The Top 10 Most Interesting Medications in your EMS Box

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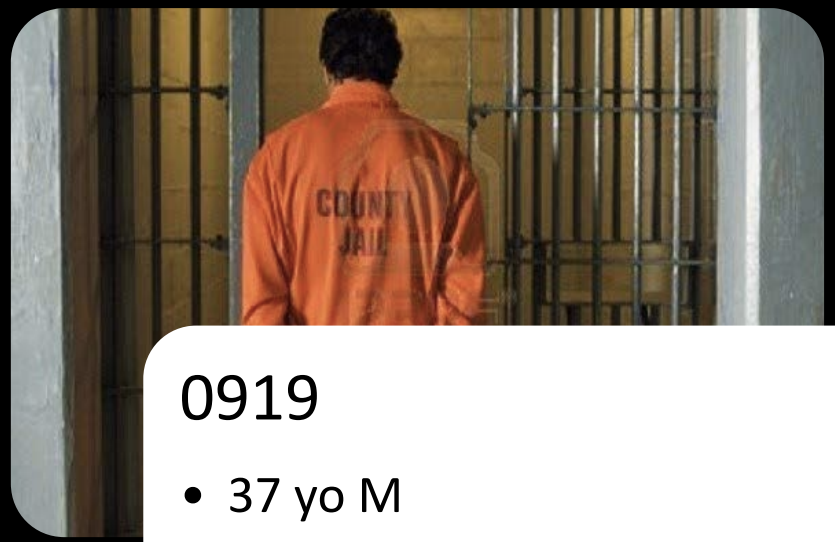
Objectives:

- Learn something new!
- There are multiple ways to use medications in the pre-hospital setting
  - Epinephrine
  - Nitroglycerin
  - Adenosine
  - Amiodarone vs. Lidocaine
  - Dextrose
  - Norepinephrine vs. Dopamine
  - The benzodiazepines
  - Ketamine

Disclosures

- None, unfortunately…
- Who am I?
  - VCU Clinical Pharmacist, Emergency Medicine
  - University of Illinois College of Pharmacy at Chicago
    - 4 years of pharmacy school (glad that's over)
    - 1 year general residency ($4/hr)
    - 1 year specialized residency in emergency medicine ($4.20/hr)

Case #1: *Diaphoretic, N/V/D, SOB*



0919

- 37 yo M
- Pale, diaphoretic, abdominal pain, N/V
- SOB

0929

- SBP 80's, BG 137
- IV access, LR infusing
- NRBR at 15L/min

Jacobsen RC et al. Case of unrec prehospital anaphylactic shock. Prehosp Emerg Care. 2011.15(1).61-6

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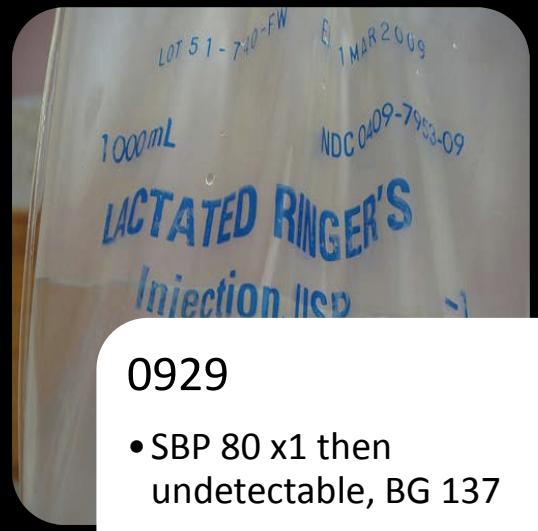


0929

- SBP 80 x1 then undetectable, BG 137
- IV access, LR infusing
- NRBR at 15L/min

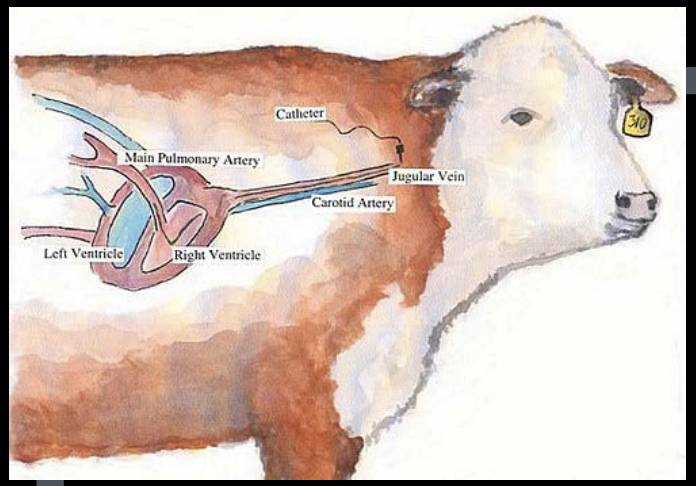
0945

- HR 125, no BP, RR 24 with O2 sat 95% on high flow
- Hives
- Epinephrine 0.3 mg IM x7, methypred 125 mg IV, diphenhydramine 50 mg IV, ranitidine 50 mg IV

Jacobsen RC et al. Case of unrec prehospital anaphylactic shock. Prehosp Emerg Care. 2011.15(1).61-6

Epinephrine

- **MOA**: ↓ inflammatory mediator release, reverses airway obstruction (β2 agonist) and cardiovascular collapse (α1, β1 agonist)
- Synonyms: Adrenaline (internationally)
- Indications:
  - Anaphylaxis
  - Respiratory distress
  - Shock
  - Cardiac arrest

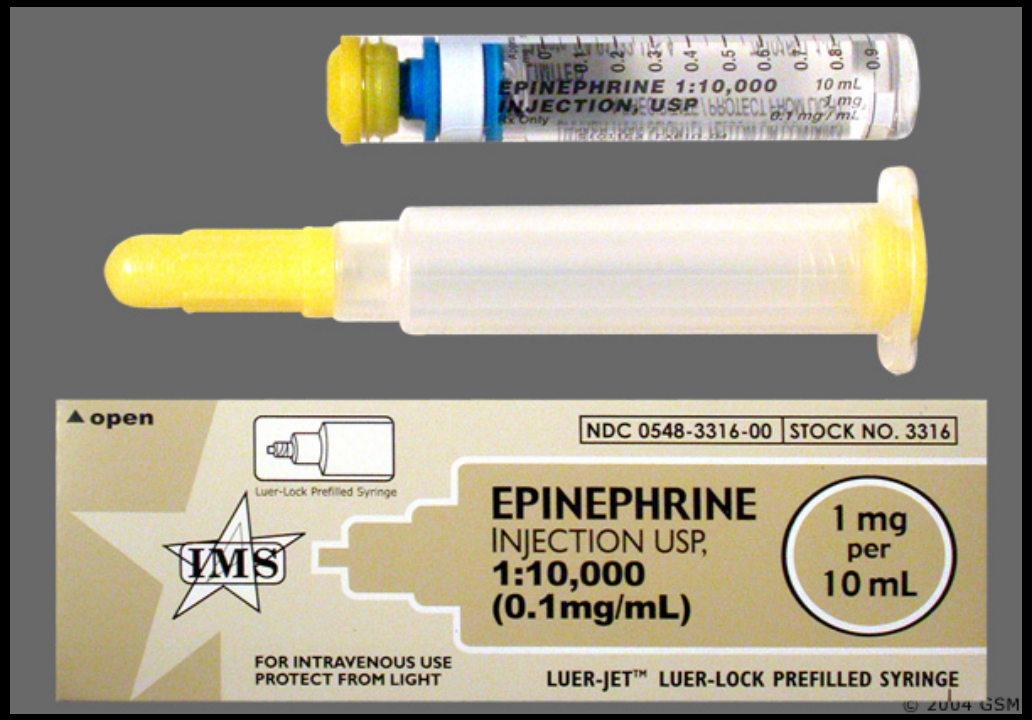


Fun Fact!

Epinephrine was the first hormone to be discovered (1890's). It was previously extracted from the adrenal glands of animals for medical use.

Epinephrine Concentration:

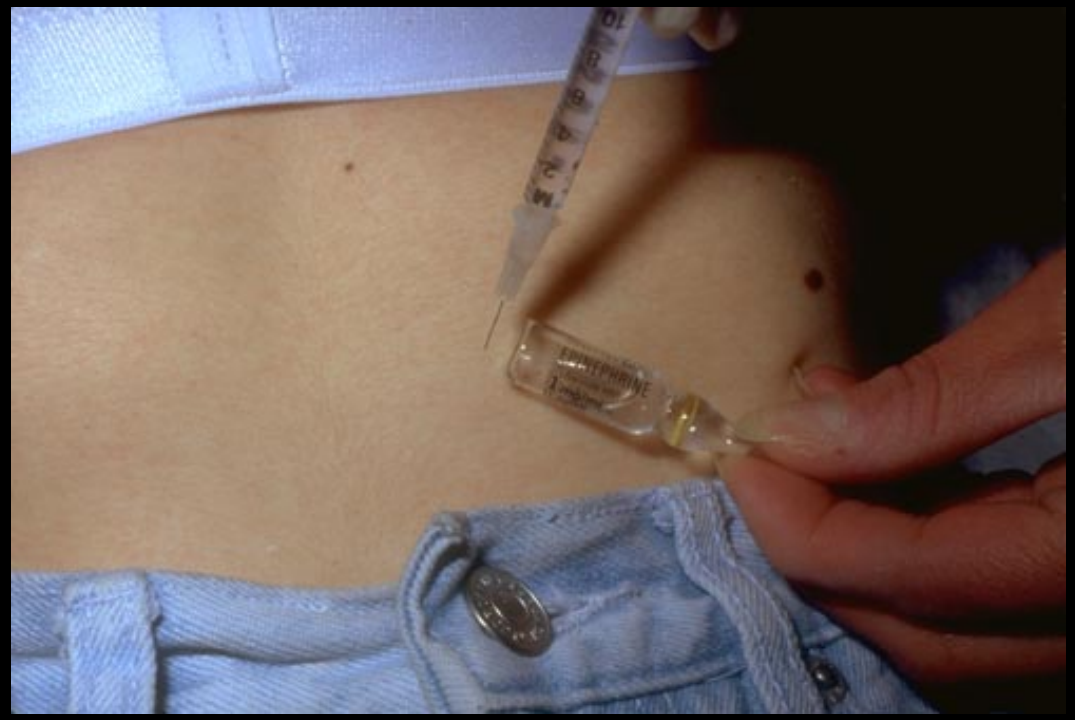
Epinephrine 1:10,000



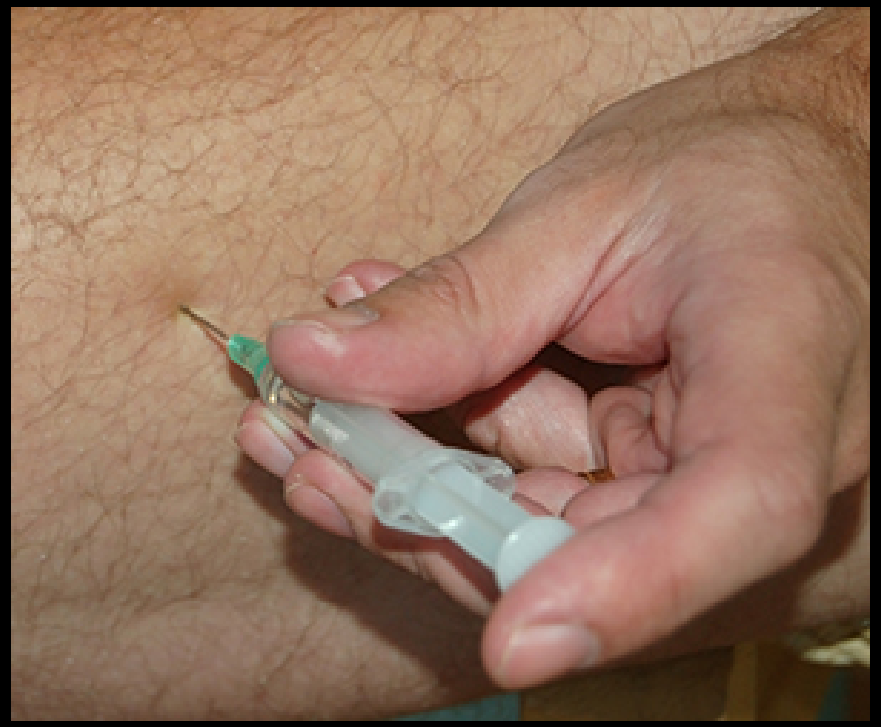
Epinephrine 1:1,000

Epinephrine Route?

