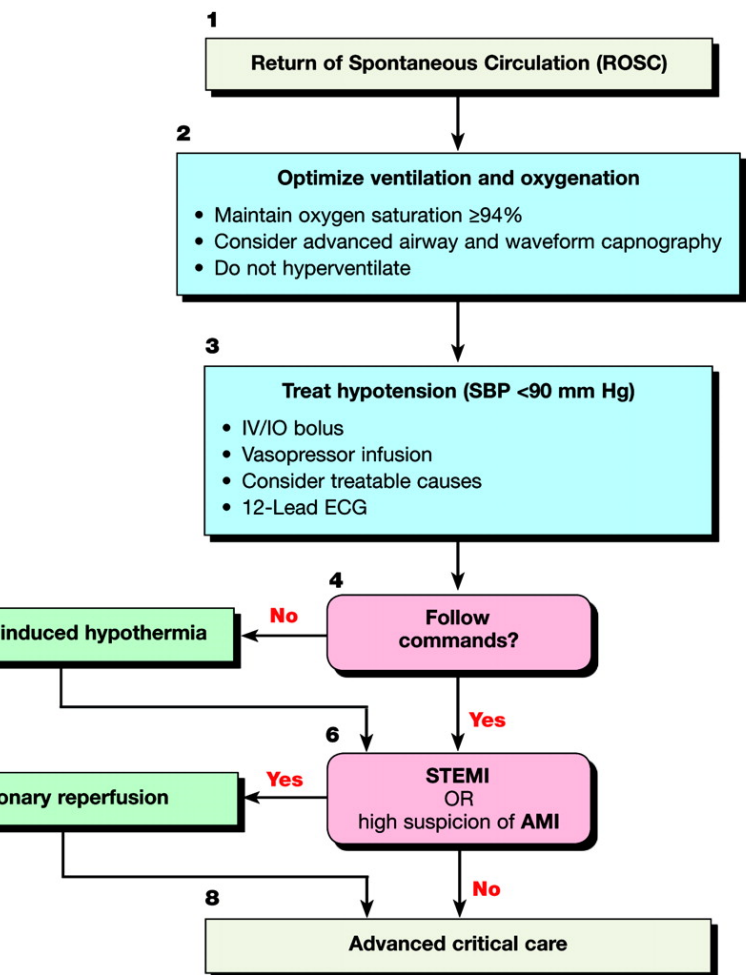
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We do this perfectly.

Always.

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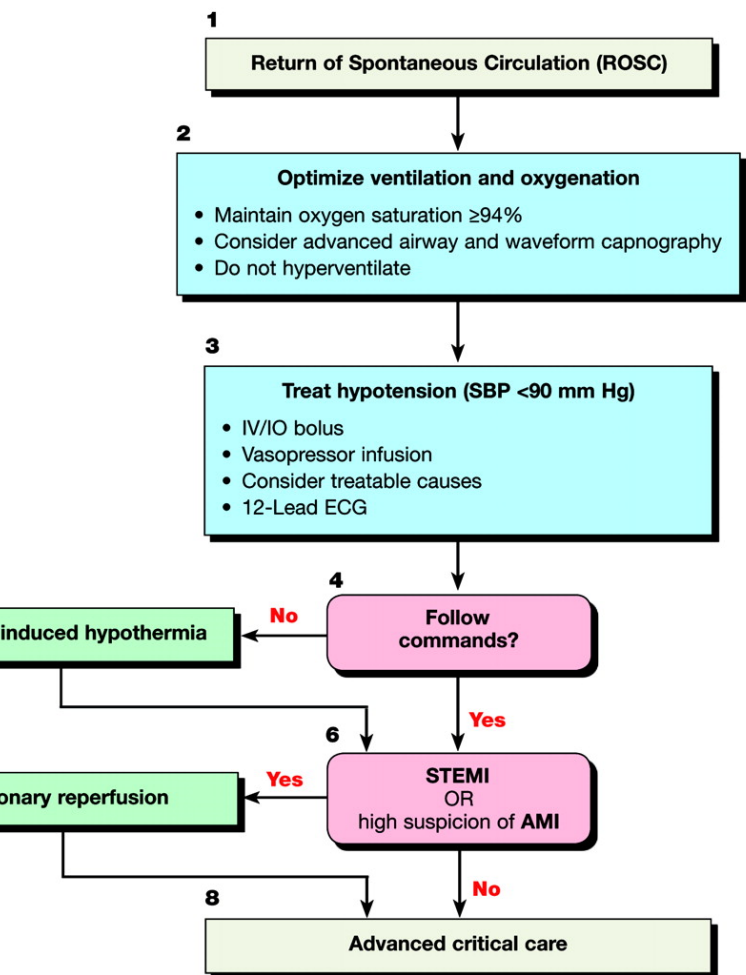
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Gone with 2015

