Septic Shock

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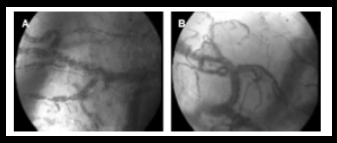
Goals:

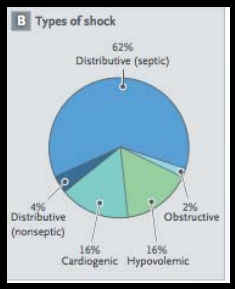
1) Understand the epidemiology of shock and how the to categorize of inflammatory response
2) Understand the general clinical approach to treating septic shock
3) Familiarize yourself with the nuance involved in septic shock resuscitation

Shock: Definition

- "Rude unhinging of the machinery of life"
- Inadequate delivery of oxygen and nutrients



Shock: Epidemiology



Systemic Inflammatory Response Syndrome (SIRS)

1) Temperature:	< 96.8° F or > 100.4° F
2) Heart Rate:	> 90 beats/min
3) Respiratory Rate:	> 20 resp/min or $PaCO_2$ < 32mmHg
4) WBC:	< 4.0/L or > 12.0/L or >10% bands

SIRS Classifications

1) SIRS (2+ criteria)
2) Sepsis (SIRS +source)
3) Severe Sepsis (Sepsis + organ dysfunction)
4) Septic Shock (hypotension refractory to IV fluid resuscitation)

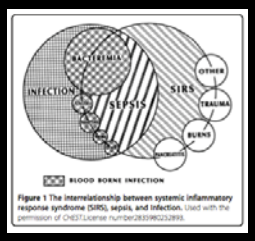
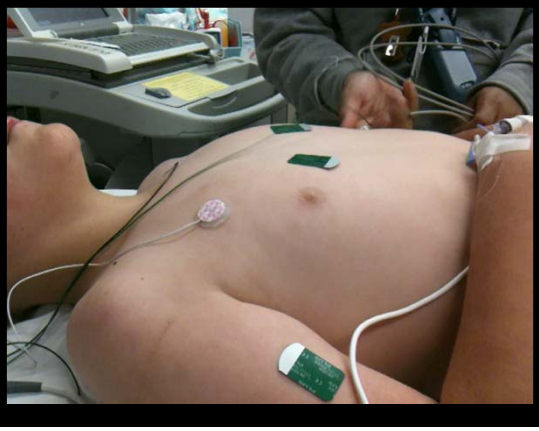


Figure 1 The interrelationship between systemic inflammatory response syndrome (SIRS), sepsis, and infection. Used with the permission of CHEST License number 2835980232899.



Systemic Inflammatory Response Syndrome (SIRS)

Table 2. Systemic Inflammatory Response Criteria and Dysfunctional Organ Systems

Variable	No. (%) of Patients: Lactate Clearance Group (n = 150)	$ScvO_2$ Group (n = 150)
SIRS criteria		
Abnormal white blood cell count	117 (78)	104 (69)
Elevated heart rate	100 (67)	108 (72)
Elevated respiratory rate	96 (64)	89 (59)
Abnormal body temperature	61 (41)	64 (43)

Systemic Inflammatory Response Syndrome (SIRS)

Temperature (°C)	Number in category	In-hospital mortality no. (%)
Infection group		
<36	480	279 (58.1)
36–36.4	1,782	536 (30.1)
36.5–36.9	4,387	978 (22.3)
37–37.4	6,345	1,282 (20.2)
37.5–37.9	5,180	1,031 (19.9)
38–38.4	4,241	806 (19.0)
38.5–38.9	2,911	594 (20.4)
39–39.4	1,924	358 (18.6)
39.5–39.9	1,099	221 (20.1)
≥40	734	200 (27.2)
Non-infection group		
<36	3,791	1,346 (35.5)
36–36.4	19,070	2,079 (10.9)
36.5–36.9	51,318	3,900 (7.6)
37–37.4	73,767	5,311 (7.2)
37.5–37.9	50,473	3,987 (7.9)
38–38.4	25,862	2,638 (10.2)
38.5–38.9	10,233	1,269 (12.4)
39–39.4	3,709	675 (18.2)
39.5–39.9	1,206	274 (22.7)
≥40	566	230 (40.6)