Subcutaneous



Intramuscular



Epinephrine Administration?

Deltoid

Anterolateral thigh

75 question survey administered by SurveyMonkey via e-mail

Random sample of nationally certified paramedics

3,537 completed survey (36.6% response rate)

98.9% identified classic anaphylaxis

2.9% identified atypical anaphylaxis

46.2% identified epinephrine as medication of choice

38.9% administered IM

60.5% deltoid

11.9% thigh

Jacobsen RC et al. Anaphylaxis knowledge among paramedics: results of a national survey. Prehosp Emerg Care 2012;16:527-34.

Epinephrine Concentration:

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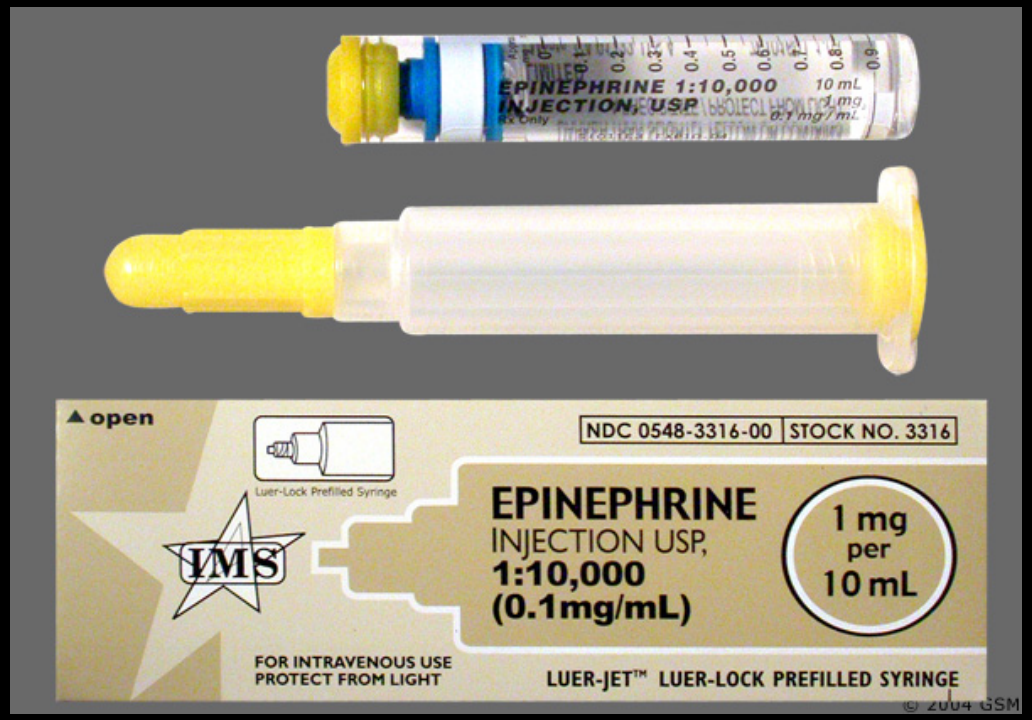

Epinephrine 1:1,000

Epinephrine Administration

- **Study**: 6 way cross over trial, blinded
- **Population**: 18-35 yo males
- Epinephrine 0.3mg SC or IM in thigh or deltoid
- Injections were given at least 1 week apart

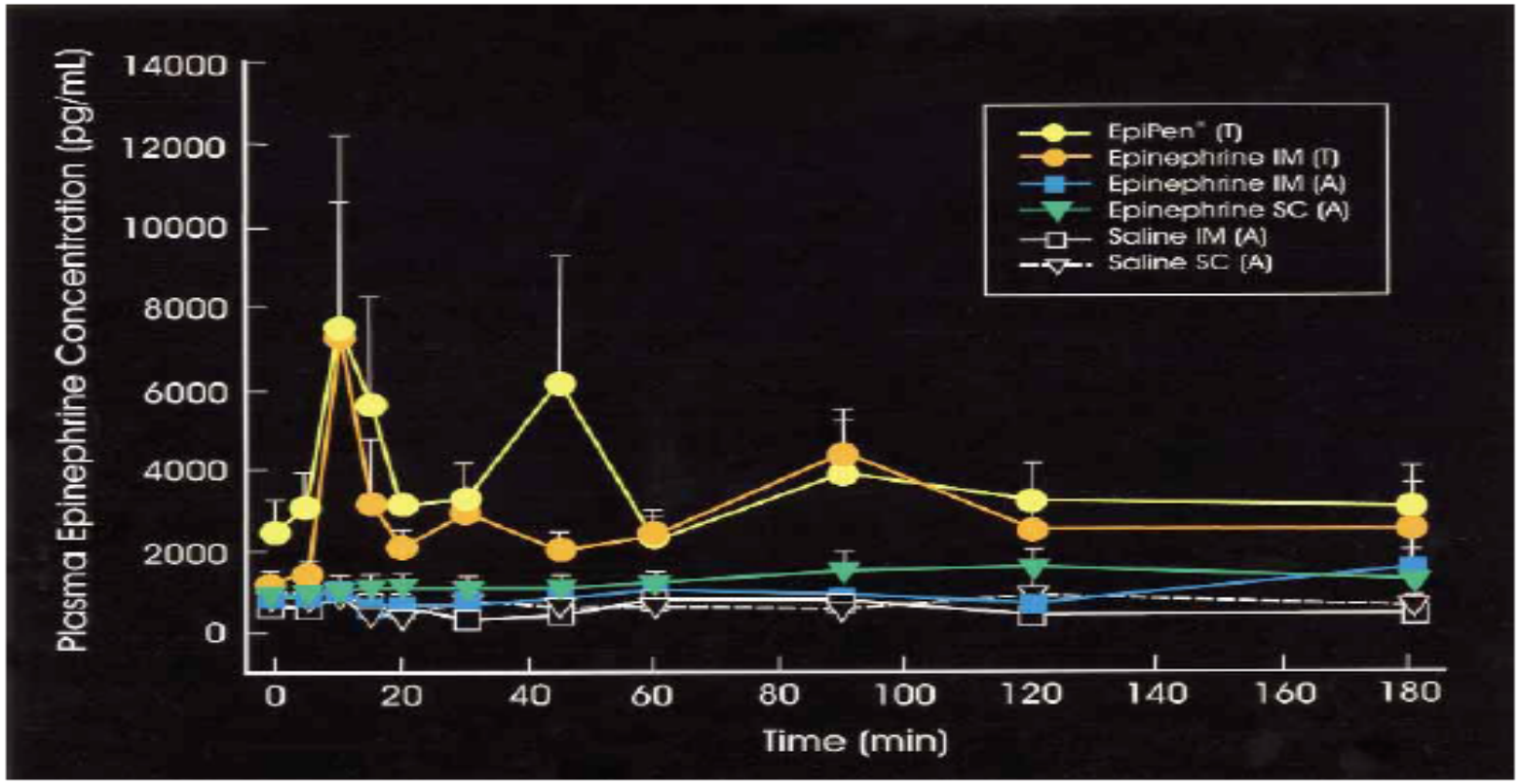

TABLE I. Mean maximum plasma epinephrine concentrations

Injection route	EpiPen IM	Epinephrine IM	Epinephrine IM	Epinephrine SC	Saline IM	Saline SC
Injection site	Thigh	Thigh	Arm	Arm	Arm	Arm
C_{max}: mean ± SEM (pg/mL)	12,222* ± 3,829	9,722* ± 4,801	1,821 ± 426	2,877 ± 567	1,458† ± 444	1,495† ± 524

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Simons FE et al. Epinephrine absorption in adults IM vs. SC. J Allergy Clin Immunol. 2001.108(5).871-3..pdf

Epinephrine in the news…

October 29th, 2015

Voluntary recall

Inaccurate dosage delivery

Failure to deliver epinephrine

Ep
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Alte

American College of Allergy, Asthma & Immunology (ACAAI) 2015 Annual Scientific Meeting

Medscape Medical News > Conference News

Epinephrine Autoinjector Shortage Predicted After Recall

Kate Johnson

November 03, 2015

2 comments Print

EDITORS' RECOMMENDATIONS

Sanofi US Recalls All Auvi-Q Epinephrine Injection

Rare but Serious Injuries With Epinephrine Autoinjectors

SAN ANTONIO — An estimated half a million epinephrine autoinjectors are coming off the market. The US Food and Drug Administration (FDA) is advising patients to call their doctor for an alternative, but some say there won't be enough supply to meet the demand.

"We're going to run out of autoinjectors in certain places. It's going to be a problem," said Bryan Martin, DO, president-elect of the American College of Allergy, Asthma & Immunology (ACAAI).

Case #2:

A 31-year-old Caucasian M was handling an Epipen.

Patient complaint: Pain and paresthesia in the thumb.

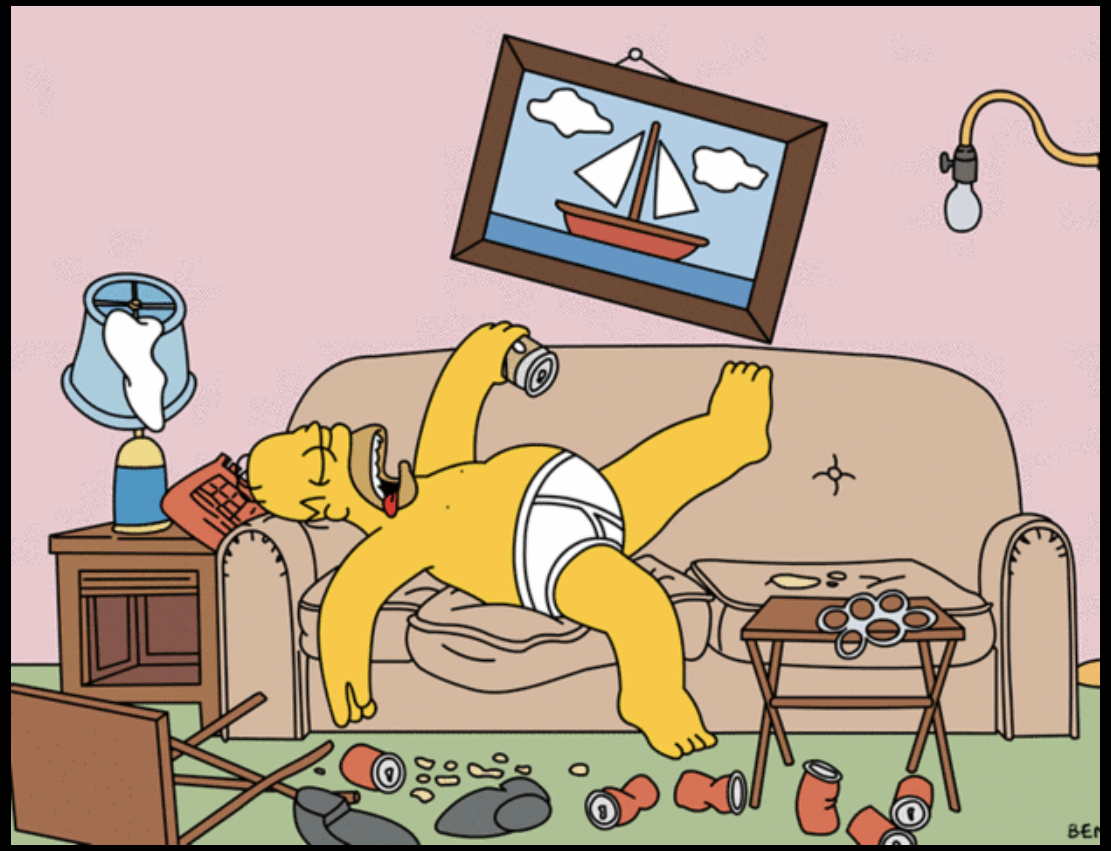
Physical exam: Entire digit was cool and pale, and a prolonged capillary refill time was seen at more than 10 seconds

BP 175/85 mmHg, HR 80/minute, and RR rate 16/minute.

Mathez C et al. Management options for accidental injection of epinephrine from an autoinjector: a case report. J Med Case Reports 2009;3:7268.

