

ACLS for the Clinical Pharmacist



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Objectives

- To review the importance of having a pharmacist attend codes
- To familiarize the pharmacist with the ACLS protocols
- To review routes of administration for medications used in code blue emergencies
- To introduce several common ECG rhythms
- To identify and discuss the most common drugs used by the ACLS algorithms

Why Involve Pharmacist?

- Improves outcomes in Code Blue
 - ◆ *Pharmacotherapy 2007. Apr 27(4):481-93.*
 - ◆ *Pharmacotherapy 1999. 19(5):556-64.*
- Calculate drug doses
- Drug information
- Preparation of drugs
- Source of quick access for medications not on crash cart
- Assessment of patient's allergies and medication usage

Common Principles in New ACLS Guidelines - 2005



1. Early, effective bystander CPR
2. Early defibrillation - Public Access Defibrillation
3. Minimal interruptions in chest compressions
4. Establishing a specific diagnosis by ECG
5. **Choose one** antiarrhythmic agent
One, and only one antiarrhythmic should be used.
6. If IV access is not established, Intraosseous cannulation is the first line alternative and endotracheal is an alternative.

Pharmacist Involvement

- Pharmacists should KNOW:
 - How? ...to use an agent
 - Why? ...we use an agent
 - When? ...to use an agent
 - What? ...to watch for

How To Use the Medication?



Routes of Medications

■ IV Push (IVP)

- Preferred route – fast, convenient, + bioavailability
- Peripheral – flush w/ 20cc bolus and elevate arm for 10-20 seconds. Peak effect takes 1-2 minutes
- Central line should be placed (however, keep in mind it is a relative contraindication for thrombolytic therapy)
 - ◆ V - vasopressin
 - ◆ A - amiodarone, atropine, adenosine
 - ◆ L - lidocaine
 - ◆ E - epinephrine

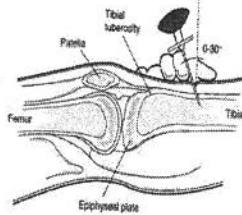
Intravenous Infusion

■ Intravenous infusion

- ◆ Medications for continuous IV infusion only
 - ◆ P – procainamide
 - ◆ I – isoproterenol
 - ◆ N – norepinephrine
 - ◆ D – dopamine
- ◆ Central line preferred, however, peripheral OK in emergency

Intraosseous Administration

- When IV access not available
- Gives access to a noncollapsible venous access route
- Important when patients are in shock with peripheral vasoconstriction



Endotracheal Administration

- When IV access is not available
- Doses usually 2-2.5 times higher
- Absorption occurs at alveolar capillary interface
- Dilute drugs with 10ml 0.9% NaCl or Water to allow for adequate delivery (H2O preferred)
 - ◆ L – lidocaine (2-4 mg/kg)
 - ◆ E – epinephrine (2-2.5 mg)
 - ◆ A – atropine (2-3 mg)
 - ◆ N – naloxone (0.8-1.6 mg)
 - ◆ V – vasopressin (80-100 Units)



HOW? Medication Administration

- Do not interrupt chest compressions
- Time to maximum effect of drug may depend on the distance from the heart
- Administer 10-20ml NS after each drug administered (20ml if peripheral administration & elevate arm)
- Have medications labeled and ready in advance
- Best to give immediately after shock

WHEN To Use WHAT Medication?



Use of Algorithms

- Meant to treat broadest range of patients
- Memory aids
- Use "wisely," not blindly
- Not meant to replace clinical judgment
 - ◆ Where to find?
 - American Heart Association
 - Attached to crash cart
 - Included in DMC Tier 2 policy
 - acls.net on the web

Check Rhythm ECG Rhythms

- Wave forms

healthcentral.org

ECG Rhythms

- Normal sinus rhythm

Heart Rate	Rhythm	P Wave	PR Interval	QRS
60-100 bpm	Regular	Before each QRS, identical	.12 to .20	<.12

healthcentral.org

ECG Rhythms

- Asystole

Heart Rate	Rhythm	P Wave	PR Interval	QRS
Absent	Absent	Absent or present	N/A	Absent