11,389/29,083 (39.1%)

19,505/239,995 (8.1%)

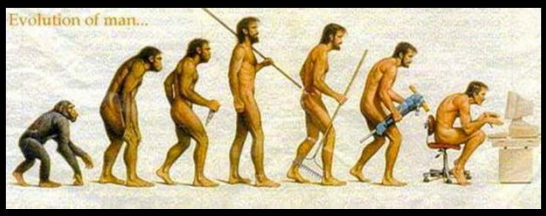
Take Home #1

- **Septic Shock is the most common cause of shock**
- **SIRS criteria are used to categorize the severity of the inflammatory response**
- **Presence of SIRS criteria does not confirm infection**
- **Absence of SIRS does not rule out septic shock**

Severe Sepsis/Septic Shock

Therapeutic approach

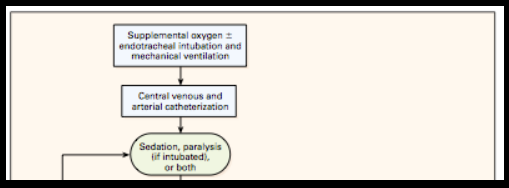
Severe Sepsis/Septic Shock
A little history: Early Goal Directed Therapy



Severe Sepsis/Septic Shock
Early Goal Directed Therapy

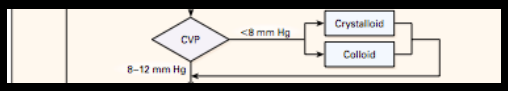
Rivers, E., Nguyen, B., Havstad, S., Ressler, J., Muzzin, A., Knoblich, B., et al. (2001). Early goal-directed therapy in the treatment of severe sepsis and septic shock. *New England Journal of Medicine, 345(19), 1368–1377. doi:10.1056/NEJMoa010307*

Severe Sepsis/Septic Shock
Early Goal Directed Therapy



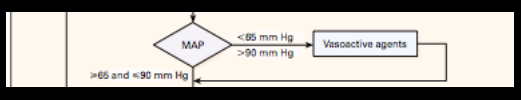
Invasive Interventions

Severe Sepsis/Septic Shock
Early Goal Directed Therapy



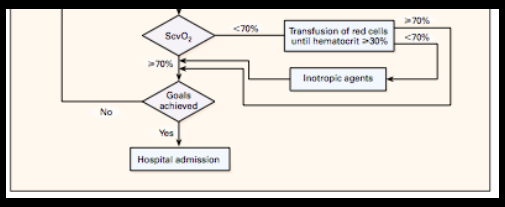
Volume Expansion

Severe Sepsis/Septic Shock
Early Goal Directed Therapy



Correct vasomotor tone

Severe Sepsis/Septic Shock
Early Goal Directed Therapy



Monitor for continued delivery deficits

Take Home #2

- Early aggressive treatment of septic shock has become the standard of care
- Care involves stabilization, volume expansion, vasomotor support and continued monitoring of tissue perfusion

Severe Sepsis/Septic Shock
EGDT: guidelines not rules to live by

ORIGINAL ARTICLE

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

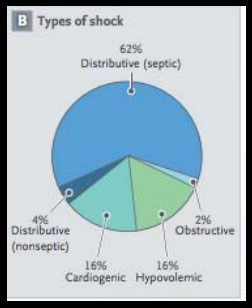
The ARISE Investigators and the ANZICS Clinical Trials Group*

NEJM 2014

Severe Sepsis/Septic Shock
ProCESS and ARISE: what now?