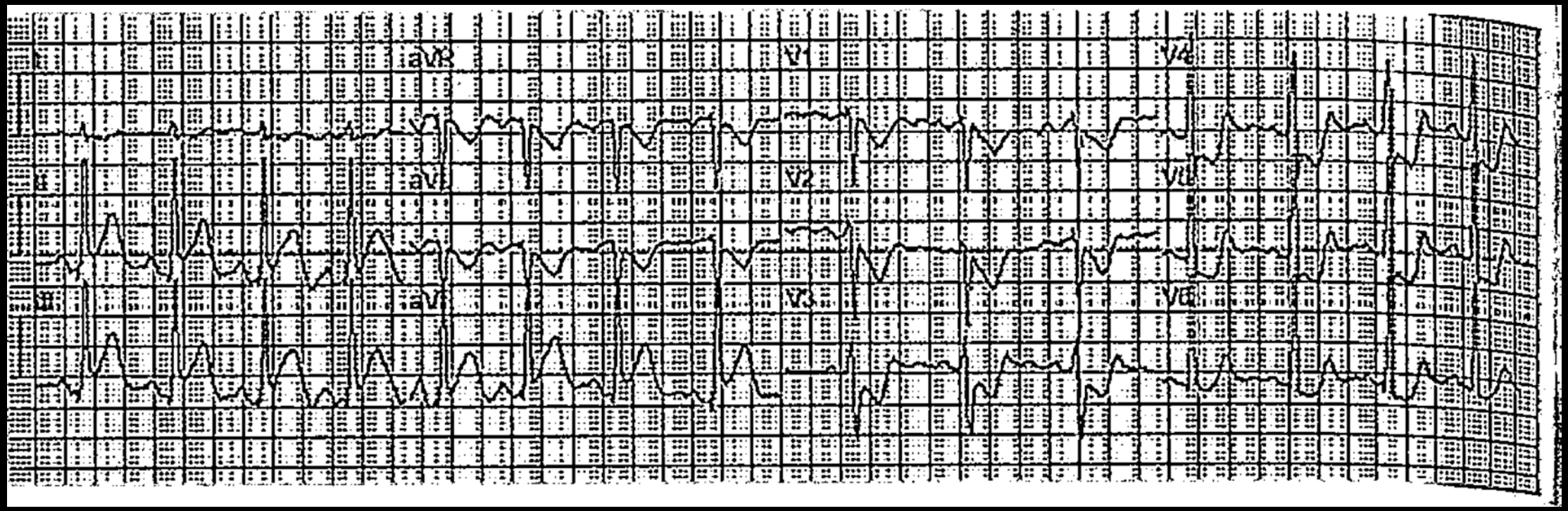
Case #3: *My chest hurts…*

- 42 yo M with no PMH called 9-1-1 with a chief complaint of gradual onset of substernal chest pain.
- The patient self-administered aspirin prior to EMS arrival.
- VS: BP 170/110, HR 88 with NSR, RR 20/min, SpO2 95% on RA.



Deltorre K, Brywczynski J, McKinney J, Slovis C. Not the nitro? Patient goes into pre-hospital V-fib arrest following nitroglycerin. JEMS 2009;34(5):34-6.

Case #3: EKG



Nitroglycerin

- **MOA**: Smooth muscle relaxation resulting in venous + arterial dilation = ↓ preload, afterload
- Indications:
  - ACS
  - CHF Exacerbation

Nitroglycerin: Which formulation?

Nitroglycerin Paste

Nitroglycerin Sublingual

Nitroglycerin: What's the difference?

	Sublingual	Paste
Dose	0.4 mg	0.5 inch
Dosing Frequency	1 tablet q5min x3	May double dose up to 2". Max of 2 doses/day
Onset	1-3 minutes	Up to 15-30 minutes
Peak Effect	5 minutes	60 minutes
Duration	>25 minutes	Up to 7 hrs
Monitoring	HR, BP, cardiac rhythm, location of infarct	

Plasma nitroglycerin levels

Fung H et al. Plasma nitroglycerin levels after sublingual, oral, and topical administration. Br J Clin Pharmac. 1997;4:241-2.

Time (min)

Figures 1 Plasma nitroglycerin concentrations after administration of a 0.3 mg sublingual tablet (●), a 6.5 mg oral capsule (■) and application of an ointment containing 16 mg of nitroglycerin (△).

ointment and administration of the 6.5 mg capsule. The peak levels achieved from these dosage forms were in the vicinity of 0.2-0.3 ng/ml, which were maintained from about 20-60 min after drug administration. A detectable level of nitroglycerin (about 0.1 ng/ml) was still observed at 120 min after administration of the 6.5 mg capsule. Blood sampling for nitroglycerin was not carried out beyond 60 min after ointment application.

The percent changes in pulse rate and mean arterial pressure after nitroglycerin administration are shown in Figure 2. Changes in these haemo-

Nitroglycerin: Topical vs. SL?

- Hemodynamics
- Onset
- Dosing
- Skin Integrity
- Ease of administration

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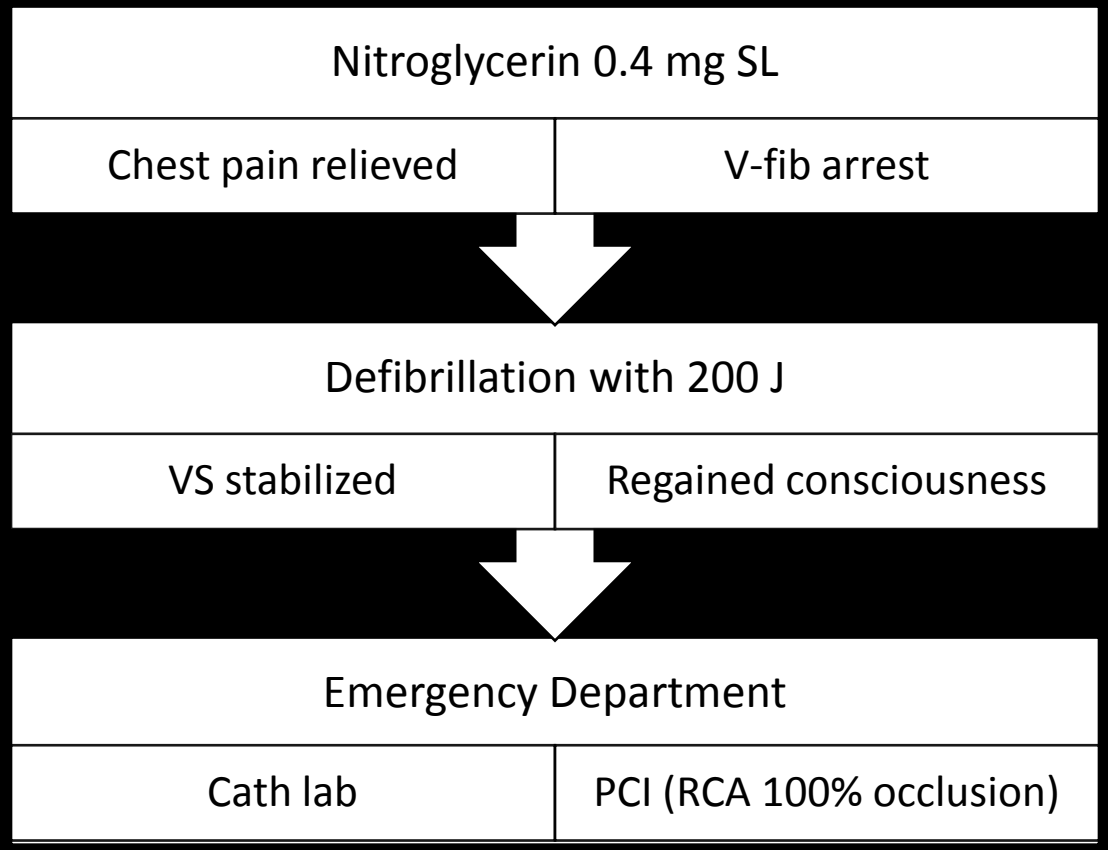


Deltorre K, Brywczynski J, McKinney J, Slovis C. Not the nitro? Patient goes into pre-hospital V-fib arrest following nitroglycerin. JEMS 2009;34(5):34-6.

Nitroglycerin: What's wrong with ED?

- Viagra, Cialis, Levitra
  - MOA: Increase in cGMP can trigger massive vasodilation + severe hypotension with nitrates
  - CONTRAINDICATED
    - Viagra, Levitra: 24 hrs
    - Cialis: 48 hrs

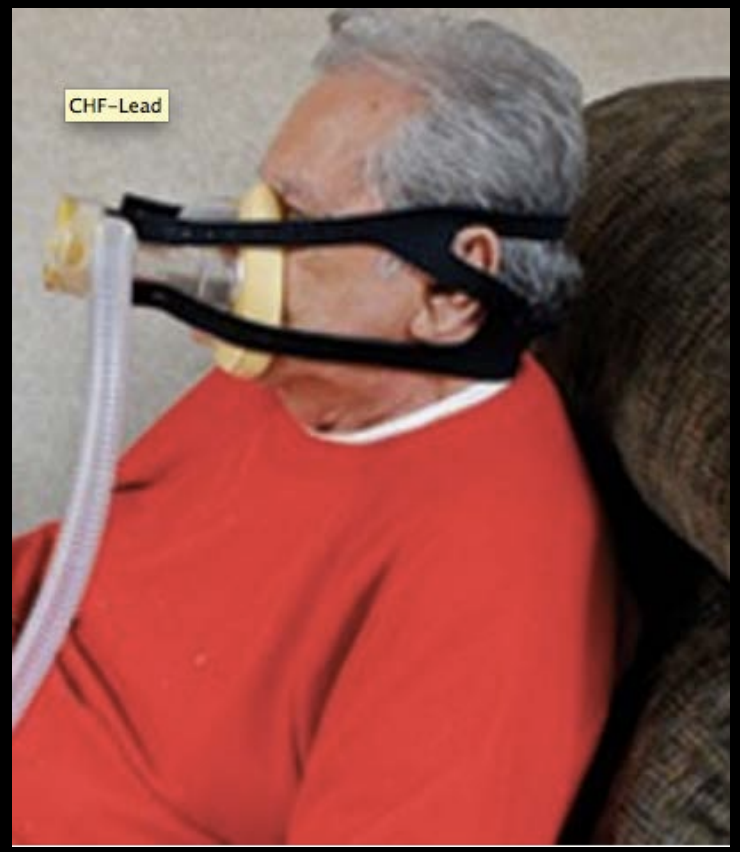
Case #4

75 yo M who called 9-1-1 with worsening SOB after missing his HD.

PMH: ESRD, HTN, CHF, obesity

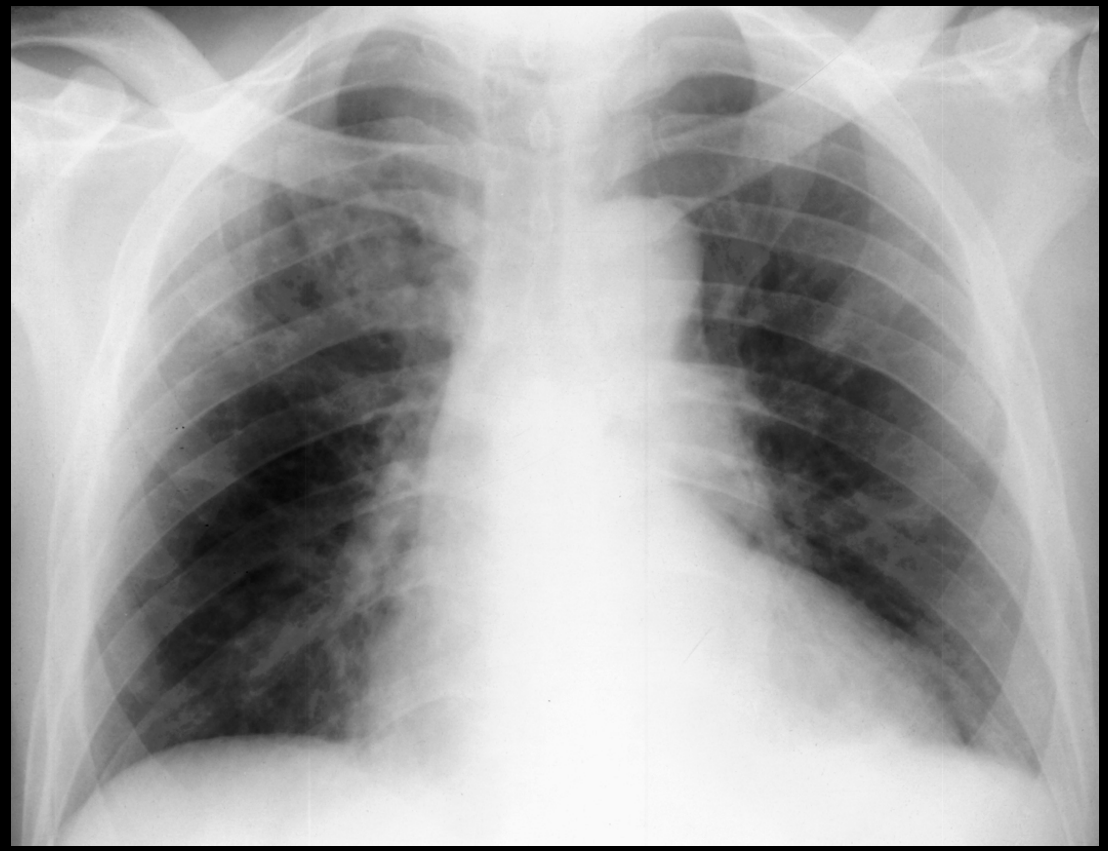
PE: Crackles

VS: HR 120, BP 240/130, RR 30 sat 85% on RA



Nitroglycerin:

- Pathophysiology:
  - R and L ventricle heart failure results in high pulmonary capillary pressure
- Treatment
  - Nitroglycerin ↓ preload (venous) and afterload (arterial) = -/↑ cardiac output



Prehospital High-dose Sublingual Nitroglycerin Rarely Causes Hypotension

Brian M. Clemency, DO; Jeffrey J. Thompson, MD; Gina N. Tundo; Heather A. Lindstrom, PhD

Based on the patient's systolic blood pressure administer:

Hold NTG SL for a systolic BP below 100 mmHg

NTG 0.4 mg SL 1 tablet every 5 minutes for a systolic BP of 100 – 160 mmHg

NTG 0.4 mg SL 2 tablets every 5 minutes for a systolic BP of 160 – 200 mmHg

NTG 0.4 mg SL 3 tablets every 5 minutes for a systolic BP over 200 mmHg

- Source: 2011 WREMAC protocols, page 15

Clemency BM et al. Prehospital high dose sublingual nitroglycerin rarely causes hypotension. *Prehosp Disaster Med* 2013;8(5):477-81.