- Bradycardia

Heart Rate	Rhythm	P Wave	PR Interval	QRS
< 60 bpm	Regular	Before each QRS, identical	.12 to .20	<.12

healthcentral.org

ECG Rhythms

- Ventricular Tachycardia

Heart Rate	Rhythm	P Wave	PR Interval	QRS
>100	Regular	Absent or not related	N/A	>.12

- Ventricular Fibrillation

Heart Rate	Rhythm	P Wave	PR Interval	QRS
300-600	Extremely irregular	Absent	N/A	Fibrillatory baseline

ECG Rhythms

- Artifact (waveform interference)

Sixty even, regular spikes in a 1 second interval caused by electrical current near the patient

healthcentral.org

Cardiac Arrest Management

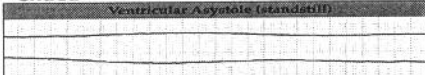
1. Pulseless Cardiac Arrest – i.e. ASYSTOLE and PEA
2. VENTRICULAR FIBRILLATION and PULSELESS V.TACH

Pulseless Arrest Algorithm

- Minimize interruptions in chest compressions
- Limit pulse and rhythm checks
- Do not check pulse immediately after shock – give 5 cycles, then check!
- Once advanced airway in place – do not interrupt compressions

Asystole and Pulseless Electrical Activity (PEA)

- Asystole is a cardiac standstill
- PEA-pt has mechanical contractions but no pulse. Any rhythm possible
- Both are non-shockable rhythms
- Most do not survive
- Asystole means the patient's life has ended



Heart Rate	Rhythm	P Wave	PR Interval (s)	QRS (duration)
Absent	Absent	Absent or present	N/A	Absent