1. Early identification and antibiotic administration
2. Volume expansion with IVF
   - CVP
   - IVC ultrasound
   - Lactate
3. Vasopressors
4. Continued monitoring
   - Lactate Clearance
   - $ScvO_2$

Severe Sepsis/Septic Shock
Early identification and antibiotic administration



Severe Sepsis/Septic Shock
Early identification and antibiotic administration

TABLE 2. Adjusted Hospital Mortality Odds Ratio and Probability of Mortality for Time to Antibiotics Based on a Generalized Estimating Equation Population Averaged Logistic Regression Model

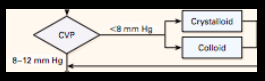
Time to Antibiotics (Hr)	OR*	95% CI	p	Probability of Mortality (%)*	95% CI
0–1†	1.00			24.6	23.2–26.0
1–2	1.07	0.97–1.18	0.165	25.9	24.5–27.2
2–3	1.14	1.02–1.26	0.021	27.0	25.3–28.7
3–4	1.19	1.04–1.35	0.009	27.9	25.6–30.1
4–5	1.24	1.06–1.45	0.006	28.8	25.9–31.7
5–6	1.47	1.22–1.76	<0.001	32.3	28.5–36.2
>6	1.52	1.36–1.70	<0.001	33.1	30.9–35.3

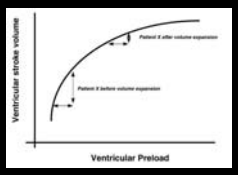
Ferrer, R., Martin-Loeches, I., Phillips, G., Osborn, T. M., Townsend, S., Dellinger, R. P., et al. (2014). Empiric Antibiotic Treatment Reduces Mortality in Severe Sepsis and Septic Shock From the First Hour. *Critical Care Medicine, 42(8), 1749–1755. doi:10.1097/CCM.0000000000000330*

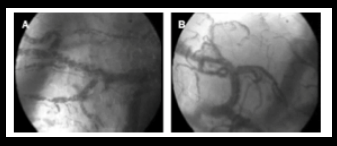
Take Home #3

- **Have a low threshold for suspecting infection in patients with shock**
- **Give early and broad empiric antibiotics**

Severe Sepsis/Septic Shock
Volume expansion—why?







Severe Sepsis/Septic Shock
Volume expansion

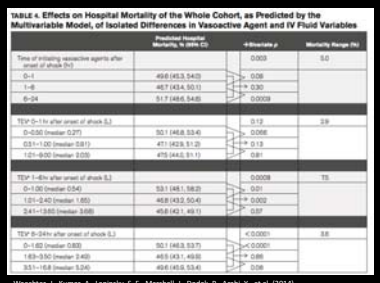
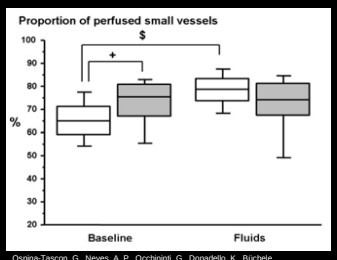


TABLE 4. Effects on Hospital Mortality of the Whole Cohort, as Predicted by the Multivariable Model, of Isolated Differences in Vasoactive Agent and IV Fluid Variables

	Predicted Hospital Mortality, % (95% CI)	↔Bivariate p	Mortality Range (%)
Time of initiating vasoactive agents after onset of shock (h)		0.003	5.0
0–1	49.6 (45.3, 54.0)	0.06	
1–6	46.7 (43.4, 50.1)	0.30	
6–24	51.7 (48.6, 54.8)	0.0003	
TEV 0–1 hr after onset of shock (L)		0.12	2.9
0–0.50 (median 0.27)	50.1 (46.8, 53.4)	0.066	
0.51–1.00 (median 0.81)	47.1 (42.9, 51.2)	0.13	
1.01–9.00 (median 2.03)	47.5 (44.0, 51.1)	0.81	
TEV 1–4 hr after onset of shock (L)		0.0008	7.5
0–1.00 (median 0.54)	53.1 (48.1, 58.2)	0.01	
1.01–2.40 (median 1.65)	46.8 (43.2, 50.4)	0.002	
2.41–3.85 (median 3.68)	45.6 (42.1, 49.1)	0.07	
TEV 8–24 hr after onset of shock (L)		<0.0001	3.8
0–1.62 (median 0.83)	50.1 (46.3, 53.7)	<0.0001	
1.63–3.50 (median 2.40)	46.5 (43.1, 49.9)	0.86	
3.51–10.8 (median 5.24)	49.4 (45.9, 53.4)	0.08	