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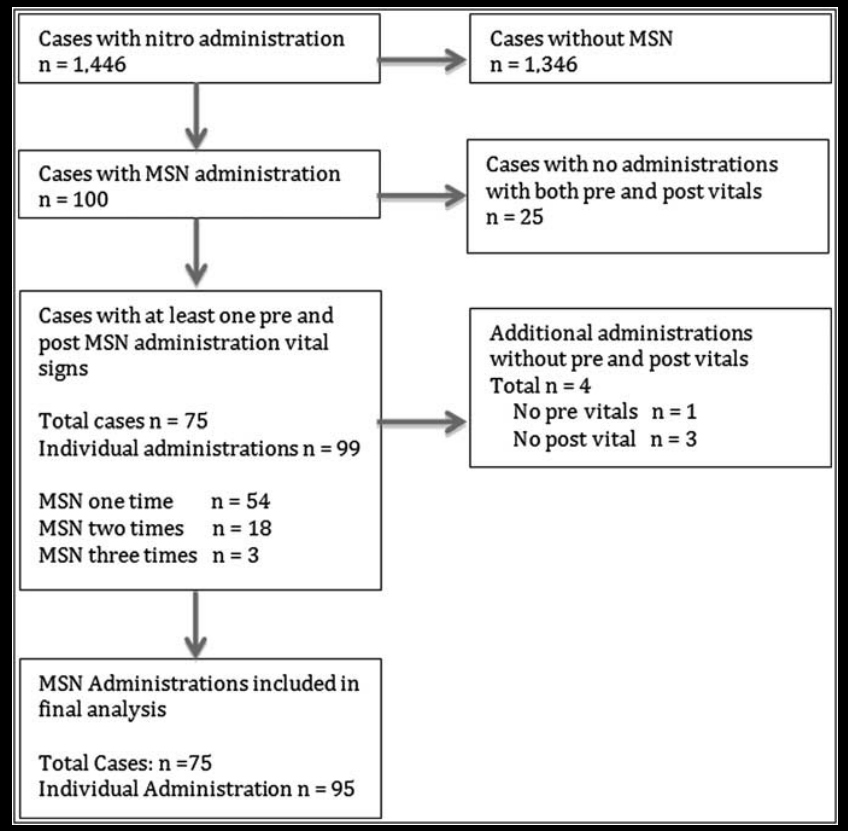

	No.	Mean SBP Δ	95% CI	Range	Incidence of Hypotension
2 tablets	65	-16.5	-8.6, -24.4	+26, -132	3
3 tablets	29	-10.1	+0.6, -20.8	+59, -79	0
4 tables	1	-31.0	N/A	N/A	0
All	95	-14.7	-8.5, -21.0	+59, -132	3

Clemency © 2013 Prehospital and Disaster Medicine

Table 1. Change in Systolic Blood Pressure by Number of Nitroglycerin Tablets Administered

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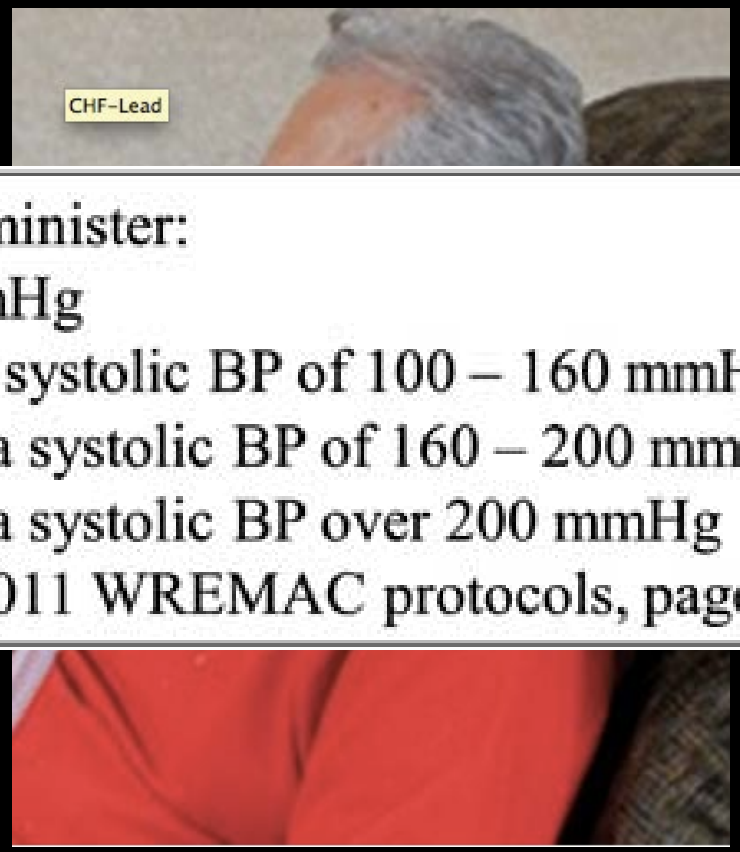
Clemency BM et al. Prehospital high dose sublingual nitroglycerin rarely causes hypotension. *Prehosp Disaster Med* 2013;8(5):477-81.

Case #4

75 yo M who called 9-1-1 with worsening SOB after missing his HD



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- NTG 0.4 mg SL 3 tablets every 5 minutes for a systolic BP over 200 mmHg

- Source: 2011 WREMAC protocols, page 15

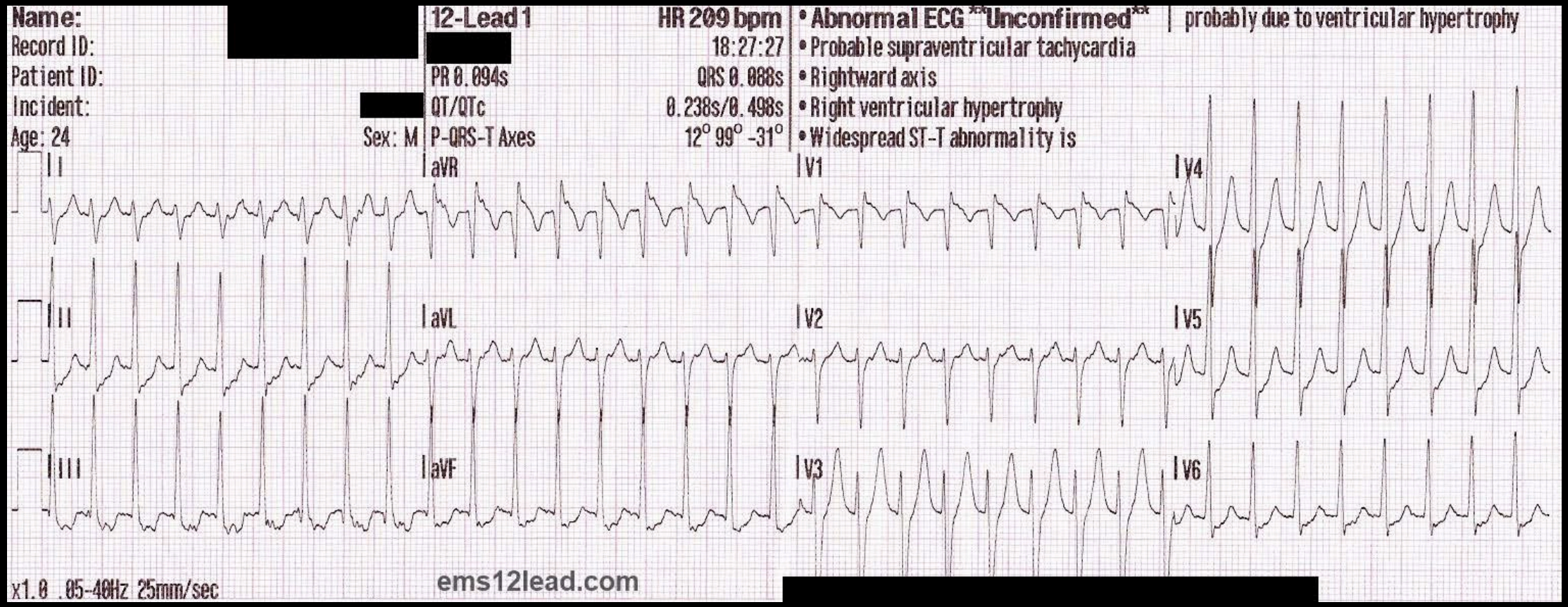
VS: HR 120, BP 240/130, RR 30
sat 85% on RA

Case #5:

- 27 yo M with a chief complaint of having an anxiety attack after a verbal altercation with his GF.
- PE: Non-labored breathing
- VS: HR 220, BP 118/64, RR 18 and SpO2 94% on RA

http://www.ems12lead.com/2012/10/08/24-year-old-male-anxiety-attack-conclusion/#sthash.IRdUW1oq.dpuf

Case #5: 12 lead



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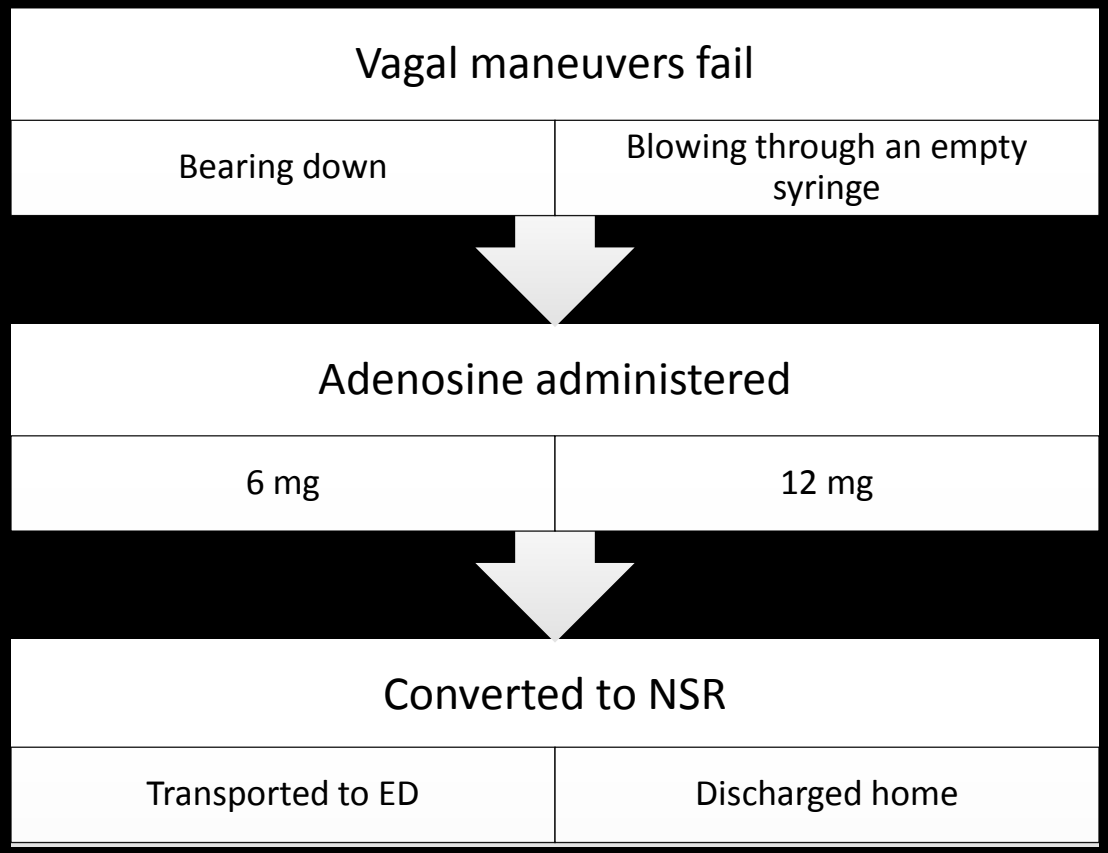
http://www.ems12lead.com/2012/10/08/24-year-old-male-anxiety-attack-conclusion/#sthash.IRdUW1oq.dpuf