Asystole & PEA Algorithm

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BLS Algorithm:
Call for help, give CPR
Give oxygen when available
Attach monitor/defibrillator when available
↓
Check rhythm: shockable? YES or NO
If NO and problem is asystole/PEA
↓
Resume CPR immediately for 5 cycles
↓
Give vasopressor: Epinephrine or vasopressin
Consider Atropine for asystole or slow PEA rate
↓
Give 5 cycles of CPR
↓
Check rhythm: shockable? If no:
  
```

Asystole and PEA Algorithm

	Interventions
P	Problem search via Differential Diagnosis table; treat accordingly. (PATCH 4MDs) Continue algorithm if indicated.
E	Epinephrine 1 mg IVP/IO q3-5 min. OR Vasopressin 40 units IV/IO, once, in place of the first or second dose of epinephrine.
A	Atropine 1 mg IVP/IO q3-5 minutes; 3mg maximum.

Problem Search: Differential Diagnosis PATCH(4) MDs

<ul style="list-style-type: none"> ■ Pulmonary embolism <ul style="list-style-type: none"> ◆ Thrombolytics ■ Acidosis <ul style="list-style-type: none"> ◆ Bicarb./hyperventilation ■ Tension pneumothorax <ul style="list-style-type: none"> ◆ Thoracostomy ■ Cardiac tamponade <ul style="list-style-type: none"> ◆ Pericardiocentesis ■ Hyperkalemia <ul style="list-style-type: none"> ◆ HCO₃, CaCl₂, Ins/Glc, HD, diuresis, kayexylate 	<ul style="list-style-type: none"> ■ Hypokalemia ■ Hypovolemia ■ Hypoxia ■ Myocardial infarct <ul style="list-style-type: none"> ◆ ACS protocol ◆ Avoid BB if cocaine ■ Drugs ■ Shivering
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Basic Pharmacology Review



Vasoactive Receptor Effects

- α_1 – VASOCONSTRICTION of arteries and veins
- α_2 – Feedback and Vasoconstriction
 - ◆ Decreases NE release
- β_1 – INOTROPE & CHRONOTROPE
- β_2 – VASODILATION (skin, kidneys, skeletal muscles, visceral and pulmonary arteries) and BRONCHODILATION

Vasopressor Therapy

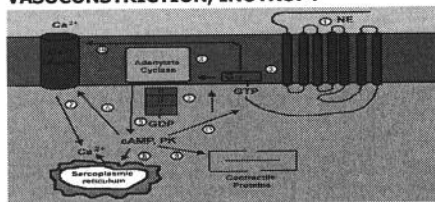
- Increases SBP by increasing preload and ventricular filling pressure
- Enhance organ perfusion, increase cerebral and coronary perfusion pressures (increases success of defibrillation)
- Mostly via α_1 stimulation and V_1 stimulation
- List the Vasopressors:
 - ◆ Epinephrine
 - ◆ Vasopressin
 - ◆ Norepinephrine
 - ◆ Phenylephrine
 - ◆ Dopamine

Inotropic Therapy

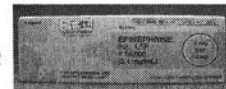
- Increase cardiac contractility and increase cardiac output (CO)
- Work via β_1 stimulation and/or by increasing cAMP and Calcium influx
- List the Inotropes:
 - ◆ Dobutamine
 - ◆ Milrinone (or inamrinone)
 - ◆ Digoxin
 - ◆ Glucagon

Catecholamine Pharmacology

- Bind to β -adrenoreceptor and stimulate Gs protein
- Stimulates adenylate cyclase, \uparrow cAMP
- cAMP acts to INCREASE Ca INFLUX
- VASOCONSTRICTION, INOTROPY



E = Epinephrine



- 1mg IVP/IO every 3-5 minutes.
- GOAL – Improve Perfusion to Essential Organs (Heart, Brain). Shifts blood centrally.
- MOA – Alpha and Beta Adrenergic Agonist
 - ◆ α_1 – Vasoconstriction. Increases BP; improves cerebral and coronary perfusion pressures
 - ◆ β_{1-2} – Stimulates the cardiac muscle increasing the strength of ventricular contraction. + inotrope and chronotrope. Does increase myocardial work

Epinephrine Side Effects

- Nervous system: anxiety, agitation
- Cardiovascular: dilated CM, LV dysfunction
- Psychiatric: disorientation, hallucinations
- Metabolic: acidosis, hypokalemia
- Renal: renal insufficiency
