


Vasopressors

Il Buono, il Brutto, il Cattivo

Joseph Miller, MD
Henry Ford Hospital
September 1, 2009

Objectives

- Identify agents
- Select "best" agent for shock states
- Identify literature with clinical outcomes
- Set goals for therapy



Case 1

- 48 year-old female presents with syncope
- History of shellfish allergy
- At a local Coney island and ate fries from cooked in the same oil as the shrimp
- Gave herself benadryl and IM epi PTA

Case 1

- She becomes delirious
- HR 140, BP 65/45, 36.5, 98% RA
- Vasopressor indicated?
- Which one?

Indications

- Maintain perfusion during hemodynamic compromise
 - Bridge while restoring preload
 - Prolonged low SVR
 - Brain and coronaries
- Consensus: MAP < 60-65 mmHg

Pharmacology – the good

- Alpha 1 – vasoconstriction
- Alpha 2 – vasodilatation
- Beta 1 – ↑ HR and contractility
- Beta 2 – vasodilatation

Pharmacology – the bad

- Alpha 1:
 - gut and limb ischemia
 - ↓ CO
- Beta 1:
 - tachycardia, dysrhythmias
 - ↑ myocardial oxygen consumption, AMI

Pharmacology

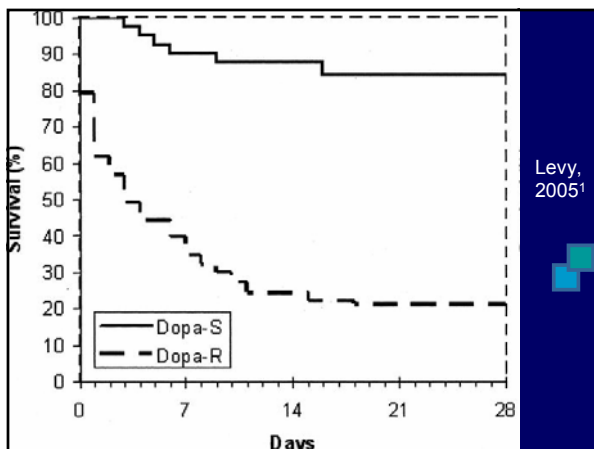
- Dopamine
- Epinephrine
- Norepinephrine
- Phenylephrine
- Vasopressin

Pharmacology

- Dopamine
- Epinephrine
- Norepinephrine
- Phenylephrine
- Vasopressin

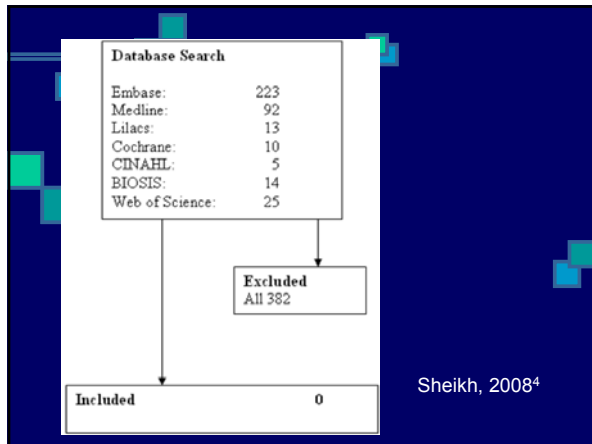
Pharmacology – the ugly

- Any pressor:
 - ↑ mortality
 - ↑ morbidity
- Marker of cellular dysfunction



Case 1- Anaphylaxis

- Best vasopressor?
 - Minimal data
 - Fatalities when epi not given
 - Limited reports of other agents
- Just give Epi²⁻³



Epinephrine


- Dose dependent (mcg/min)
 - < 0.1 - Beta
 - 0.1-2.0 - Alpha + Beta
 - > 2.0 - mostly Alpha
- Anaphylaxis
 - 1 mcg/min if IM route fails
 - Bronchodilation, mast cell stabilization⁵