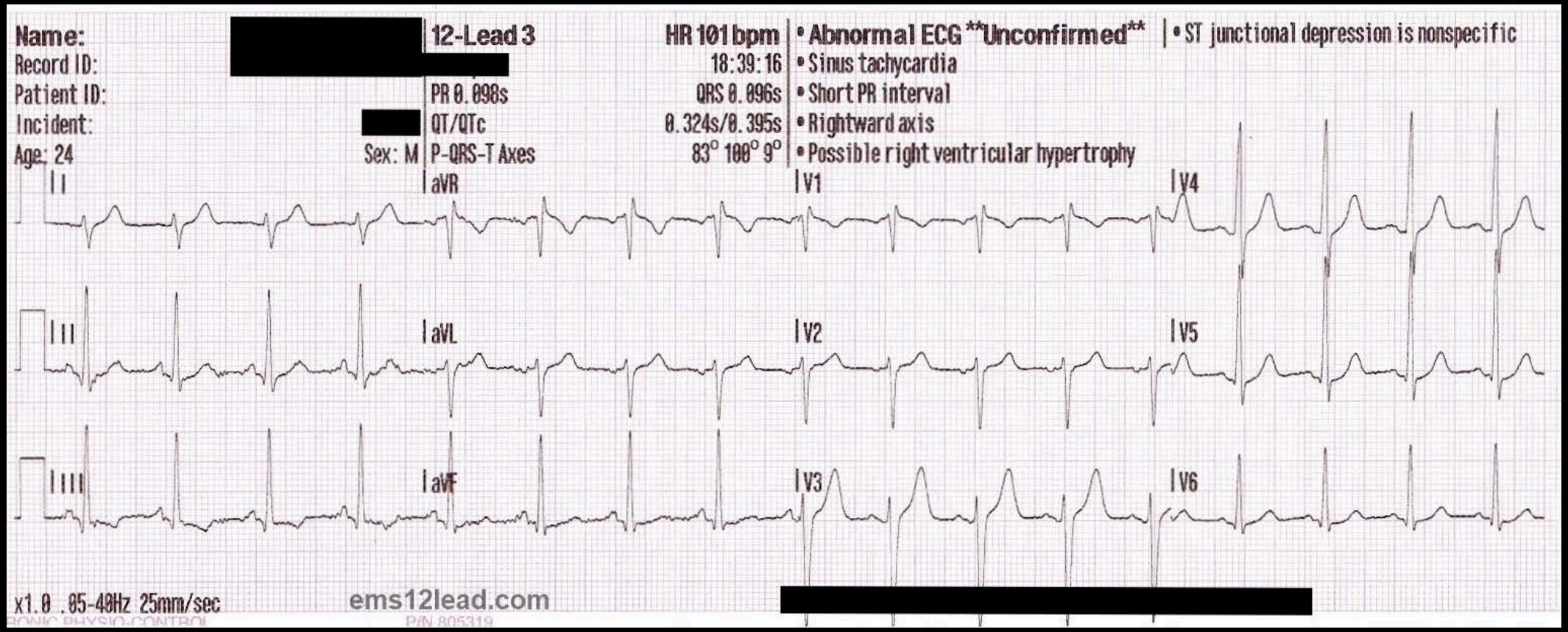
Case #5:

- 27 yo M with a chief complaint of having an anxiety attack after a verbal altercation with his GF.
- PE: Non-labored breathing
- VS: HR 220, BP 118/64, RR 18 and SpO2 94% on RA
- What would you do?



http://www.ems12lead.com/2012/10/08/24-year-old-male-anxiety-attack-conclusion/#sthash.IRdUW1oq.dpuf

Case #5: Repeat EKG



http://www.ems12lead.com/2012/10/08/24-year-old-male-anxiety-attack-conclusion/#sthash.IRdUW1oq.dpuf

Adenosine

- MOA:
  - Slows conduction time through the AV node, interrupting re-entry pathways, and restoring NSR
- Indications:
  - Paroxysmal supraventricular tachycardia
- Pharmacokinetics
  - Onset: Rapid
  - Duration: 6 seconds

Fun fact!

Caffeine provides an opposite effect to adenosine by blocking the adenosine receptor. As a result, patients who have ingested caffeine may need larger doses of adenosine to see a response.

Adenosine: Administration

Administer over 1-2 seconds at an area proximal as possible to the trunk. Follow with rapid normal saline flush.

1. Draw up adenosine 6 mg in 2 mL
2. 3 way stop cock
3. Administer adenosine rapid IVP
4. Raise arm above heart + flush rapidly
5. Counsel on “strange feeling”

Case #6:

- A 57-year-old M collaps suddenly. Two bystande physicians begin CPR
- EMS continues CPR wh ventilating the patient wi bag-valve device conne oxygen.
- Patient was found to be ventricular fibrillation (V 200-joule biphasic shoc epinephrine was deliver
- What's next?

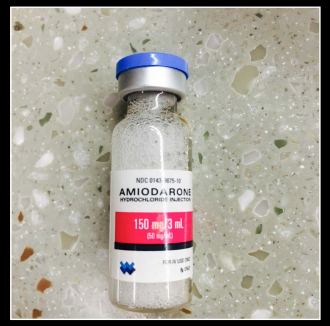
Amiodarone vs. Lidocaine

Amiodarone

Lidocaine

Antiarrhythmics: Amiodarone

- MOA: Inhibits α + β adrenergic stimulation; affects Na, K, Ca channels
- Indication/Dose:
  - Pulseless VF/VT: 300 mg IVP, then 150 mg IVP if no response
  - Stable VT: 150 mg over 10 minutes



Prepared in Tween 80

Onset: ?

Duration: 5-70 days

Amiodarone 37.3% iodine by weight

Antiarrhythmics: Lidocaine

- MOA: Na channel blocker
- Dose: 1-1.5 mg/kg IV, may repeat 0.5 mg/kg q5-10 min (max 3 mg/kg)
- Indication:
  - VF or pulseless VT
  - Hemodynamically stable monopmorphic VT

Fun Fact:
Lidocaine is the most widely used cocaine derivative.

Antiarrhythmics: Amiodarone vs. Lidocaine

Study	ARREST	ALIVE
Design	Randomized, double blind, placebo controlled	
Population	Out of hospital cardiac arrests with refractory VF or pulseless VT	
Arms	N= 246 Amiodarone 300mg IVP N= 258 Placebo	N= 180 Amiodarone 5 mg/kg IVP N= 167 Lidocaine 1.5 mg/kg IVP
Results	**Survival to hospital admission 44% vs 34%, p=0.03**	**Survival to hospital admission 22.8% vs 12%, p=0.009**

Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. N Engl J Med. 1999;341(12):871–878

Dorian P, Cass D, Shwartz B, et al. Amiodarone as compared with lidocaine for shock resistant ventricular fibrillation. N Engl J Med. 2002;346(12):884–890

Amiodarone vs. Lidocaine?

Amiodarone

Lidocaine

Iodides: Iodine Allergy + Amiodarone

	Study	Population	Results
Brouse SD et al. Pharmacotherapy. 200 5;25(3):429-34.	Retrospective	N=3 Inclusion: Amiodarone naïve, documented allergy to iodine containing products	No documented ADR to amiodarone IV or PO
Stafford L. Ann Pharmacother. 2007;41(7):1310-4.	Case Report	55 yo M w/ facial urticaria after intra-arterial injection of iohexol tx successfully with promethazine + hydrocortisone.	Treated with amiodarine IV for atrial fibrillation. Initiated on amiodarone 400mg po TID, 60 min after 1st dose- lip swelling/tingling. Tx with promethazine.
Lakshmanadoss U et al. Pharmacotherapy. 2012;32(7):618-22	Retrospective	N=234 - Anaphylaxis: 20 (8.5%) - Hives: 34 (14.5%) - Rash/nonspecific 180 (77%) Inclusion: Documented allergy to iodine or iodinated contrast who received IV or PO amiodarone	ADR due to amiodarone based on the Naranjo: - 1 of 234 (0.4%): - 68 yo F admitted for sepsis. Tx with amiodarone 600mg IV for atrial fibrillation. Facial flushing, hives, worsening hypoxia, tachycardia. Amiodarone stopped, tx with steroids and antihistamines. Sx resolved 30 min later

Case #6:

- A 57-year-old M collapses suddenly. Two bystander physicians begin CPR
- EMS arrives <10 minutes after the call.
- EMS continues CPR while ventilating the patient with a bag-valve device connected to oxygen.
- Patient was found to be in ventricular fibrillation (VF). A 200-joule biphasic shock x2 and epinephrine was delivered

Amiodarone 300 mg IVP x1

↓

ROSC

↓

Amiodarone 1 mg/min infusion

↓

Transported to ED

Mark S. Link et al. Circulation. 2015;132:S444-S464

Amiodarone in the news…

Untested Ebola drug given to patients in Sierra Leone causes UK walkout

Use of amiodarone heart drug at Lakka centre in Freetown deemed 'reckless' by scientist as 14 medical staff withdraw over safety fears

British health workers help an Ebola patient in Freetown, Sierra Leone. Photograph: Baz Ratner/Reuters

- Amiodarone:
  - Proposed MOA: Prevention of Ebola virus from entering the body
  - Dose: 20 mg/kg/day IV x3 days then switch to oral

Case #7:

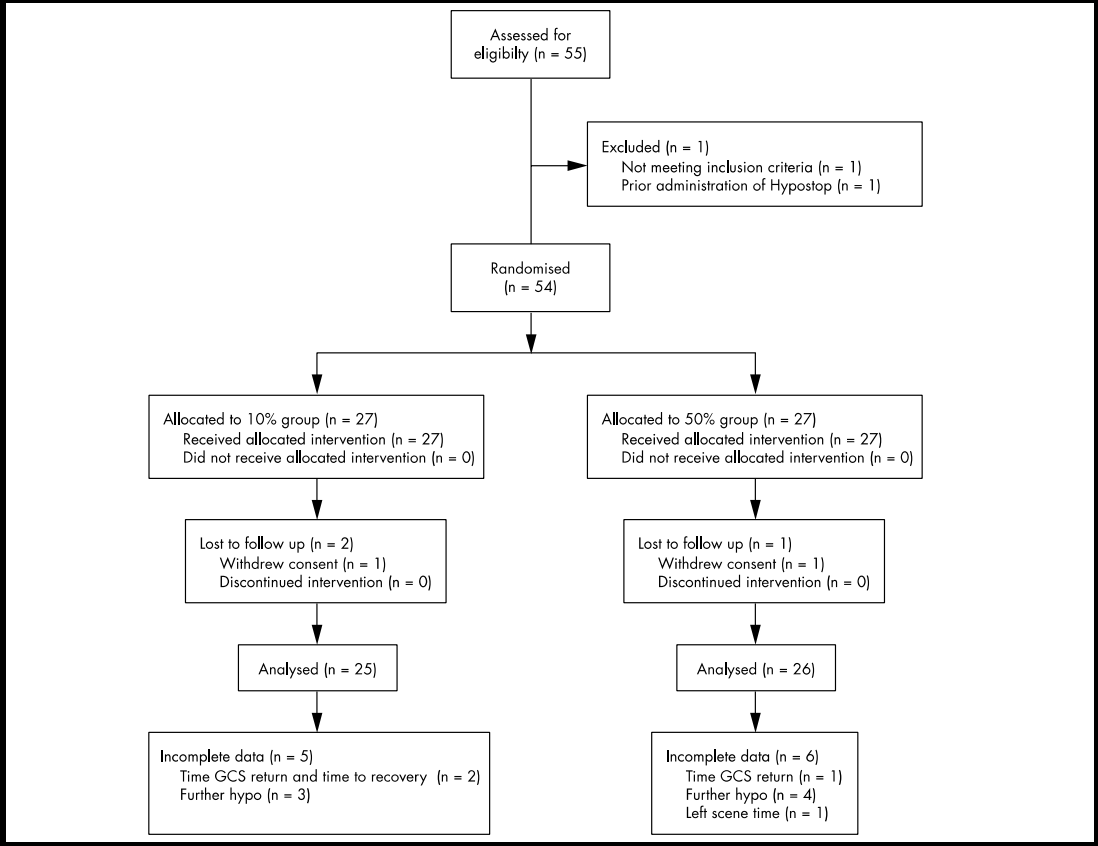
- 57 yo F found with a GCS of 3 with snoring respirations
- Exam:
  - Diaphoretic
  - T37, BP 158/94, HR 120, RR 14
  - Accucheck: 14

Dextrose 50% vs. 10%

PREHOSPITAL CARE

Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomised controlled trial

- Study Design: Randomized controlled trial
- Setting: United Kingdom EMS System
- Population: Unresponsive adults with BG < 72 mg/dL (N=51)
- Intervention: 5g aliquots of D10% or D50% to max of 25g



Moore C et al. Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomized controlled trial. Emerg Med J 2005;22:512-5.