- Other: extravasation, skin necrosis

Vasopressin



- Vasopressin 40 units IVP/IO x 1 (2 vials required. Each vial = 20 Units)
- May replace 1st or 2nd dose of epinephrine
- **Pharmacology:** Endogenous ADH
 - ◆ Causes vasoconstriction at high doses by directly stimulating smooth muscle V₁ receptors
 - ◆ Dilates cerebral blood vessels
 - ◆ Coronary & renal vasoconstriction

Vasopressin Rationale

- Enhance organ perfusion
- Advantages over epinephrine?
 - ◆ Longer half-life (10-20 minutes)
- Not affected by acidosis
- Unique MOA - nonadrenergic
- Best outcomes in ASYSTOLE?

Pharmacotherapy 2006;26(6):828-839

Vasopressin Side Effects

- GI: nausea, intestinal cramps
- Increased mesenteric vascular resistance
- Bronchial constriction
- Uterine contractions
- Extravasation - necrosis

A = Atropine



- 1mg IVP/IO every 3-5 minutes up to a maximum of 3 mg
 - ◆ Excessive parasympathetic tone may play a role in stopping ventricular and supraventricular pacemaker activity
 - ◆ Avoid if lack of cardiac activity has a clear explanation such as hypothermia

Atropine Pharmacology

- Competitive antagonist of acetylcholine
- Vagolytic action causes restoration of heart rate and blood pressure
- Reverses cholinergic-mediated decreases in:
 - ◆ Heart rate
 - ◆ Systemic vascular resistance
 - ◆ Blood pressure

Atropine Side Effects

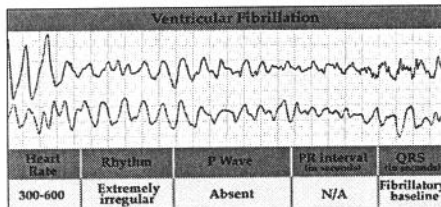
- Anticholinergic
 - ◆ Confusion
 - ◆ Blurred vision
 - ◆ Dry mouth, skin, nose
 - ◆ Constipation
 - ◆ Urinary retention
 - ◆ Lightheadedness

VF and PVT

- VF = ventricular fibrillation
 - ◆ Fibrillary contractions of the ventricular muscle due to rapid repetitive excitation of myocardial fibers without coordinated contraction of the ventricle
- PVT = pulseless ventricular tachycardia
 - ◆ An abnormally rapid ventricular rhythm with aberrant ventricular excitation most commonly associated with atrioventricular dissociation
 - ◆ The patient has no pulse

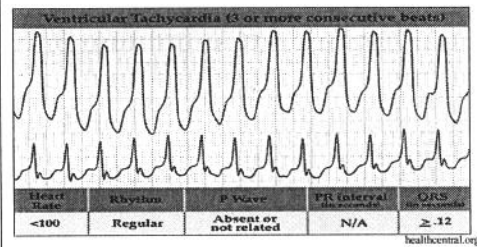
ECG Rhythms

- Ventricular fibrillation

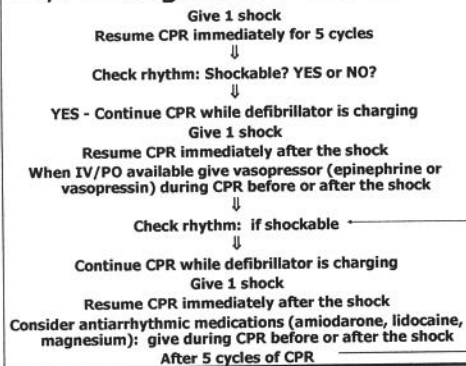


ECG Rhythms

- Ventricular tachycardia

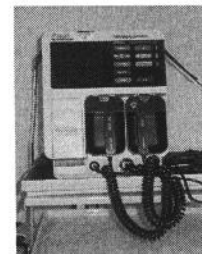


VF/PVT Algorithm: SCREAM



Shock

- Manual biphasic
 - ◆ Device specific
 - ◆ Typically 120-200 J
 - ◆ If unknown, use 200 J
- AED
 - ◆ Device specific
- Monophasic
 - ◆ 360 J



VF/PVT Algorithm: SCREAM

S	Shock	360J monophasic, 1 st and subsequent shocks. Shock every 2 minutes if indicated.
C	CPR	After shock, immediately begin chest compressions followed by respirations for 2 minutes. Do not check rhythm or pulse.
R	Rhythm	Rhythm check after 2 minutes of CPR (and after every 2 minutes of CPR thereafter) and shock again if indicated. Check pulse only if an organized or non-shockable rhythm is present

Implement the Secondary ABCD Survey. Continue this algorithm if indicated. Give drugs during CPR before or after shocking. Minimize interruptions in chest compressions to < 10 seconds. Consider differential diagnosis.

VF/PVT Algorithm: SCREAM

E	Epinephrine	1mg IVP/IO q3-5 minutes or vasopressin 40 units IV/IO, once, in place of the 1 st or 2 nd dose of epinephrine.
A M	Antiarrhythmic Medications	Consider antiarrhythmics: <ul style="list-style-type: none"> Any Legitimate Medication Amiodarone 300mg IVP/IO, may repeat once at 150mg in 3-5 minutes if VF/PVT persists or Lidocaine (if amiodarone unavailable) 1-1.5mg/kg IVP/IO, may repeat X2, q5-10 min at 0.5-0.75mg/kg Max LD= 3mg/kg Magnesium Sulfate 1-2 gm IVP/IO diluted in 10m D5/W (5-20 min push) for torsades de pointes or suspected/known hypomagnesemia.