Epi IV Dosing

- 1:10,000 solution = 0.1 mg/mL
- = 100 mcg/mL
- Add 1 mL to 100 mL of 0.9% NS
- = 1mcg/mL infusion

Case 2

- 18 year-old female presents intoxicated & quadriplegic
- Dive in the shallow end
- HR 50, BP 58/39



Neurogenic shock

- No randomized, prospective studies
- Sympathetic denervation
 - vasodilation and venous pooling
 - cardiac - bradycardia and reduced myocardial contractility
- Dopamine often 1st line⁶⁻⁷

Dopamine

- Dosing (mcg/kg/min)
 - 0.5-2 – D1 (renal, mesenteric, cerebral, coronary vasodilation)
 - 5-10 – Beta 1 and a little Alpha
 - 10-20 – more alpha
- Low-dose benefit disproven⁸

Neurogenic Shock

- Any vasopressor may do
- Consider MAP goal of 85 mmHg
 - Perfuse the penumbra
 - Uncontrolled studies⁹⁻¹⁰
- MAP goal of 65 mmHg?



Goal MAP?

- MAP which improves perfusion but minimize side-effects
- Aiming high (MAP > 65) confers no clear benefit in sepsis¹¹⁻¹²

	MAP			F/LT
	65 mm Hg	75 mm Hg	85 mm Hg	
DO ₂ (mL/min/m ²)	620 ± 59	670 ± 59	703 ± 74	.07/.02
VO ₂ (mL/min/m ²)	119 ± 12	138 ± 20	153 ± 20	.24/.11
SO ₂ (%)	76 ± 3	76 ± 2	70 ± 2	.94/.76
Lactate (mEq/L)	3.1 ± 0.9	2.9 ± 0.8	3.0 ± 0.9	.55/.77

Case 3

- 41 year-old male with a history of IVDA
- Temp 39.2, HR 130, BP 65/42 (50) after 6L of crystalloid
- + Delirium



Case 3

- Sepsis bundle
- Start a vasopressor?
- What vasopressor?



Surviving Sepsis¹³

- 1st line: Norepi or Dopamine
- Epi as 1st alternate
- May add low-dose vasopressin

Norepinephrine

- Primarily an alpha agent
- Start: 8 to 12 mcg/min
- Max = 5 mcg/kg/min

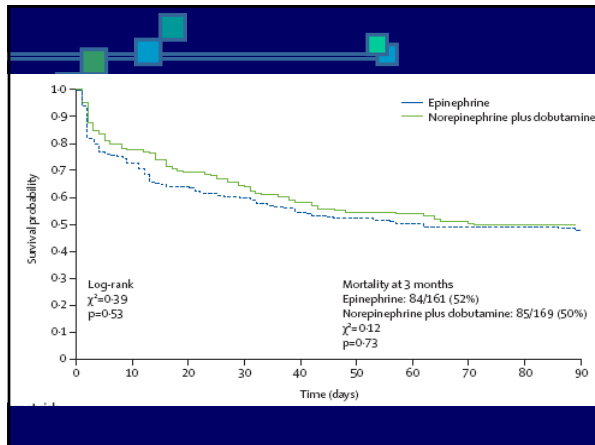
Norepi vs. Dopamine?

- Cochrane: 3 small studies, n=62¹⁴
 - slightly favors norepinephrine
 - RR of death of 0.88 (95% CI 0.57 to 1.36)
- Sakr (SOAP): observational, n=1,058¹⁵
 - higher mortality trend for Dopamine
 - 49.9% vs. 41.7%, p .01
 - not observed in Norepi group

Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial

Djillali Annane, Philippe Vignon, Alain Remault, Pierre-Edouard Ballaert, Claire Charpentier, Claude Martin, Gilles Trechê, Jean-Damien Ricard, Gérard Nitenberg, Laurent Papazian, Elie Azoulay, Eric Bellissant, for the CATS Study Group*

- 330 patients¹⁶
- Epi alone comparable to Norepi + Dobutamine
- RR death at 28 days: 0.86 (95% CI 0.65-1.14)