PREHOSPITAL CARE

Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomised controlled trial

Table 2 Differences in outcome measures between the two study groups. Values are median (range, interquartile range)

	10% Group (n = 25)	50% Group (n = 26)	Difference, p value
Total dose of dextrose (g)	10 (5 to 30, 10 to 15)	25 (10 to 25, 15 to 25)	+15, p<0.001
Post-treatment blood glucose (mmol/l)	6.20 (4 to 17, 5.15 to 9.10)	9.40 (4.30 to 18.50, 8.28 to 11.60)	+3.2, p = 0.003
Post-treatment GCS	15 (6 to 15, 15 to 15)	15 (3 to 15, 15 to 15)	0, p = 0.400
Time to GCS 15 (min)	8 (1 to 30, 5 to 15)	8 (2 to 19, 4 to 11)	0, p = 0.733
Time on scene (min)	40 (13 to 75, 30 to 51)	35 (15 to 61, 23 to 45)	−5, p = 0.162
Ease of administration score	2 (1 to 4, 1 to 3)	1 (1 to 5, 1 to 2)	−1, p = 0.142
	Proportion (%)	**Proportion (%)**	**Difference (95% CI, p value)**
Subjects receiving the maximum permitted dose of 25 g	3/25 (12%)	17/26 (65%)	+53% (+28 to +72%, p<0.0001)
Subjects with a post-treatment GCS of <15	2/25 (8%)	1/26 (4%)	−4% (−12 to +22%, p = 0.360)
Subjects with a further hypoglycaemic episode within 24 h	4/22 (18%)	4/22 (18%)	0% (−24 to +24%, p = 1)

GCS, Glasgow Coma Scale

Moore C et al. Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomized controlled trial. Emerg Med J 2005;22:512-5.

What's wrong with good ole D50?

Dextrose Content

D50:
25 g in 25 mL

Body:
5 g in 5 L

Hyperglycemia = ↑ mortality?

- Stroke
- Head injury
- Sepsis
- Trauma
- MI

Levy SB et al. Images in emergency medicine. Dextrose extravasation causing skin necrosis. Ann Emerg Med. 2006 Sep;48(3):236, 239.

What's wrong with good ole D50?

Rebound hypoglycemia

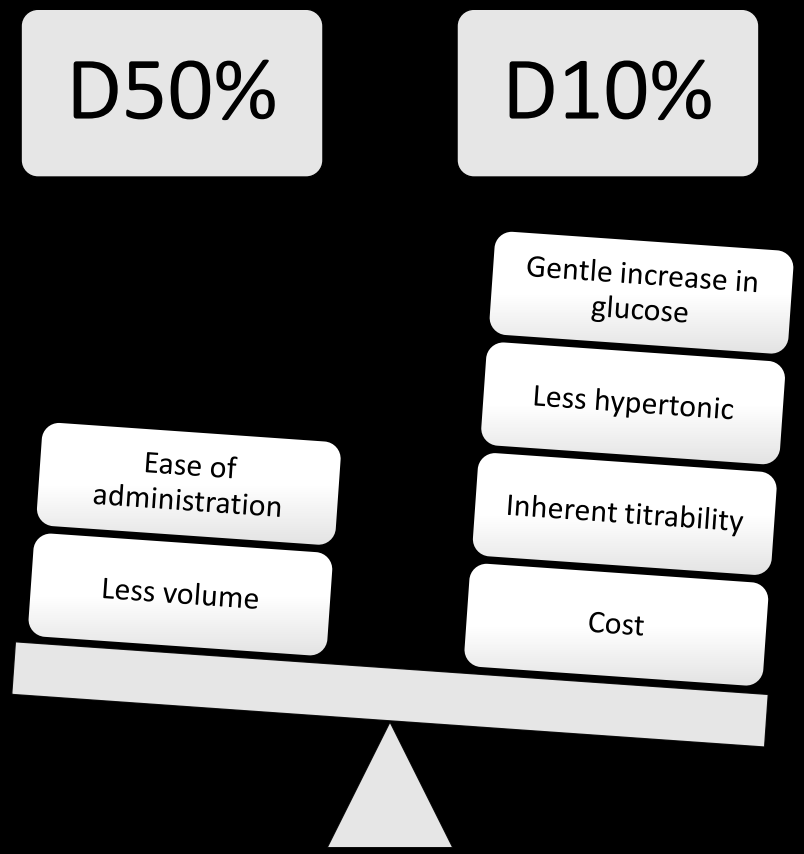
- Rapid increase in blood glucose
- Further release of insulin
- Rapid renal clearance of glucose
- Rebound hypoglycemia

Viscosity

VCU Medical Center

Levy SB et al. Images in emergency medicine. Dextrose extravasation causing skin necrosis. Ann Emerg Med. 2006 Sep;48(3):236, 239.

Choices, choices…



Patient administered 150 mL of D10 en route. Repeat glucose 94 with a GCS of 12

Further history obtained from the ED. She has been seen multiple times for hypoglycemia 2/2 to EtOH abuse.

Blood EtOH serum level = 0.13

Case #8:

- 72 yo F with DM type II, HTN, AF, CKD from a SNF for AMS.
- VS: Temp 101F, BP 70/45, HR 140, RR 20, O2 Sat 95% RA.
- After adequate 3L of NaCl 0.9%, pt continues to remain hypotensive BP 60-70s/30-40s and tachycardic HR 130s.
- Construction: 25 min ETA to ED

Vasopressor?

Pick a vial, any vial?

Norepinephrine

- Clinical Effect: ↑ SVR, ↑/- CO
- Indication: Sepsis, cardiogenic shock
- AE: Extravasation

Pointers:

- Initial dose: 5-10 mcg/min

Dopamine

- Clinical Effect: ↑CO and ↑SVR
- Indication:
  - Requiring ↑CO and ↑SVR
- AE: Tachydysrhythmias
  - MOA: Endogenous release of NE by DA entering the sympathetic nerve terminal

:

- Initial dose: 5 mcg/**kg**/min

Vasopressor Indications: General Shock

Study	Description	Conclusion
Myburgh JA et al. Intensive Care Med. 2008;34(12):2226-34.	Norepinephrine vs. Epinephrine Prospective, double-blind, RCT of shock patients to NE or epinephrine (N=280)	**No statistically significant difference** in time to goal MAP or 28 day mortality. Epinephrine associated with more metabolic abnormalities resulting in discontinuation.
De Backer D et al. N Engl J Med. 2010;362(9):779-89.	Norepinephrine vs. Dopamine Prospective, RCT of shock patients to NE or DA (N=1679)	**No statistically significant difference** in 28 day mortality. **More arrhythmias in DA vs. NE group (207 events vs. 102, P<0.001)**
Havel C et al. Cochrane Database Syst Rev. 2011;(5):CD00379.	Multiple vasopressors 23 randomized controlled trials involving 3212 patients, with 1629 mortality outcomes. Six different vasopressors, alone or in combination, were studied in 11 different comparisons.	**No difference in mortality between NE and DA.** Insufficient evidence for other comparisons. **↓ risk of arrhythmias with NE compared to DA (RR 0.43, 0.26-0.69)**

Vasopressor Indications: General Shock

Study	Description	
Myburgh JA et al. Intensive Care Med. 2008;34(12):2226-34.	Norepineph Prospective (N=280)	**gnificant difference** in time to ay mortality. Epinephrine ore metabolic abnormalities ntinuation.
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Havel C et al. Cochrane Database Syst Rev. 2011;(5):CD00379.	Multiple va 23 randomi outcomes. S in 11 differe	**mortality between NE and DA.** nce for other comparisons. **mias with NE compared to DA 59)**

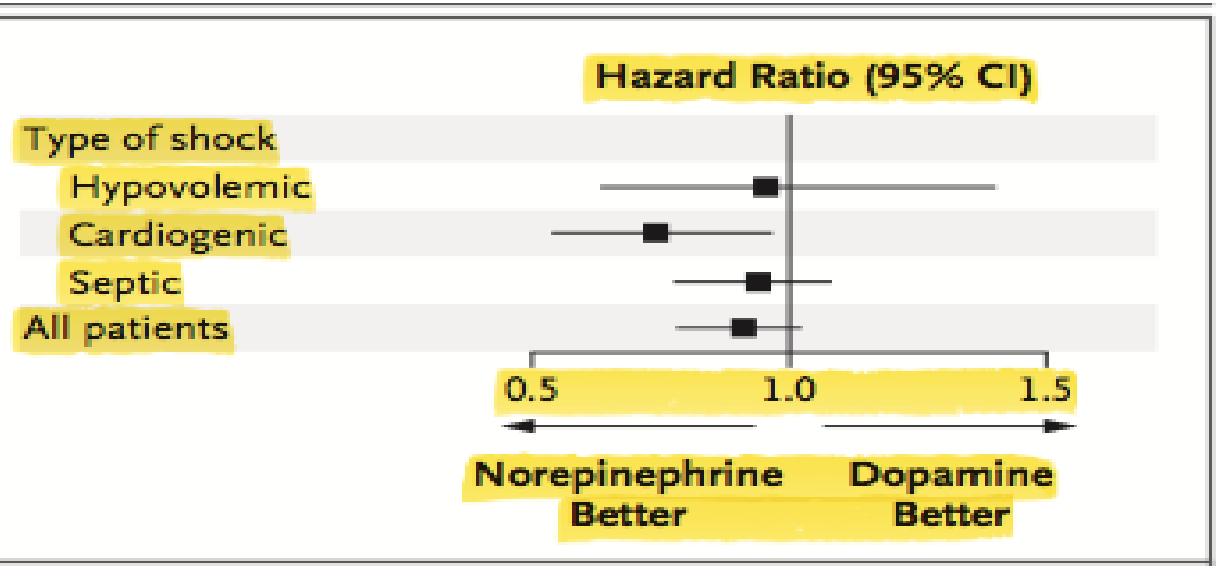

Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.