Amiodarone



- 300mg IVP/IO once, then consider additional 150mg IVP/IO once
 - ◆ If pt is pulseless, give IVP, otherwise dilution with 20-30ml and a slower infusion results in less bradycardia, hypotension and phlebitis
 - ◆ Infusion OK peripherally if < 2mg/ml
 - ◆ Not for ET administration

Amiodarone

- MOA: Inhibits conduction through Sodium, Potassium and Calcium channels and α & β adrenergic blocking ability
- Inhibits adrenergic stimulation, prolongs the action potential and refractory period in myocardial tissue, and decreases AV conduction and sinus node function
- Based on ARREST and ALIVE Trials
- Side effects: hypotension, bradycardia, nausea, vomiting, tremor, dizziness, headache, phlebitis

Lidocaine



- 1-1.5 mg/kg first dose then 0.5-0.75mg/kg IVP/IO q5-10 minutes
- Maximum of 3 doses or 3 mg/kg
- After return of ROSC infuse at 1-4 mg/min (50% reduction if cardiac or liver failure)
- Suppresses automaticity of conduction tissue and blocks both the initiation and conduction of nerve impulses
- Side effects: hypotension, headache, shivering

Magnesium



- 1-2 grams IVP/IO diluted in 10ml D5W over 5-20 minutes. If patient has pulse, can slow down infusion to 30-60 min
- INDICATION: torsades de pointes
 - ◆ Low magnesium causes inhibition of conduction through K⁺ channels in heart – prolongs AP and QT prolongation
- Side effects: flushing, somnolence, complete heart block, respiratory paralysis

Arrhythmia Management

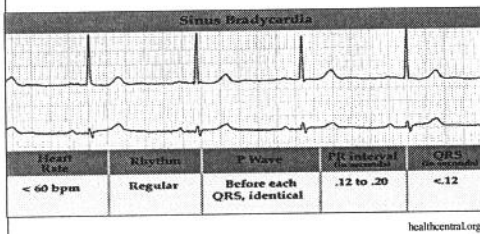
- Bradycardia
- Tachycardia: SVT

Bradycardia

- Bradycardia:
 - ◆ HR < 60 beats/minute or when the heart rate is slower than expected
- Signs and symptoms might include:
 - ◆ Chest pain, shortness of breath
 - ◆ Hypotension, pulmonary edema, congestive heart failure

ECG Rhythms

- Sinus bradycardia



Bradycardia Algorithm: Pacing Always Ends Danger

Maintain patient airway; assist breathing as needed
 Give oxygen
 Monitor ECG, blood pressure, oximetry
 Establish IV access
 ↓
 Signs/symptoms of poor perfusion caused by the bradycardia?
 If yes:
 ↓
 Prepare for transcutaneous pacing
 Consider atropine IV while awaiting pacer; if ineffective begin pacing
 Consider epinephrine or dopamine infusion while awaiting pacer or if pacing ineffective
 ↓
 Prepare for transvenous pacing
 Treat contributing causes
 Consider expert consultation

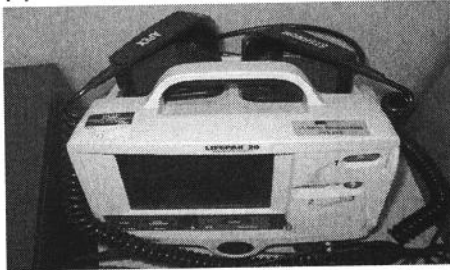
Bradycardia Algorithm: Pacing Always Ends Danger

Mnemonic	Intervention	Note
Pacing	TCP	Immediately prepare for TCP with serious circulatory compromise due to bradycardia (especially high-degree blocks) or if atropine failed to increase rate
Consider medications while pacing is readied.		
Always	Atropine	First line drug, 0.5mg IV/IO q3-5 min (maximum 3mg)
Ends	Epinephrine 2-10mcg/min	Second line drugs to consider if atropine and/or TCP are ineffective. Use with extreme caution
Danger	Dopamine 2-10 mcg/kg/min	

Transcutaneous Pacing

- Used to speed up a cardiac rhythm that is too slow
- If considered, start immediately
- To be effective, must be performed early and combined with drug therapy

Transcutaneous Pacing Apparatus



Atropine



- Atropine 0.5 mg IV while awaiting pacer