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Norepi? There's a rhyme about that.

# Norepinephrine

Alpha and Beta adrenergic actions

- Specificity can be a good thing

Dose

- 0.1-0.5 mcg/kg/min (common 2-10 mcg/min)

More familiar thanks to shortages

Why the bad rep?

- Previous use as a secondary vasopressor for hypotension refractory to dopamine

# Pharmacology with the living

Mistakes may be more readily evident...

# ACS

xygen

- Define hyperoxia
- Pullalarevu et al. Association Between Duration of Hyperoxia, Organ Failure and Survival After Cardiac Arrest

SA

- MoA
- Daily ASA concerns

# ACS Pharm

## Nitrates

- Concerns?

## Pain management

- What medication

## Beta-Blockers

- Reasonable in severe hypertension or tachyarrhythmias (IIa, B)
- Absent contraindications, administer PO within first 24 hours (I, A)



# Bradycardia

- 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

3

## Persistent bradyarrhythmia causing:

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

No

Monitor and observe

Yes

5

## Atropine

If atropine ineffective:

- Transcutaneous pacing  
OR
- Dopamine infusion  
OR

## 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

# 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?  
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Ischemic chest discomfort?  
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## Atropine

If atropine ineffective:

- Transcutaneous pacing  
OR
- **Dopamine** infusion  
OR
- **Epinephrine** infusion

# Bradycardia

ropine

Nonselective muscarinic acetylcholinergic antagonist  
(AKA Anticholinergic)

MoA - Parasympathetic NS guerilla warfare

# Bradycardia

propine

Nonselective muscarinic acetylcholinergic antagonist  
(AKA Anticholinergic)

MoA - Parasympathetic NS guerilla warfare

Caution/considerations

What about 'high blocks'?

# Bradycardia

Vasopressors haven't changed, just more emphasis

- Dopamine
- Epinephrine
- Norepinephrine

# Bradycardia

## Dopamine

Chronotropic and Inotropic effects

### Dose Specificity

- 0.5 – 2.0 – Low (aka renal dosing)
- 2.0-10.0 – Intermediate
- 10.0-20.0 - High

