

Severe Sepsis: Recognition and Treatment

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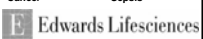
Severe Sepsis: A Growing Healthcare Challenge

- #1 cause of death in non-coronary ICU
- 11th leading overall cause of death
- 28-day mortality rate of 30-50%
- >750,000 cases in US annually
- Incidence is growing faster than overall population

Incidence


Mortality

Source: Sands KE, et al. JAMA 1997; Murphy, NVSR; Angus DC et al. Crit Care Med. 2001
National Center for Health Statistics, 2001. American Cancer Society, 2001.
American Heart Association, 2000; Angus DC et al. Crit Care Med. 2001.




Economic Burden of Severe Sepsis

- Total national healthcare costs associated with severe sepsis = \$16.7 billion
- Average LOS = 19.6 days
- Average cost per patient = \$22,100
- Increased costs compared to other patients:
 - 141% higher total hospital costs
 - 7x greater ventilator usage
 - 2x longer length of stay
- Whereas the incidence of septic shock has steadily increased during the past several decades, the associated mortality rates have remained constant or have decreased only slightly.




Source: Angus DC, et al. Critical Care Medicine, 2001; 29: 1303-1310; www.sepsis.com; Friedman, et al; Has the mortality of septic shock changed with time. Critical Care Medicine, 1998; 26: 208-86.




Finding the Solution - Surviving Sepsis Campaign

- Goal: To increase awareness and improve outcomes in severe sepsis, leading to a 25% reduction in mortality in 5 years.
- Includes evidence-based guidelines developed by group of international experts and endorsed by 11 international organizations.
- Guidelines include EGDT, for which ScvO₂ monitoring is a key component.



Sponsors of Guidelines:
 American Association of Critical-Care Nurses
 American College of Chest Physicians
 American College of Emergency Physicians
 American Thoracic Society
 Australian New Zealand Intensive Care Society
 European Respiratory Society
 European Society of Chemotherapy, Microbiology and Infectious Diseases
 European Society of Intensive Care Medicine
 Infectious Disease Society of America
 Society of Critical Care Medicine
 Surgical Infection Society




How Does Severe Sepsis Compare to Your Current Care Priorities?

Quality Projects	US Incidence	# of Deaths	Mortality Rate
AMI ¹	895,000	171,000	19%
Stroke ¹	700,000	157,800	23%
Pneumonia ²	1,300,000	61,800	4.8%
Severe Sepsis ³	751,000	215,000	29%

Why do you think that severe sepsis has not received the same focus as these other common disease states?

1. American Heart Association, Heart Disease and Stroke Statistics 2006 Update. 2. National Center for Health Statistics. Available at: www.cdc.gov/nchs/data/np/neumonia.htm. Accessed 2/04/05. 3. Angus DC et al. Crit Care Med 2001;29:1303-1310.



Life after severe sepsis

- Almost 60 percent of hospitalizations for severe sepsis were associated with worsened cognitive and/or physical function among survivors in the first survey following hospitalization.
- The risk of progression to moderate or severe cognitive impairment in sepsis survivors was 3.33 times higher than their risk before hospitalization.
- Severe sepsis was associated with the development of 1.57 new functional limitations among patients with no limitations before sepsis.

Iwashyna, et al. 2010 (NIH study)

What is Sepsis??

- Mortality rate 20%
- Defined as infection plus systemic manifestations of infection
- Gradual onset
- Occurs in microcirculation
- Symptoms manifestation late in disease process
- Time is of the essence for survival!



Systemic Inflammatory Response Syndrome (SIRS)

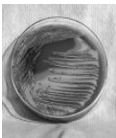
TWO or more of the following criteria:

- Temperature >101F or <96.8F
- HR >90
- RR > 24 or PaCO₂ <32
- WBC >12,000 or <4000
- Bands >10%



Severe Sepsis

- Sepsis AND acute dysfunction of at least one organ, hypoperfusion, or hypotension. (30-50% mortality)



Septic Shock resulting in MODS (Multiple organ dysfunction syndrome)

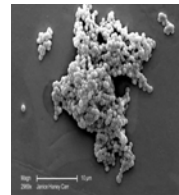
- MODS--presence of altered function of two or more organs in an acutely ill patient, such that homeostasis cannot be maintained without intervention.
- Mortality about 50-70%
 - Occurs when sepsis-induced hypotension persists despite adequate fluid resuscitation. (Bone, 1992)

Is the occurrence of sepsis increasing over time?