 - ◆ 50% reduction in dose when compared with PEA algorithm
- May repeat to a total dose of 3 mg
- If ineffective, begin pacing

Epinephrine



- Consider epinephrine 2-10 mcg/min continuous infusion while awaiting pacer
- Use 1ml of the 1:1000 or 10 ml of the 1:10,000 in 500ml D5W
- Alternatively, 0.5 mg IVP boluses
 - ◆ To avoid tachyarrhythmias
 - ◆ Until continuous infusion available
 - ◆ Until pacemaker available
- Or if pacing ineffective

Dopamine



- Or consider dopamine 2-10 mcg/kg/min infusion while awaiting pacer or if pacing ineffective
- MOA: Precursor of norepinephrine, stimulates heart through both alpha- and beta-adrenergic receptors
- Increases both cardiac output and arterial perfusion pressure

Dopamine Side Effects

- **Cardiovascular:** ectopic heartbeats, tachycardia, vasoconstriction, hypotension, ventricular arrhythmias
- **CNS:** headache
- **GI:** nausea, vomiting
- **Respiratory:** dyspnea
- **Other:** Adrenal insufficiency

Tachycardia Algorithm

Assess and support ABCs as needed
Give oxygen
Monitor ECG, blood pressure, oximetry
Identify and treat reversible causes
↓
Symptoms persist and patient stable
Establish IV access
Obtain 12-lead ECG or rhythm strip
Is QRS narrow or wide?
↓
Narrow QRS (<0.12 sec) with regular rhythm
↓

Tachycardia Algorithm (continued)

Attempt vagal maneuvers
 Give adenosine 6mg rapid IVP
 If no conversion, give 12mg rapid IVP
 May repeat 12mg dose once

↓


Does rhythm convert?
 Note: Consider expert consultation

↓

Yes: Probable reentry SVT. Observe for recurrence. Treat recurrence with adenosine or diltiazem (Cardizem) or beta-blockers.

or

No: Possible atrial flutter, ectopic atrial tachycardia, or junctional tachycardia. Control rate with diltiazem (Cardizem) or beta-blockers. Treat underlying cause. Consider expert consultation.



Tachycardia Algorithm

- Tachycardia is stable, narrow, and regular:
 - ◆ Yes 1-2-3, think SVT, then V-A-C

1. Stable?	Yes: see question 2	No: unstable = immediate electrical cardioversion
2. Narrow?	Yes: see question 3	No: wide = consult an expert with QRS ≥ 0.12 sec
3. Regular?	Yes: see mnemonic	No: irregular = consult an expert

Tachycardia Algorithm


- Yes 1-2-3, think SVT, then V-A-C
 - ◆ Vagal maneuvers, if this fails...
 - ◆ Adenosine 6 mg rapid IVP (may repeat X2, q1-2 min at 12mg)
 - ◆ Cardizem (diltiazem) managed by an expert if stable, narrow, regular tachyarrhythmia continues

www.acs.net

Vagal Maneuvers

- Valsalva's maneuver
 - ◆ A forcible exhalation effort against a closed glottis which results in an increase in intrathoracic pressure which interferes with venous return to the heart
- Carotid sinus massage
 - ◆ Firm rotatory pressure applied to one side of the neck over the carotid sinus in a supine patient to cause vagal stimulation in order to slow or terminate tachycardia

Adenosine



- To convert SVT: 6 mg rapid IVP over 1-3sec followed by 20ml saline flush; if rate dose not convert in 1-2 min give 12mg IVP & repeat 12mg in 1-2 minutes again
 - ◆ Larger doses required for patients with significant blood levels of theophylline, caffeine, or theobromine
 - ◆ Reduce initial dose to 3 mg in patients taking dipyridamole or carbamazepine or those with transplanted hearts *or if given by central venous access*

Adenosine

- Slows conduction time through AV node, interrupts reentry pathways through AVN and restores NSR