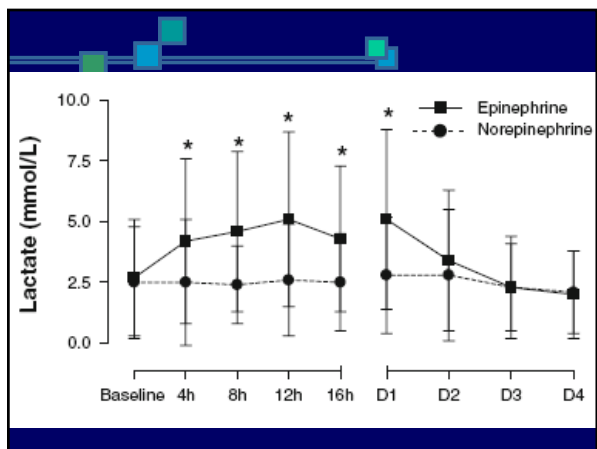


	Overall (n=330)	Epinephrine (n=161)	Norepinephrine plus dobutamine (n=169)
During catecholamine infusion			
Supraventricular tachycardia >150 bpm	41 (12%)	19 (12%)	22 (13%)
Ventricular arrhythmias	20 (6%)	12 (7%)	8 (5%)
Acute coronary event	8 (2%)	5 (3%)	3 (2%)
Limb ischaemia	8 (2%)	2 (1%)	6 (4%)
Stroke	4 (1%)	2 (1%)	2 (1%)
Central nervous system bleeding	3 (0.9%)	3 (2%)	0 (0%)
After catecholamine infusion			
Arrhythmias	13 (4%)	6 (4%)	7 (4%)
Stroke	4 (1%)	2 (1%)	2 (1%)
Other neurological sequelae	2 (0.6%)	1 (0.6%)	1 (0.6%)
Others	6 (2%)	3 (2%)	3 (2%)

John A. Myburgh
Alisa Higgins
Alina Jovanowska
Jeffrey Lipman
Naresh Ramakrishnan
John Santamaria
the CAT Study investigators

A comparison of epinephrine and norepinephrine in critically ill patients

- 277 randomized to Epi or Norepi¹⁷
- No difference in endpoints
 - Primary - time to achieve MAP goal
 - Secondary - 28 and 90-day mortality
- 10% withdrawal from Epi group

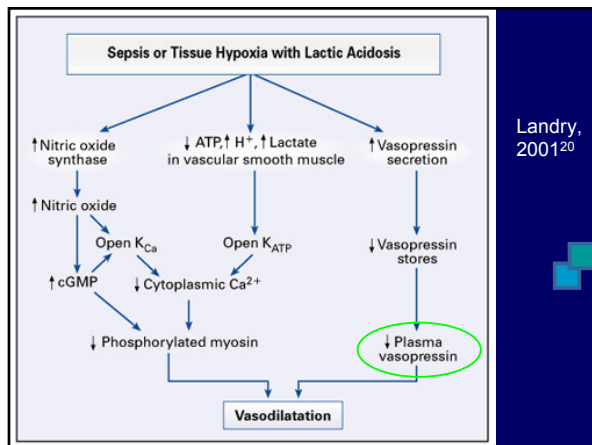


Epi and Lactate

- Increases lactate concentration¹⁸⁻¹⁹
 - increase in Na,K-ATPase pump activity
 - independent of cellular hypoxia

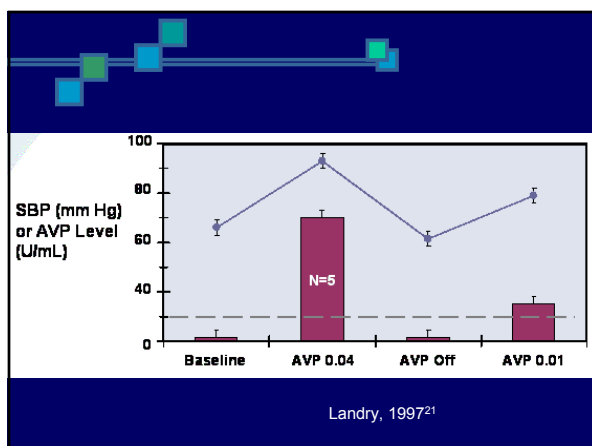
Case 1

- Rapidly titrate Norepinephrine to 100mcg
- MAP 55
- Do you add arginine vasopressin (AVP)?