- Yes, sepsis is becoming more common, especially in the hospital, as a result of:
- Medical and technological advances associated with treatments
- The increasing number of elderly or debilitated people, and patients with underlying diseases such as cancer, who require therapy
- The widespread use of antibiotics, which encourages the growth of drug-resistant microorganisms

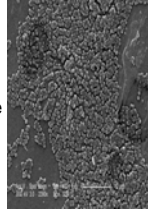
Common Sources

- Skin- Bacteria enter the skin through wounds and skin inflammations; IV catheters and Foley catheters
- Bone- Inflammation and infections of the bone, the bone marrow, the sinuses, etc.
- Nervous System- Inflammation and infections in the brain (eg, meningitis or encephalitis) or spinal cord.
- **In 50% of cases of severe sepsis or septic shock, blood cultures are negative.**

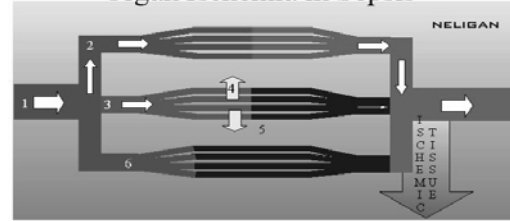


Common Sources

- Lungs- Major source of infection in severe sepsis (especially with hospital-acquired infections), with sepsis usually associated with pneumonia.
- Abdomen- Appendicitis, bowel problems, gallbladder infections. When the outer surface of the abdominal organs (called the peritoneum) is involved in the infection, it is called "peritonitis."
- Urinary tract- Common source of infection, particularly in patients needing a urinary catheter. Diabetic patients are also at increased risk of urinary infections leading to sepsis.

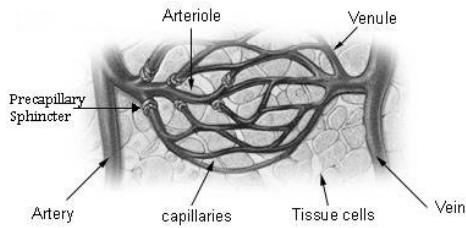


Organ Ischemia in Sepsis

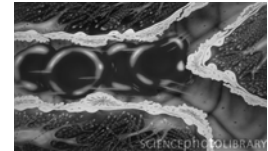


1. Due to vasodilatation, organ perfusion pressure is low and sluggish.
2. Some capillary beds perfuse normally.
3. Others are badly damaged, and there is 4. capillary leak, 5. The tissues become edematous, compressing normal tissues, preventing oxygen exchange.
6. Due to venous stasis and activation of coagulation pathways, small vessels become obstructed, and blood flow stops.

Microcirculation

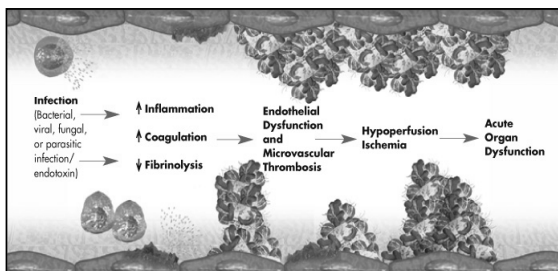


Microcirculation



- Function is to permit transfer of substances between tissues and circulation. This transfer occurs predominantly across the walls of the capillaries but some exchange occurs in the small venules also.
- Substances involved include water, electrolytes, gases (O₂, CO₂), nitrogenous wastes, glucose, lipids and drugs.

Sepsis Pathophysiology



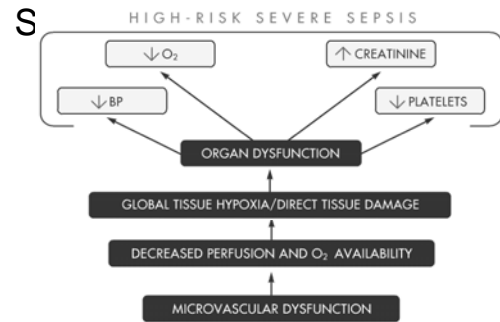
Understanding Sepsis

- Evidence suggests that severe sepsis is a disease of the microvasculature characterized by:
 - 1. Decreased perfusion and oxygen availability
 - Microvascular thrombosis
 - Reduced functional capillary density
 - 2. Endothelial dysfunction
 - Endothelial apoptosis
 - Increased expression of adhesion molecules
 - Increased capillary permeability
 - 3. Reduced vasomotor tone
 - 4. Increased leukocyte-endothelium interactions