## Epinephrine

- Chronotropic and Inotropic effects

# Review

## Inotrope

- Force of contraction

## Chronotrope

- Speed of contraction

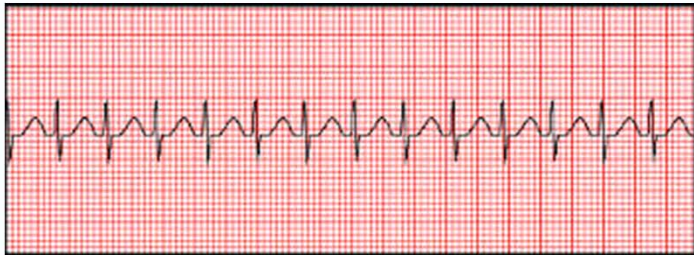
## Dromotrope

- AV node conduction speed

# Tachycardia



The Good



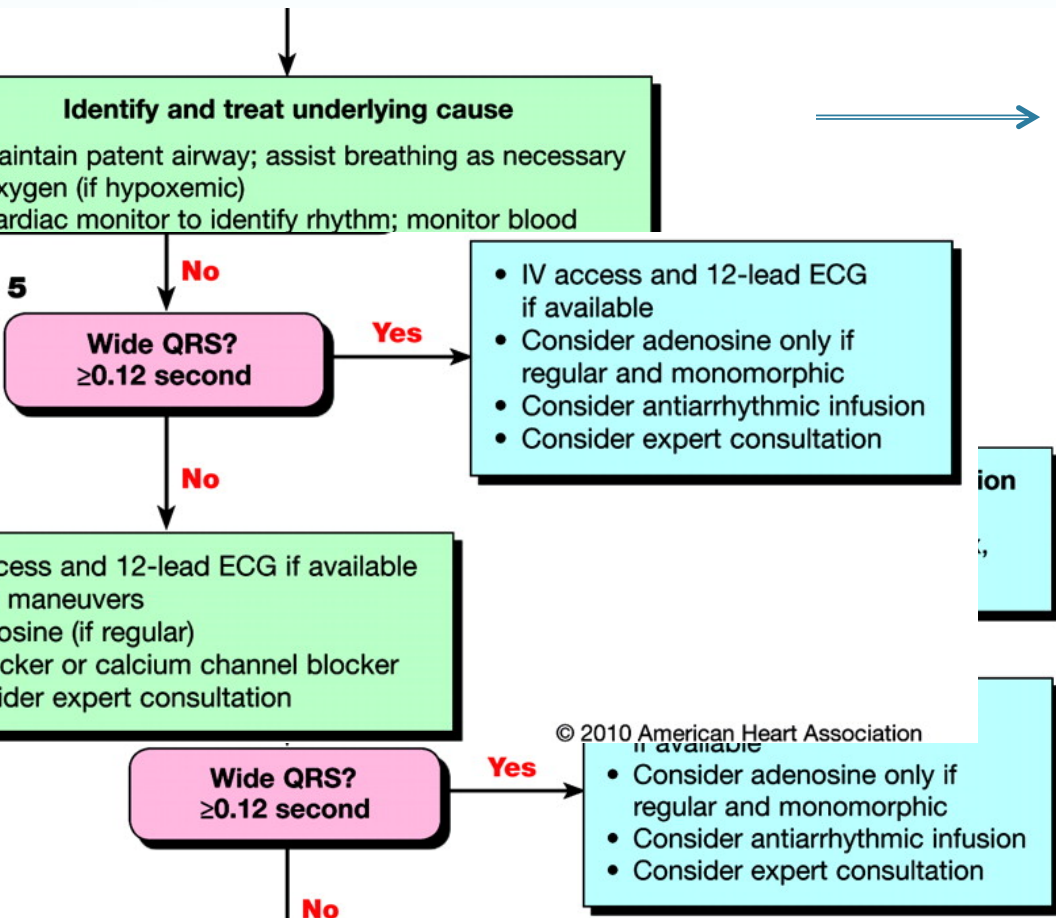
The Bad



The Ugly



# Adenosine



**Doses/Details**

**Synchronized Cardioversion**  
Initial recommended doses:

- Narrow regular: 50-100 J
- Narrow irregular: 120-200 J biphasic or 200 J monophasic
- Wide regular: 100 J
- Wide irregular: defibrillation dose (NOT synchronized)

**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

© 2010 American Heart Association

# Adenosine

Classification – antiarrhythmic (V)

MoA

Limitations

Dose

Why consideration for wide, regular, monomorphic tachycardia

# Rate Control

## Cardiazem

Prolongs AH conduction time  
and AV node EFR

0.25-0.35 mg/kg bolus with  
10 mg/hr infusion

## Metoprolol

- Blocks response to beta adrenergic stimulation
- 5 mg IV, repeated in 5 min to max of 15 mg

# Procainamide

Class – Antiarrhythmic – (Ia)

## Effects

- Increased atrial effective refractory period (decreased impulse conduction)
- Variable A-V node effects (direct slowing with weak vagolytic)
- Decreased myocardial excitability – from atria to ventricle
- Decreased CO (profound in myocardial damage)

Dosing – 20-50 mg/min loading dose

# Procainamide

## ECG Changes

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

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Questions, Concerns,  
Discussion?