Case #8:

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- VS: Temp 101F, BP 70/45, HR 140, RR 20, O2 Sat 95% RA.
- After adequate 3L of NaCl 0.9%, pt continues to remain hypotensive BP 60-70s/30-40s and tachycardic HR 130s.
- Construction: 25 min ETA to ED

Case #9:

- EMS called by coworker of a 48 yo M with only a PMH of HTN for witnessed seizure.
- Pt states “I don’t think I’m goin to make it today”
- 5 min prior to ED arrival, pt begins seizing again.
- BP: 221/134, HR: 120, BG: 131

The Benzodiazepines:

Lorazepam	Midazolam	Diazepam

The Benzodiazepines:

Benzodiazepine Fun Fact:

Benzodiazepines were discovered accidentally in 1955 during a lab clean up. The first benzodiazepine developed was chlordiazepoxide (Librium) then diazepam (Valium). Valium became the #1 selling medication from 1960-1970's

The Benzodiazepines: IV

Lorazepam

Dose: 2-4 mg

(0.1 mg/kg, max 4 mg)

Onset: Within 10 minutes

Duration: Up to 8 hrs

The Benzodiazepines: IV

Midazolam

Dose: 5-15 mg (0.2 mg/kg)

Onset: 3-5 minutes

Duration: <2 hrs

The Benzodiazepines: IV

Diazepam

Dose: 5-10 mg

Onset: Immediate, time to peak 10 minutes

Duration: Variable, accumulates in fat tissue

The Benzodiazepines: IV Access

Lorazepam

Dose: 2-4 mg
(0.1 mg/kg, max 4 mg)

Onset: Within 10 minutes

Duration: Up to 8 hrs

Midazolam

Dose: 5-15 mg
(0.2 mg/kg)

Onset: 3-5 minutes

Duration: <2 hrs

Diazepam

Dose: 5-10 mg

Onset: Immediate, peak 10 minutes

Duration: Variable

The Benzodiazepines: No IV Access

	Lorazepam	Midazolam	Diazepam
Intramuscular	**Dose:** 0.1 mg/kg (max 4mg) **Onset:** Slow **Duration**: Up to 8 hrs	**Dose:** 5 mg **Onset**: Up to 15 min **Duration**: Up to 6 hrs	-
Intranasal	-	**Dose:** 0.2 mg/kg (max 10 mg) **Onset:** 4-8 min **Duration:** 18-41 min	-
Rectal	-	-	**Dose:** Age+ weight **Onset:** Within 10 min **Duration**: 20-30 min

Case #9:

- EMS called by coworker of a 48 yo M with only a PMH of HTN for witnessed seizure.
- Pt states “I don’t think I’m goin to make it today”
- 5 min prior to ED arrival, pt begins seizing again.

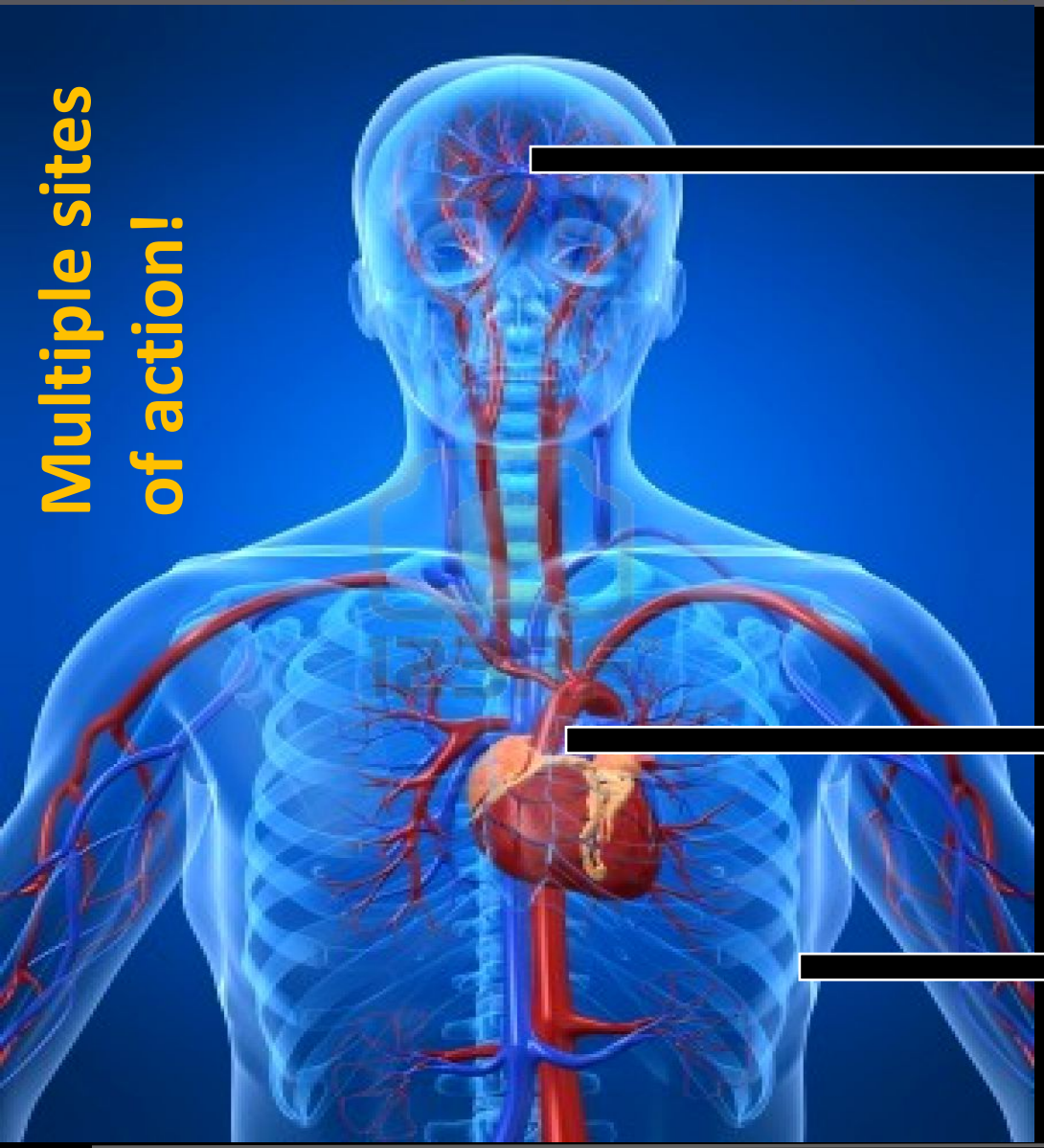
Midazolam 5 mg IV x1	
Unable to obtain intubation	Arrived to ED with respirator support via bag valve mask

Intubated in the ED with midazolam 10mg IV x1 and rocuronium 100 mg	
Sedated with midazolam and fentanyl	CT head negative. Suspected EtOH withdrawal

Admitted to MRICU	
Extubated the next day	HTN emergency

Don’t be scared of the K hole…

Multiple sites of action!



Analgesia
Amnesia
Dissociation
Antidepressant?

HTN
Tachycardia
Increased cardiac output

Bronchodilation

Dosing + Clinical Effect

Route	Dose	Onset	Time to Peak	Duration of Action
Intravenous	Analgesia: 0.1-0.2 mg/kg Sedation/RSI: 1-2 mg/kg	<1 minute	3-5 minutes	5-10 minutes
Intramuscular	Analgesia: 1-2 mg/kg Sedation: 4-5 mg/kg	2-5 minutes	20 minutes	30 minutes
Intranasal	Analgesia: 0.5 mg/kg Sedation: 1-2 mg/kg	2-5 minutes	3-5 minutes	30-60 minutes

Indications for Ketamine

Excited Delirium

- 35 yo M, 103 kg
- Bizarre behavior
- Does not react to manual pain compliance-control techniques
- 8 law enforcement officers on scene struggling with the subject, 2 become injured.

Excited Delirium

Midazolam

- Dose: 2-5 mg IM
- Onset: 5-20 minutes
- Duration: 2-6 hrs

Haloperidol

- Dose: 5-10 mg IM
- Onset: 10-30 minutes
- Duration: 4-6 hours

Ketamine

- Dose: 4-5 mg/kg IM
- Onset: 3-5 minutes
- Duration: 20-30 minutes

Ho JD et al. *Prehosp Emerg care* 2013;17:274-79.
http://www.zombieagency.org/wp-content/uploads/2012/10/cot-01.jpeg

Prehospital Use of IM Ketamine for Sedation of Violent and Agitated Patients

Kenneth A. Scheppke, MD*
Joao Braghiroli, MD†
Mostafa Shalaby, MD‡
Robert Chait, MD§

*University of Miami Miller School of Medicine Palm Beach Regional Campus, JFK Medical Center, Department of Emergency Medicine, Atlantis, Florida
†University of Miami, Miller School of Medicine, Miami, Florida
‡Metrohealth Medical Center Case-Western Reserve University, Department of Hospital Medicine, Cleveland, Ohio
§University of Miami Miller School of Medicine Palm Beach Regional Campus, JFK Medical Center, Department of Cardiology, Atlantis, Florida

- Retrospective review
  - Ketamine: 4 mg/kg IM +/- midazolam 2-2.5 mg IM/IV
  - N=52
    - 50 of 52 had medical control
  - 3 cases = Respiratory depression
  - Time to ED = 19 minutes
  - No emergence reactions

Original Contribution

The association between ketamine given for prehospital chemical restraint with intubation and hospital admission☆,☆☆

Aaron M. Burnett, MD [a,*,1], Bjorn K. Peterson, MD [a,2], Samuel J. Stellpflug, MD [b,3], Kristin M. Engebretsen, PharmD [b,4], Katherine J. Glasrud, MD [c,5], Jordan Marks, MSII [d,6], Ralph J. Frascone, MD [a,7]

[a] Regions Hospital, Department of Emergency Medical Services, Saint Paul, MN
[b] Regions Hospital, Department of Clinical Toxicology, Saint Paul, MN
[c] Regions Hospital Emergency Medicine Residency, Saint Paul, MN
[d] University of Kansas College of Medicine, Kansas City, KS

- Retrospective review
  - Ketamine 5 mg/kg IM
  - N=49
    - Mean dose 5.26 +/- 1.65 mg/kg
  - 14 required intubation in the ED
  - 35 (71%) required admission to the hospital

Excited Delirium

- Intramuscular ketamine dose required for control:

  A. 50 mg?

  B. 100 mg?

  C. 250 mg?

  D. 500 mg?

Ho JD et al. *Prehosp Emerg care* 2013;17:274-79.
http://www.zombieagency.org/wp-content/uploads/2012/10/cot-01.jpeg

Excited Delirium

- Intramuscular ketamine dose required for control:

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  C. 250 mg?

  D. 500 mg

Ho JD et al. *Prehosp Emerg care* 2013;17:274-79.
http://www.zombieagency.org/wp-content/uploads/2012/10/cot-01.jpeg

Analgesia

- 9 yo M
- Patent airway
- HR 94, BP 110/60, RR 20, O2 sat 98% on RA
- Requiring transport to nearby hospital 30 minutes away by flight
- Repeatedly stating "*It hurts so bad, no needles.*"

Reid C et al. *Emerg Med J* 2011;28:328-9.
http://www.aafp.org/afp/2012/0101/afp20120101p25-f5.jpg

Analgesia

- Utilize as primary or adjunctive agent
- Occurs at sub-dissociative dosing
  - IV: 0.1-0.2 mg/kg
  - IM: 0.5-1 mg/kg
  - Nasal: 0.5 mg/kg
- Indication
  - Respiratory compromise
  - Hemodynamic instability
  - Lack of IV access

Acta Anaesthesiol Scand 2011; **55**: 638–643
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2011.02446.x

Review Article

Ketamine as an analgesic in the pre-hospital setting: a systematic review

P. A. Jennings[1,2], P. Cameron[2] and S. Bernard[1,2]
[1]*Ambulance Victoria, Melbourne, Vic., Australia and* [2]*Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Vic., Australia*

- Systematic review
- 6 publications included
  - No difference between morphine and ketamine for pain relief
  - No difference in level of sedation, N/V, itching
  - Ketamine associated with more neuropsychological effects

Analgesia

- Ketamine:
  - Route?
    A. PO
    B. IV
    C. IM
    D. Intranasal
  - Dose?
    A. 5 mg
    B. 15 mg
    C. 30 mg
    D. 50 mg

Reid C et al. *Emerg Med J* 2011;28:328-9.
http://www.aafp.org/afp/2012/0101/afp20120101p25-f5.jpg

Analgesia

- Ketamine:
  - Route?
    A. PO
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    D. 50 mg

Reid C et al. *Emerg Med J* 2011;28:328-9.
http://www.aafp.org/afp/2012/0101/afp20120101p25-f5.jpg

Rapid Sequence Intubation

- 35 yo M with GSW to the head, exposed brain matter
- EMS: Self inflicted, 9 mm hand gun
- Med Evac arrives: Patient ventilations being assisted by EMS with a BVM
- VS: HR 120, **BP 96/70**, SpO2 99% via BVM

Respiratory Distress: Rapid Sequence Intubation (RSI)

- Patients:
  - Concern for hemodynamic instability
  - Reactive airway disease
- Options for induction:
  - Etomidate: 0.3 mg/kg IV
  - Ketamine: 1-2 mg/kg IV, 10 mg/kg IM
  - Midazolam: 0.2-0.3 mg/kg IV
  - Propofol: 1 mg/kg IV

http://airway.jems.com/wp-content/uploads/2011/04/using-2.jpg

Traumatic Brain Injury + Systolic Blood Pressure

Chesnut RM et al. 1993;59:121-5.