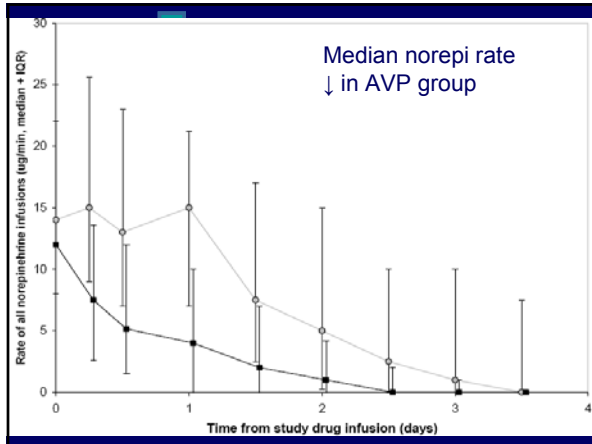
AVP pharmacology

- V1 receptors on vascular smooth muscle
- ↑ vascular response to catecholamines
- Inhibits vascular smooth muscle nitric oxide production



AVP vs. Norepi

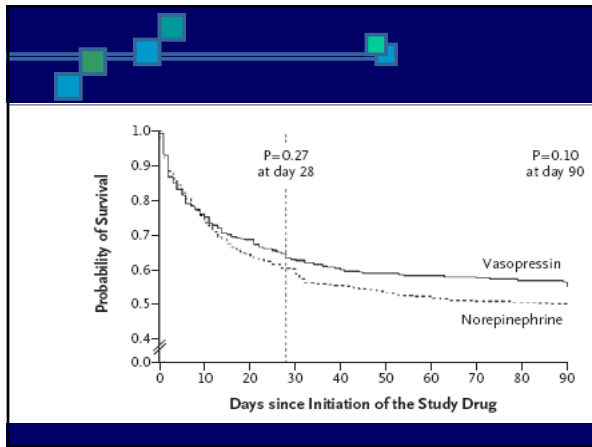
- Russell, 2008 NEJM
- 778 patients with septic shock
 - 0.01–0.03 U/min AVP
 - 5–15 mcg/min Norepi
- 28-day mortality



AVP vs. Norepi Survival

Vasopressin vs norepinephrine infusion for septic shock†

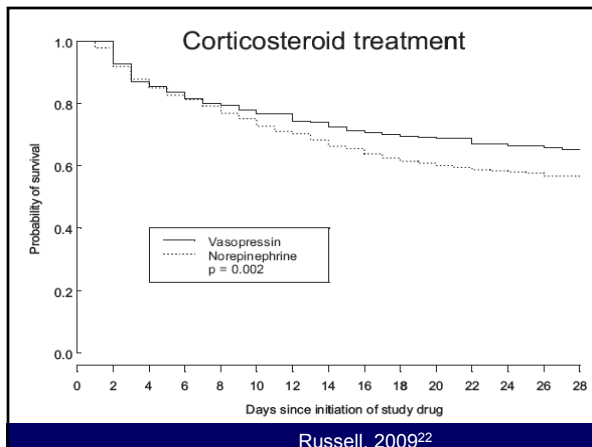
Outcomes	Vasopressin	Norepinephrine	RRR (95% CI)	NNT (CI)
28-day mortality	35%	39%	7.6% (-14 to 27)‡	NS
90-day mortality	44%	50%	11% (-7 to 28)§	NS
≥ 1 serious adverse event	10.4%	10.5%	1.1% (-49 to 34)	NS