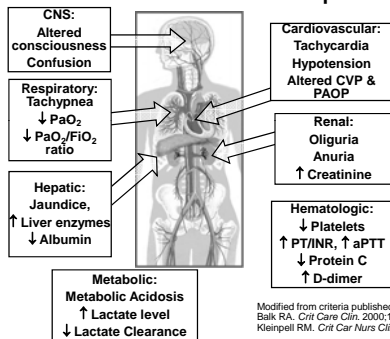
The Problem

- **#1. Recognition that is it occurring**
- Inconsistency in the early diagnosis of severe sepsis and septic shock
- Frequent inadequate volume resuscitation without defined endpoints
- Late or inadequate use of antibiotics
- Frequent failure to support the cardiac output when depressed
- Frequent failure to control hyperglycemia adequately
- Frequent failure to use low tidal volumes and pressures in acute lung injury
- Frequent failure to treat adrenal inadequacy in refractory shock

Microvascular Dysfunction in



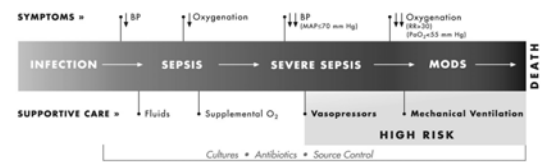
Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis



Modified from criteria published in:
Balk RA. *Crit Care Clin*, 2000;16:337-352
Kleinpell RM. *Crit Care Nurs Clin N Am* 2003;15:27-34.

Identification of High-Risk Severe Sepsis

- Clinical indicators can alert you to high risk of death.*



* The mortality rate (risk of death) of standard therapy patients who had an APACHE II score of 25 in the trial was 25%. The mortality rate of standard therapy patients who required vasopressors was 30%.

† Need for dopamine ≥ 5 $\mu\text{g}/\text{kg}/\text{min}$ or norepinephrine, epinephrine, or phenylephrine at any dose. Single organ dysfunction alone may not represent high risk of death.

Of the measures used in the PROWESS (Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis) clinical trial, the APACHE II score was most effective in classifying patients by risk of death and by likelihood of benefit from Xiglis.

Goals of Treatment

- Control underlying infection
- Interrupt coagulation
- ↓ Inflammation
- Restore fibrinolysis

Goal is to ↑ microvascular flow and perfusion of dysfunctional organs.

Screening

Key areas for screening programs include:

- Medical-Surgical Units
- ICU—1 in 10 admissions to the ICU involves severe sepsis (Angus,2001)
- Emergency department—37% of severe sepsis patients present in the emergency department
- Pharmacy—combination of therapies can signal possible clinical indicators of severe sepsis (vasopressors and antibiotics)

Triggers

- Upon admission to ED/ICU
- At nurse shift changes
- During medical or multidisciplinary rounds
- Upon deterioration in patient's clinical/laboratory parameters

Sepsis Identification Tool

Systemic Inflammatory Response Syndrome (SIRS)	<ul style="list-style-type: none"> * Temp > 101 F or < 96.8 F * HR > 90 bpm * RR > 24 or PaCO₂ < 32 * WBC > 12,000 or < 4,000 * Bands > 10%
Sepsis	2 or more SIRS criteria present AND suspected or confirmed infection
Severe Sepsis	Sepsis AND dysfunction of one or more organs: <ul style="list-style-type: none"> • SBP < 90 for one hour despite adequate fluid therapy • UO < 30 ml/hr (< 0.5 ml/kg/hr) • Cr ↑ > 0.5 from baseline or requires acute dialysis • Platelets < 10,000 • pH < 7.30 or lactate > 4 mmol/L or 36mg/dL • Liver enzymes > 2x normal • Bilirubin > 4 • Ileus • AMS or ↓ GCS • P/F ratio < 250, PEEP > 7.5
Septic Shock	Severe sepsis AND, despite adequate fluid therapy, SBP < 90 or MAP < 70

Identifying At-Risk Patients

Screening patients at risk of developing severe sepsis can aid in early diagnosis. The following patient types receiving anti-infective therapy and organ support are among those who should be screened:

- ICU and Med-Surg patients receiving antibiotics
- Severe CAP (community-acquired pneumonia)
- Intra-abdominal surgery
- Meningitis
- Chronic diseases (including diabetes, heart failure, chronic renal failure, and hepatitis)
- Compromised immune status (HIV/AIDS, use of cytotoxic and immunosuppressive agents, malignant neoplasms, and alcoholism)
- Cellulitis
- Urinary tract infection

Patients at Greater Risk

Predictors of higher mortality for severe sepsis patients include the following patient characteristics:

- Older age
- Underlying co-morbidity
- Higher body weight

Surviving Sepsis Campaign

- Early recognition and diagnosis
- Initial resuscitation-fluid therapy using Early Goal Directed Therapy
- Early initiation of broad spectrum antibiotic therapy
- Source control (surgery)
- Vasopressors (levophed or dopamine)
- Inotropic therapy (dobutamine)
- Corticosteroids for septic shock
- (Recombinant Human Activated Protein C) rhAPC
- Blood product administration

Initial Resuscitation

- Fluid therapy Goals (1st 6 hours):
 - CVP 8-12 mmHg (12-15 if vented)
 - MAP >65 mmHg
 - Urine output >0.5 mL/kg/hr
 - ScvO₂ >70% SVO₂ >65% (PA cath)

Diagnosis and Source Control

- Lactic acidosis (>4mmol/L or >36 mg/dL)
- Obtain blood cultures preferably prior to antimicrobial therapy if no delay.
- 2 cultures with one drawn percutaneously and one through vascular access
- >50% of severe sepsis cases will have negative cultures but many cases likely caused by bacterial or fungi.
- Remove IV if access device possible source and replace
- Surgical intervention for abscess or necrotic tissue

Antibiotic Therapy

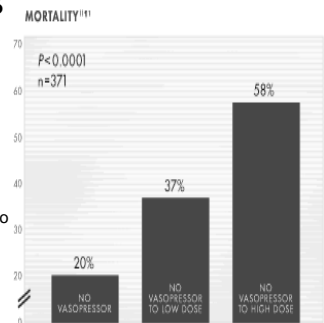
- Antibiotic therapy be started as early as possible and within the first hour of recognition of severe sepsis.
 - Initial empirical broad spectrum for greater coverage of pathogens (bacterial and fungal)
 - Reassess daily
 - 7-10 day therapy

Vasopressors

- MAP >65%
- Norepinephrine or dopamine to correct hypotension
- Epinephrine if poor response to norepi or dopamine
- Vasopressin not recommended initially

Vasopressors

- Mortality rates doubled to nearly 40% in those patients who required no vasopressors at baseline, but required low-dose vasopressors by Day 1.
- Nearly 60% of patients who required high-dose vasopressors by Day 1 did not survive.



Inotropic Therapy

- Dobutamine in presence of myocardial dysfunction AEB low CO
- If the CVP is 8-12 and
- If the MAP is >65 and
- If the Hct 30% BUT
- ScVO₂ <70% then start dobutamine

Blood Product Administration

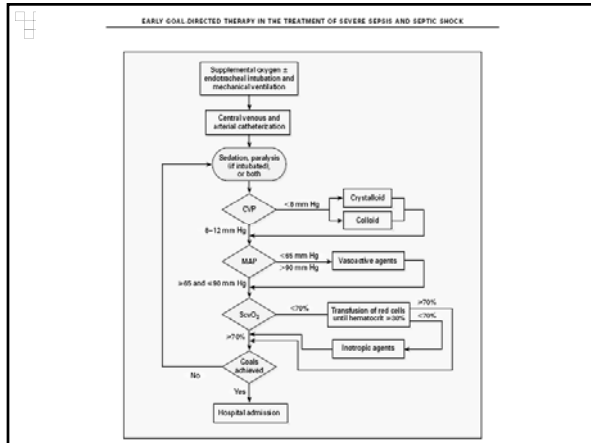
- Once tissue hypoperfusion resolved
- Recommended when hgb <7.0 g/dL to target 7.0-9.0 g/dL in adults
- Not based on sepsis patients
- When compared with 10-12 g/dL no association with increased mortality.
- Recommend platelets if <5000/mm³
- Erythropoietin, FFP (in absence of bleeding) and antithrombin therapy not recommended.

Corticosteroid Therapy

- Recommended given only to adults after it has been confirmed that BP poorly responsive to fluid resuscitation and vasopressor therapy.
- Shown to reverse septic shock
- Mortality benefit not clear
- Side effects include increased risk of infection and myopathy.
- JURY STILL OUT on efficacy.
- ACTH stimulation test not suggested

Recombinant Human Activated Protein C (rhAPC)

- APACHE II >25 or multiple organ failure if no contraindications
- PROWESS study- 1,690 patients with documented 6.1% reduction in mortality
- Bleeding-major side effect



Supportive Therapy of Severe Sepsis

- Mechanical ventilation
- VTE/stress ulcer prophylaxis
- Sedation and analgesia
- Glucose management (<180 mg/dL)
- Renal replacement therapy
- Bicarbonate therapy
- Consideration for limitation of support