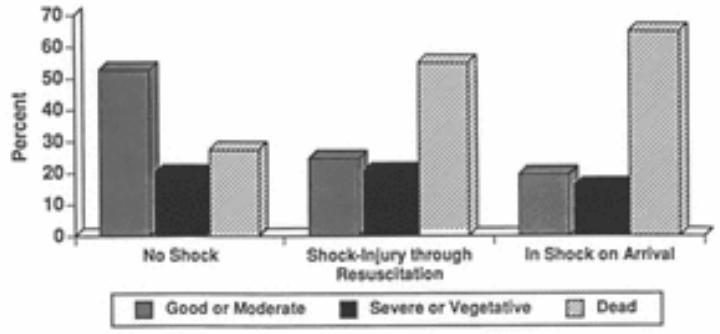

Fig. 1. Outcome as influenced by early shock (one or more episodes of systolic blood pressure ≤90 mmHg) for 717 patients in the Traumatic Coma Data Bank. Patients in shock on arrival are a subset of those experiencing shock during the time period from injury through resuscitation

- Traumatic Coma Data Bank
  - TBI, GCS ≤8
- Early hypotension:
  - SBP <90 mmHg from time of injury through resuscitation
- N= 717
  - Mortality: 55% vs. 27% with early hypotension

Respiratory Distress: Rapid Sequence Intubation (RSI)

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  - Concern for hemodynamic instability
  - Reactive airway disease
- Options for induction:
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http://airway.jems.com/wp-content/uploads/2011/04/using-2.jpg

Respiratory Distress: Rapid Sequence Intubation (RSI)

- Patients:
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- Options for induction:
  - Etomidate: 0.3 mg/kg IV
  - **Ketamine: 1-2 mg/kg IV, 10 mg/kg IM**
  - Midazolam: 0.2-0.3 mg/kg IV
  - Propofol: 1 mg/kg IV

http://airway.jems.com/wp-content/uploads/2011/04/using-2.jpg

Rapid Sequence Intubation

- Intubated: Etomidate + succinylcholine with EtCO2 = 32
- 15 min later: HR 70, BP 77/50, EtCO2 = 17
- 20 minutes later: Traumatic arrest

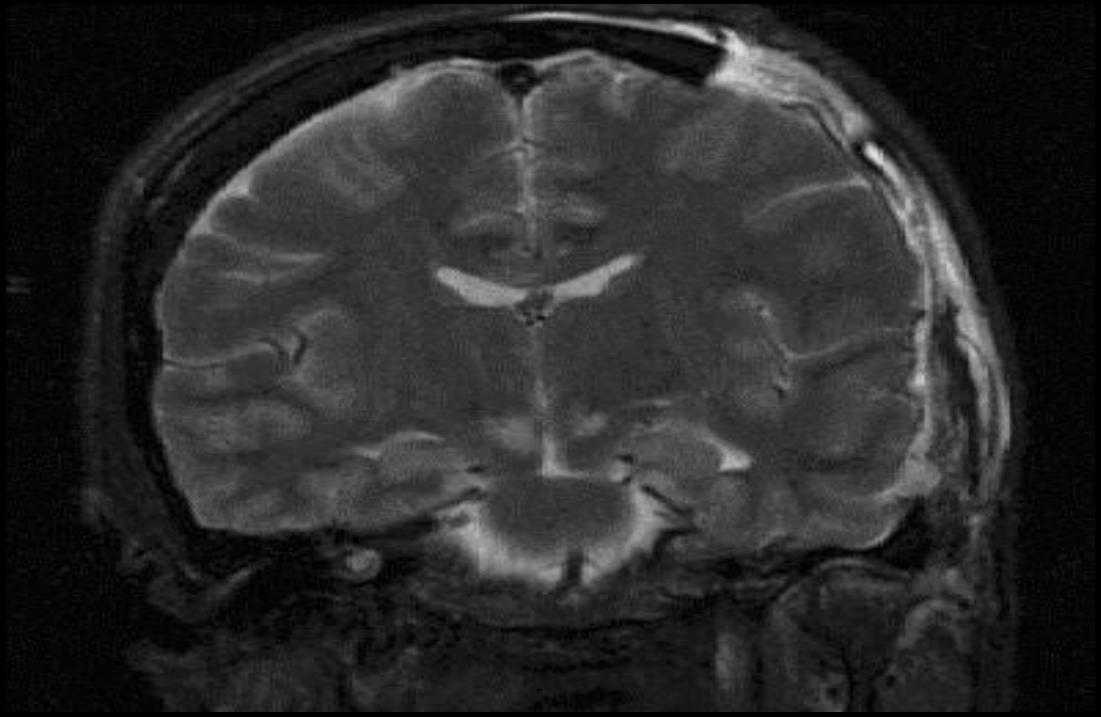
The Ugly Side of Ketamine?

Increased Intracranial Pressure

Clinical Effect

- Cerebral vasodilator
  - Increased cerebral blood flow
  - Increase in cerebral metabolic rate
- Clinical Effect
  - Minimal evidence
    - Increased in ICP (?)
    - Neuroprotective (?)
- Indication
  - Risk vs. Benefit

Consequence: Brain herniation ?

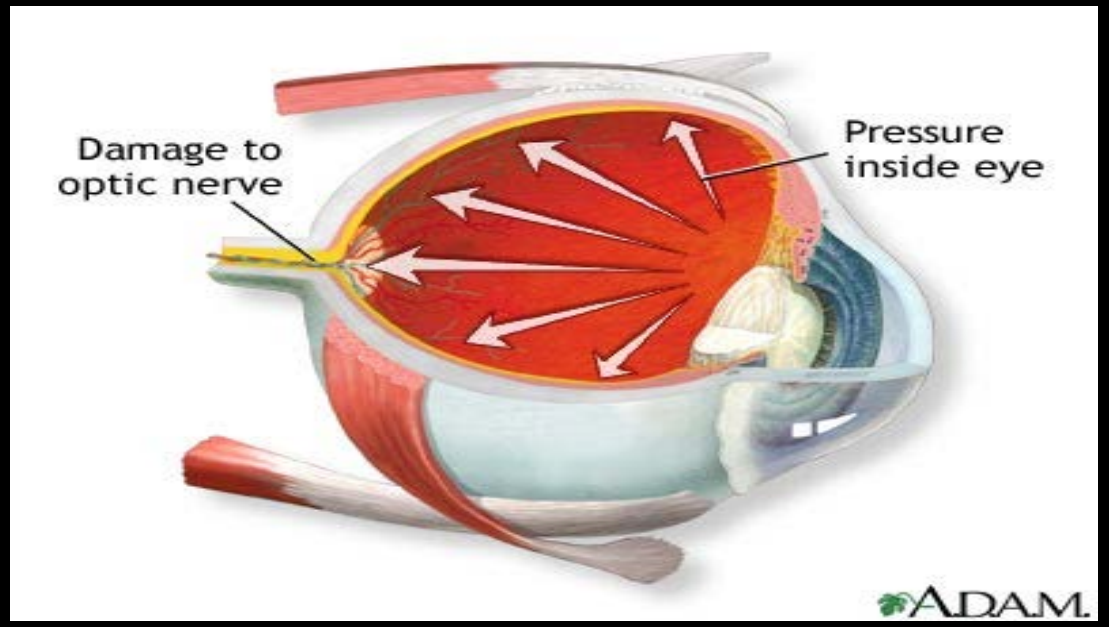


http://upload.wikimedia.org/wikipedia/commons/5/5c/Brain_herniation_MRI.jpg

Ketamine + ICP

Literature	Description	Findings
Zeiler FA et al. Neurocrit Care. 2014;21(1):163-73.	Systematic review on the use of ketamine **in TBI** and its effect on ICP. 7 articles were included, 3 addressed bolus dose ketamine (n=63)	2 **of 3 studies showed decrease in ICP of ~30%** 1 of 3 showed statistically significant but non-sustained decrease in ICP
Zeiler FA et al. J Crit Care. 2014	Systematic review on the use of ketamine in **nontraumatic neurological illness** and its effect on ICP. 16 articles were included, 12 addressed bolus dose ketamine.	Mixed results in adult and pediatric population. **Elevations in ICP were associated with no control for pCO2.**
Cohen L et al. Ann Emerg Med. 2014;1-9.	Systemic review that looked at effect of ketamine (bolus, continuous) on intracranial and cerebral perfusion pressures, neurologic outcomes, ICU LOS, and mortality. 10 articles were included (n=953)	Variable effect on ICP. **No difference in neurologic outcomes, ICU LOS, or mortality**

Elevated Intra-Ocular Pressure

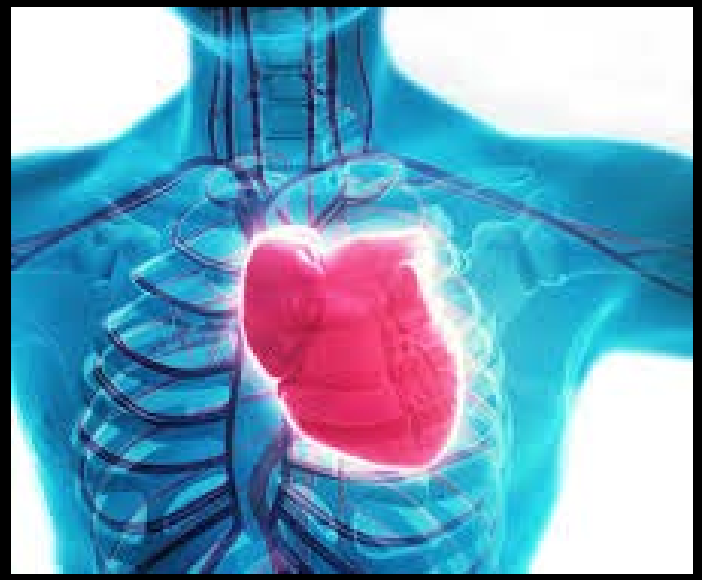


- Concern in:
  - Glaucoma
  - Acute globe injury
- Why?
  - Sympathomimetic effect results in ↑ in IOP
  - Dose dependent
    - Estimated ~10% ↑
  - Controversial
    - Clinical significance is unclear
    - Pre-medications with BZD may negate this effect

Cardiovascular Disease

Use with caution in:

- Heart failure
- Angina
- History of MI



Currently Hypertensive +/- Tachycardic

- May exacerbate current status
  - HR: ↑ 20-30%
  - SBP: ↑ 10-30%
  - DBP: ↑ 10-20%

Anesth Analg. 1968;47:769-778
https://www.cardiolaborate.org/wp-content/uploads/2014/05/Myocardial-infarction-and-remodeling-CARDIOLABORATE.jpg

Emergence Reaction: The Set Up

- Highest risk
  - Patient
    - Within 60 min of administration
    - >10 yo
    - Female
    - Personality disorder
    - Anosognosia
    - Paranoia
  - Environment
    - Ketamine rapidly administered IV
    - Excessive stimuli

Hypersalivation

- Occurs within minutes of administration

- **Management**
  - Suction
  - Atropine: 0.01 mg/kg (min 0.1 mg, max 0.5 mg) IM or IV
  - Glycopyrrolate: 0.1 mg IV every 2-3 minutes PRN

http://www.jamesfriedmanphotographer.com/photos/l1281061968Hypersalivation-1.jpg

Airway Protection + Laryngospasm

Respiratory, airway reflexes

- Ketamine preserves laryngeal and pharyngeal protective reflexes **more** than any other anesthetic agent
- ↑ risk in:
  - Additional sedatives on board (analgesics, etc.)
  - Rapid administration
  - Larger doses

Laryngospasm

- Stridor
- Abrupt cyanosis, hypoxia
- Management
  - Jaw thrust and O2
  - Bag valve mask ventilation
  - Endotracheal intubation

The Top 10 Most Interesting Medications in your EMS Box

Tammy Nguyen, PharmD, BCPS
Clinical Pharmacy Specialist, Emergency Medicine
Tammy.Nguyen@vcuhealth.org

VCU Medical Center

Prehospital care

Ketamine sedation for patients with acute agitation and psychiatric illness requiring aeromedical retrieval

Minh Le Cong,[1] Bruce Gynther,[2] Ernest Hunter,[2] Peter Schuller[3]

- Cairns Royal Flying Doctor Service in Australia
  - Ketamine: Initial bolus at 0.5-1 mg/kg x2, then infusion at 1-1.5 mg/kg/hr.
  - Target: Calm, cooperative, able to respond to verbal commands

- N=18
  - Age: 12-43 years old
  - Primary diagnosis: Exacerbation of schizophrenia
  - Flight duration: 30 min – 3 hrs
  - AE:
    - HTN, tachycardia (N = 4)
    - No airway compromise
    - No worsening of agitation or psychiatric sx