Waechter, J., Kumar, A., Lapinsky, S. E., Marshall, J., Dodek, P., Arabi, Y., et al. (2014). Interaction Between Fluids and Vasoactive Agents on Mortality in Septic Shock. *Critical Care Medicine, 42(10), 2158–2168. doi:10.1097/CCM.0000000000000520*

Severe Sepsis/Septic Shock
Volume expansion

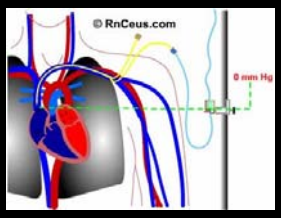


Ospina-Tascon, G., Neves, A. P., Occhipinti, G., Donadello, K., Büchele, G., Simion, D., et al. (2010). Effects of fluids on microvascular perfusion in patients with severe sepsis. *Intensive Care Medicine, 36(6), 949–955. doi:10.1007/s00134-010-1843-3*

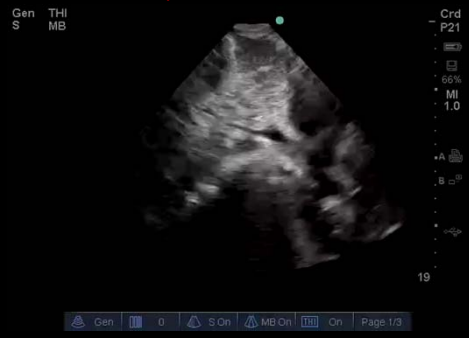
Severe Sepsis/Septic Shock
Volume expansion: Methods of monitoring

Severe Sepsis/Septic Shock
Volume expansion: Central Venous Pressure

- Measures pressure in SVC
- Requires central venous catheter: either IJ or SC
- Inherent variability in measuring
- Measurements affected by patient physiology

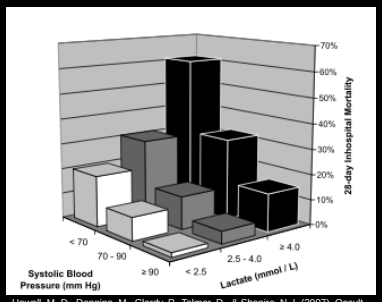


Severe Sepsis/Septic Shock
Volume expansion: IVC ultrasound

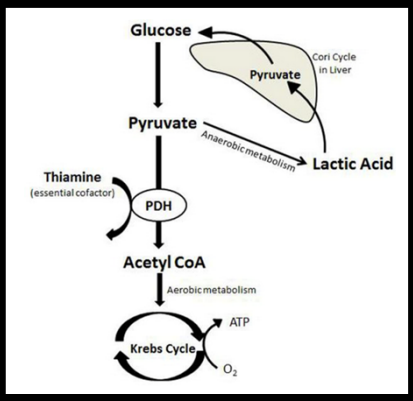


Severe Sepsis/Septic Shock
Volume expansion: Lactate

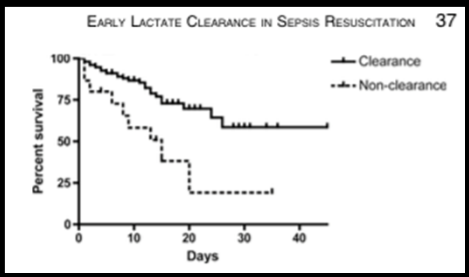
Severe Sepsis/Septic Shock
Volume expansion: Lactate



Howell, M. D., Donnino, M., Clardy, P., Talmor, D., & Shapiro, N. I. (2007). Occult hypoperfusion and mortality in patients with suspected infection. *Intensive Care Medicine, 33(11), 1892–1899. doi:10.1007/s00134-007-0680-5*



Severe Sepsis/Septic Shock
Volume expansion: Lactate



Severe Sepsis/Septic Shock
Volume expansion: Lactate

I know it's bad. If it's getting better, then there's less bad.