AVP in less severe shock

Table 4. Rates and Risks of Death from Any Cause According to the Severity of Shock.^a

Stratum	Norepinephrine Group no./total no. (%)	Vasopressin Group no./total no. (%)	P Value†	Absolute Risk Reduction (95% CI) %
More severe septic shock				
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76	-1.5 (-11.2 to 8.2)
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84	1.0 (-8.8 to 10.8)
Less severe septic shock				
28-day mortality	65/182 (35.7)	52/196 (26.5)	0.05	9.2 (-0.1 to 18.5)
90-day mortality	83/180 (46.1)	69/193 (35.8)	0.04	10.4 (0.4 to 20.3)



Case 4

- 68 year-old male with chest pain and an anterior STEMI on EKG
- HR 120, BP 65/39, confused
- Cardio Team Uno is in another case
- Vasopressor?

Cardiogenic

- Interventional problem
 - IABP
 - Revascularization
 - Address any surgical cause
- What vasopressor?

Cardiogenic

Systolic BP 70 to 100 mm Hg NO signs/symptoms of shock	Systolic BP 70 to 100 mm Hg Signs/symptoms of shock	Systolic BP Less than 70 mm Hg Signs/symptoms of shock
Dobutamine • 2 to 20 mcg/kg per minute IV	Dopamine • 5 to 15 mcg/kg per minute IV	Norepinephrine • 0.5 to 30 mcg/min IV

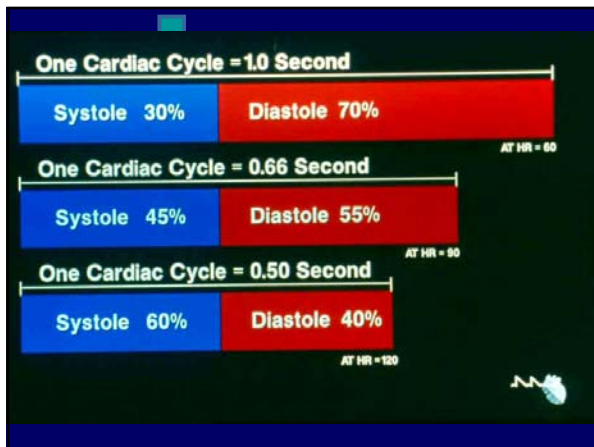
ACC/AHA Guidelines, 2004²³

Cardiogenic

- Dopamine?
 - Tachycardia, arrhythmogenicity, but + inotropy
- Norepi?
 - Makes sense, limited clinical data
- Vasopressin?
 - retrospective study of 36 patients: hemodynamic effects comparable to norepinephrine²⁴
- Phenylephrine?

Phenylephrine

- Selective alpha-1 agonist
- Limited data in shock states
- Dose: start 20 mcg/kg/min
- Reflex bradycardia
 - Coronary Perfusion



Pulmonary Embolism

- 44 year-old female returns from CT with BP 71/40, 140, 24
- No response to 1st bolus
- Worse with 2nd bolus
- Rads calls ...

Pulmonary Embolism

- No human trials
- Case reports of every agent
- Norepi may cause less ↑ pulmonary vascular resistance²⁵
- Canine model favors Norepi²⁶

Conclusions

- The good:
 - Can buy time
 - ? Sparing effect of vasopressin
 - Anaphylaxis, neurogenic do well
- The bad:
 - Scarce data outside of sepsis
 - Tachycardia is no friend of the heart
 - Can mask impending doom

Conclusions

- Have endpoints in mind
 - Preload
 - End-organ, cellular markers
 - MAP > 65 mmHg (? 85 for neurogenic)
- The ugly
 - Sepsis, LV failure, RV failure
 - Marker of cellular dysfunction

Conclusions

- Anaphylaxis – Epinephrine
- Neurogenic – Dopamine
- Sepsis – Norepinephrine
- Cardiogenic – Norepinephrine or Phenylephrine
- RV Failure - Norepinephrine