Mechanical Ventilation

- Sepsis-induced acute lung injury (ALI)/Acute Respiratory Distress Syndrome (ARDS) Nearly 50 percent of patients with severe sepsis will develop acute lung injury (ALI)/acute respiratory distress syndrome (ARDS).
- 9% reduction in mortality shown when:
 - target tidal volume of 6 mL/kg body weight often called "low tidal volume"
- Permissive hypercapnia to minimize plateau pressures and tidal volumes (exception in metabolic acidosis and increased ICP)
- Usage of PEEP >5 to avoid lung collapse
- Prone positioning
- Weaning protocols
- NO ROUTINE USE OF SALINE INSTILLATION OF ETT
- HOB 30-45 degrees if not contraindicated
 - PUD and VTE protocols in place

Sedation and Analgesia

- Sedation protocol recommended
 - Ramsey or RASS (Richmond Agitation and Sedation Scale)
 - Daily interruptions for readiness to wean vent
 - Impact on LOS and VAP
 - Watch out for delirium!
 - Assess and treat for pain and discomfort

■ Case Study

The curious case of Mr. Jones

- HPI: 76 y/o who presented to the ED at 10 AM with CC of 3-day hx of SHOB that has gotten worse today. He saw his PCP for same complaint yesterday and was prescribed an abx.
- PMH: COPD, HTN, CAD
- FH: CAD, Diabetes
- PSH: CABG x 4 (10 years ago)
- SH: Smokes 1 ppd x 38 years, denies ETOH and illicit drug use.

In the ED

- VS: BP 108/67, HR 108, RR 22, T 100.9 O2 sat 91% on RA
- Lungs with crackles to bases
- Non-productive cough
- Heart RRR but tachy
- EKG Tachycardia but otherwise normal
- Placed on O2 2Ln/c with sat 96%
 - Chest XRay shows bilateral infiltrates with consolidation on base of right side
- WBC 11,000

Hospital course

- At 1:00 PM he is admitted to the GMF floor with community-acquired pneumonia.
- First dose of IV abx given in the ED.
- IV NS at 75 mL/hr.
- VS on admission to floor:
 - BP 98/54, HR 115, RR 24, T 101 (gave anti-fever)
 - O2 sat 94% on 2 L n/c
- He ate 50% of supper but has no appetite.

Hospital course

- At 6:00pm he becomes slightly lethargic and is pulling at his IV tubing and nasal cannula
- VS at shift change:
 - BP 92/48, HR 115, RR 22, T 100
 - O2 sat 93% on 2L n/c
 - Physician notified
 - order to ↑ IVF to 100mL/hr
 - Keep O2 sat >95%--O2 ↑4Ln/c

- At 9:00 pm his wife becomes worried and comes out to the nurse's station asking for help.
- You go into the room and find the following.....

“Now Mr. Jones.....”

- He is lethargic, cool pale skin.
- Keep pulling at nasal cannula.
- VS show BP 86/38, HR 122, RR 26, T 102
- Urine output 0.3 mL/kg/hr past 2 hours
- O2 sat 90% 4L n/c (84% on RA)
- *What is going on and what are you going to do about it?*

Questions to ask yourself

- What is the patients current condition?
- Why are his VS worsening?
- Should I call the doctor and what do I say?
- SBAR (situation, background, assessment, recommendation)
 - S: Pt has become increasingly lethargic.
 - B: Admitted today with pneumonia.
 - A: Give VS, physical assessment and describe the trend. Consider possible sepsis.
 - R: May need to call the RRT and transfer to higher level of care.



RRT and ICU Orders

- Place on 15L NRB mask
- Give initial 500 mL bolus NSS with goal to keep CVP 8-12 mmHg after placing CL (preferably with ScVO2 monitoring capability)
- Start sepsis order set
- Start additional abx
- If BP <90 after multiple boluses then start a pressor keep MAP >65

RRT and ICU Orders

- Respiratory status deteriorates and is placed on vent
 - Preliminary blood cultures negative
 - Lactate 48 mg/L
 - WBC 28,000
- When did this patient become septic?

Always.....

Watch for SIRS!!

- Review VS and monitor trends (lose false sense of well-being if SPB >90mmHg)
- Monitor for acute changes in mental status
- Get another set of eyes if you are unsure
- Utilize your resources-charge nurse, RRT
- plan what you will tell the physician
- Suspect sepsis until proven otherwise especially with central line catheter, Foley, or any other foreign object or device
- Listen to the family. They know the patient better than anyone.

Questions.....

- Thank you for your attention and for caring for our patients with sepsis!

www.survivingsepsis.org/guidelines
www.sccm.org