Take Home #4

- **Surviving Sepsis recommends 30cc/kg IVF bolus to start**
- **Each monitoring technique has limitations, but can provide some data to help decide if further IVF will be beneficial**
- **You will likely see all of these modalities used in the ED at some point**

Severe Sepsis/Septic Shock
Vasoactive agents

Norepinephrine
- α-agonist (primary)
- β1-agonist (secondary)

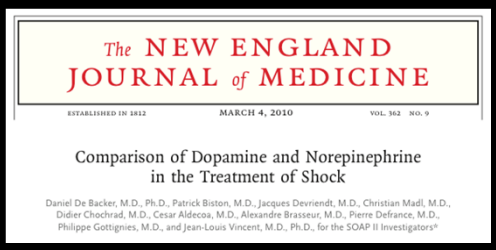
Phenylephrine
- α1-agonist

Epinephrine
- α-agonist
- β-agonist

Dopamine
- β1-agonist (primary)
- α-agonist (secondary)
- Dopamine receptors

Vasopressin
- V1 smooth muscle receptors

Severe Sepsis/Septic Shock
Vasoactive agents


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 4, 2010 VOL. 362 NO. 9

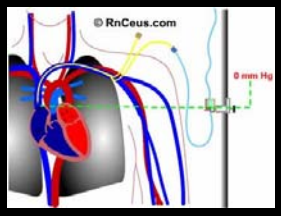
Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators*

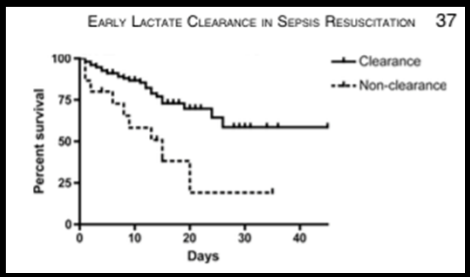
Severe Sepsis/Septic Shock
Continued monitoring:

Severe Sepsis/Septic Shock
Continued monitoring: $ScvO_2$

- O_2 saturation taken from the SVC
- Requires central venous catheter: either IJ or SC
- Can be continuous with "Sepsis Catheter"
- Affected by the extraction of oxygen by the tissues—high or low values (>89 or <70 can be abnormal and predict adverse outcomes)



Severe Sepsis/Septic Shock
Continued monitoring: Lactate Clearance



Severe Sepsis/Septic Shock

Continued monitoring: $ScvO_2$ vs Lactate Clearance

Variable	Lactate Clearance Group (n = 150)	$ScvO_2$ Group (n = 150)	Proportion Difference (95% Confidence Interval)	*P* Value[b]
In-hospital mortality, No. (%)[a]				
Intent to treat	25 (17)	34 (23)	6 (−3 to 15)	
Per protocol	25 (17)	33 (22)	5 (−3 to 14)	

Take Home #5

- **Continue to monitor patients with shock physiology**
- **Lactate clearance and $ScvO_2$ can both be used to monitor the course of resuscitation and determine if further interventions are necessary.**

Severe Sepsis/Septic Shock

Summary!

1) Have a low threshold for suspecting infection and giving antibiotics
2) Aggressively resuscitate patients with IVF and continue to assess volume status to optimize cardiac output
3) Add vasopressor agents when hypotension persists after initial resuscitation (my general starting point is 2L IVF)
4) Continue to monitor blood pressure and lactate