- Side effects common but transient: flushing, dyspnea, chest pain

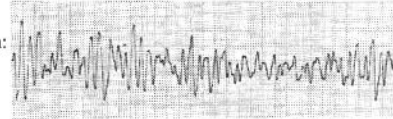
Diltiazem (Cardizem)



- Use if adenosine fails
- 15-20mg (0.25mg/kg) IVP over 2 min; if needed in 15 minutes give an IVP dose of 20-25mg (0.35mg/kg)
- Maintenance infusion dose is 5-15mg/hr
- Blocks conduction through the AV node
- Harmful if given to patients with atrial fibrillation or atrial flutter associated with known pre-excitation such as Wolf-Parkinson-White

Cases:

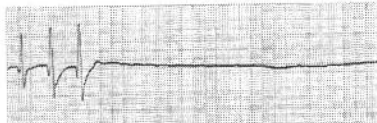
■ Rhythm:



- What is this?
- Algorithm?
- Drugs/Doses?
- Ventricular Fibrillation
- SCREAM
- Epi 1 mg q3-5min
- Amiodarone 300mg IVP, may repeat with 150mg

Cases:

■ Rhythm:



- What is this?
- Algorithm?
- Drugs/Doses?
- Asystole
- PEA
- Epi 1 mg q3-5min (or vasopressin 40 Units IVP)
- Atropine – 1mg q3-5 min to max dose = 3mg

Cases:

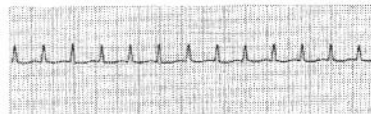
■ Rhythm:



- What is this?
- Algorithm?
- Drugs/Doses?
- Bradycardia
- Pacing Always Ends Danger
- Atropine 0.5 mg q3-5min to max = 3mg
- Epi 2-10 mcg/min
- Dopamine 2-10 mcg/kg/min

Cases:

■ Rhythm:



- What is this?
- Algorithm?
- Drugs/Doses?
- SVT
- Yes 1, 2, 3, then think VAC
- Adenosine 6mg IVP then 12mg IVP, then 12mg IVP
- Cardizem 15-20 mg IVP then 5-15 mg/hr

Other Code Situations

- Anaphylaxis:
 - ◆ Epi 0.3-0.5 mg IV, steroids, ranitidine, diphenhydramine
- AFib:
 - ◆ diltiazem, β B, digoxin, amiodarone, ibutilide
- Hyperkalemia:
 - ◆ Insulin + D50; CaCl; Bicarb; albuterol, dialysis, kayexylate, furosemide
- Hypotension:
 - ◆ Norepinephrine 5-20 mcg/min, Phenylephrine 20-180 mcg/min; Vasopressin 0.01-0.03 Units/min, Dopamine 10-20 mcg/kg/min

Other Code Situations

- **Pulmonary Embolism:**
 - ◆ Massive PE with shock or hemodynamic instability should receive tPA 100mg IVPB over 2 hr
- **Status Epilepticus:**
 - ◆ Lorazepam 0.1mg/kg IVP, Phenytoin 10-20 mg/kg IVPB or Fosphenytoin
- **Prolonged Code:**
 - ◆ Systemic acidosis ensues – NaBicarb may be appropriate

Induced Hypothermia

- Hypothermia for 24 hr
- Hypothermia After Cardiac Arrest (HACA) *NEJM 2002;346:557-63*
- Ice packs, Arcti Sun Protocol, Cooling blankets
- Requires continuous sedative and analgesic infusions, meperidine for shivering and avoidance of anticoagulation

Take Away Points

- **Most frequently used medications**
 - ◆ Epinephrine: asystole, bradycardia, PEA, VF/PVT
 - ◆ Atropine: asystole, bradycardia, PEA
 - ◆ Vasopressin: asystole, PEA, VF/PVT

Take Away Points

- **Medications IVPB only**
 - ◆ P - procainamide
 - ◆ I - isoproterenol
 - ◆ N - norepinephrine
 - ◆ D - dopamine
- **Medications IVP or IVPB**
 - ◆ V - vasopressin
 - ◆ A - amiodarone, adenosine, atropine
 - ◆ L - lidocaine
 - ◆ E - epinephrine
- **Tracheal administration**
 - ◆ L - lidocaine
 - ◆ E - epinephrine
 - ◆ A - atropine
 - ◆ N - naloxone
 - ◆ V - vasopressin
- Doses usually 2-2.5 times those given IVP
- Follow each dose with 10 ml NS flush down tracheal tube if not diluted to that volume for administration

Supplemental Reading

- Cardiovascular complications of cocaine use. *N Engl J Med 2001;345(5):351-358*
- Evolving role of vasopressin in the treatment of cardiac arrest. *Pharmacotherapy 2006;26(6):828-839*
- Pharmacotherapy considerations in advanced cardiac life support. *Pharmacotherapy 2006;26(12):1703-1729*

