Exploring the Cutting Edge of Sepsis

Perianesthesia Potpourri
February 6, 2016

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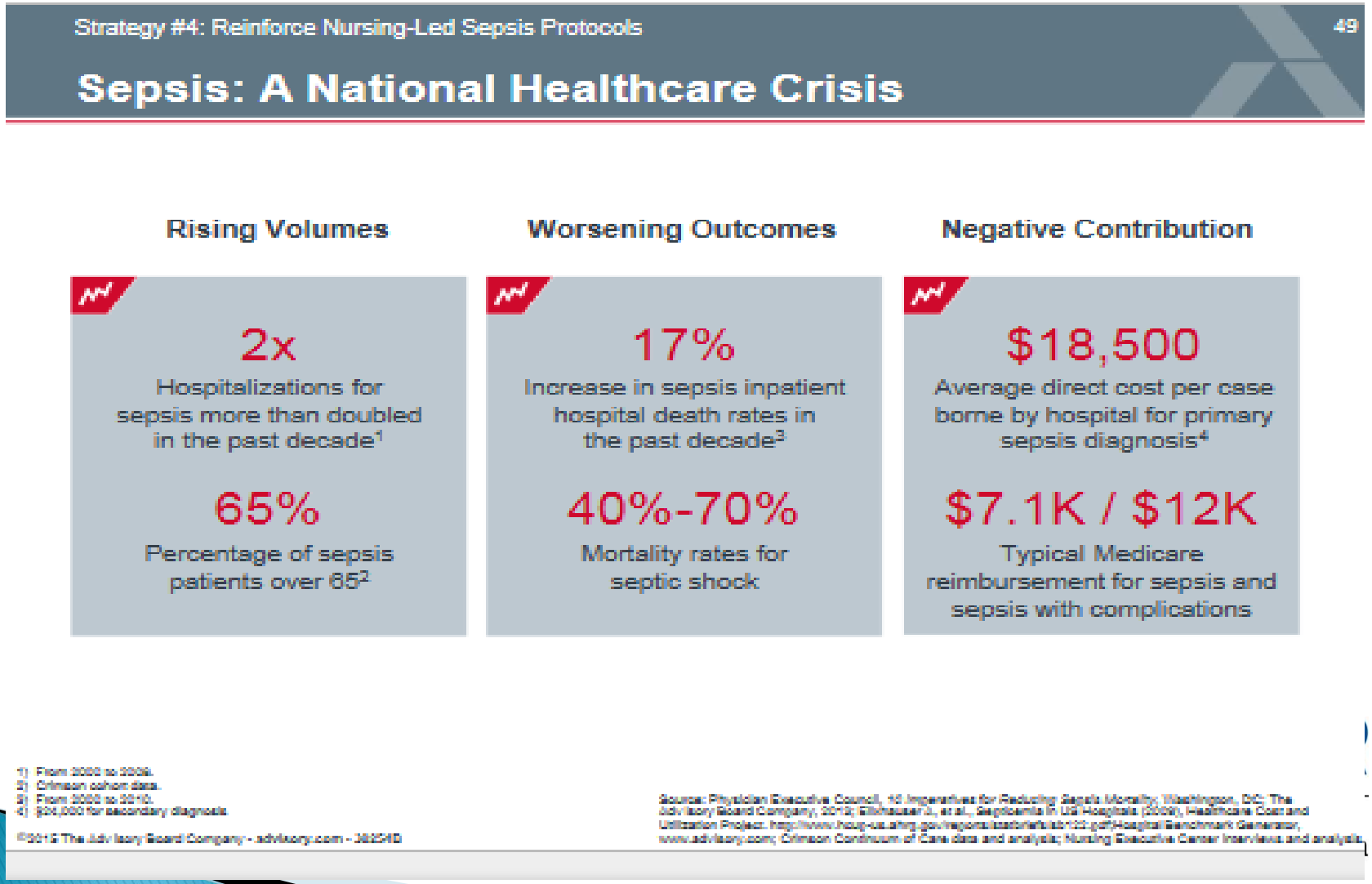
Exploring the Cutting Edge of Sepsis

- Distinguish between sepsis, severe sepsis, and septic shock
- Identify treatment priorities in the first 24 hours after presentation

- I have no conflicts of interests to disclose.

National Attention on Sepsis



National Attention on Sepsis

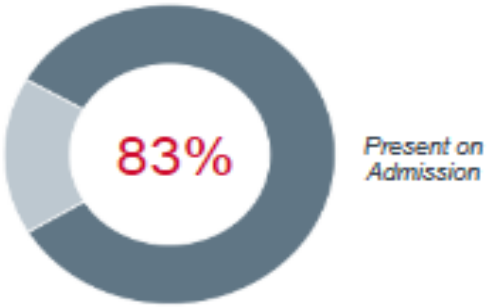
50

Vast Majority of Cases Present on Admission

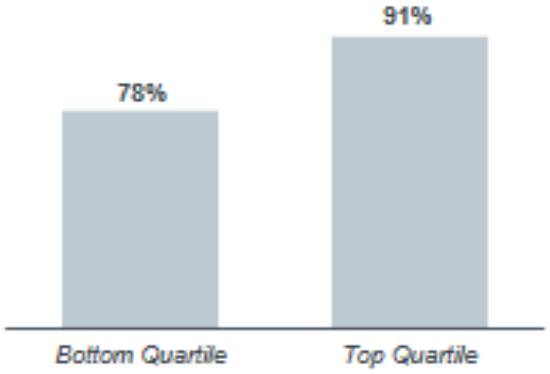
Overwhelmingly Not a Hospital Acquired Condition

Percent of Sepsis Cases Present on Admission

n=283,000 Cases



Percent of Sepsis Cases Present on Admission, Interquartile Range



1) Top quartile indicates the organizations with the most cases of sepsis present on admission, rather than top-quartile overall performance.
2) Present on admission.

Source: Physician Executive Council, 10 Imperatives for Reducing Sepsis Mortality; Washington, DC; The Advisory Board Company, 2013.

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Sepsis Facts

- In the U.S. there are more than 750,000 new cases of sepsis each year, with 225,000 being fatal (1/4 of patient die)
- In the U.S. severe sepsis is the leading cause of death in Non-ICU patients
- Sepsis is the leading cause of death by infection in the world
- More people are hospitalized for sepsis than for MI
- Mortality rate of severe sepsis is 20-50%
- When shock is present, mortality 50-60%
- The annual cost of hospital care for patients with septicemia is $14 billion in the U.S.

Definitions: Infection

- **Infection**: The invasion of normally sterile tissue by organisms
  - Bacteria
  - Fungi
  - Virus
  - Parasites

Definitions: SIRS

- **Systemic Inflammatory Response Syndrome**: (SIRS) The clinical syndrome that results from an inflammatory response to a noninfectious insult. The response is manifested by two or more of the following:
  - Temp >38 or <36
  - Heart rate>90
  - RR >20 or pC02<32
  - WBC> 12,00 or <4000, >10% immature forms

Definitions: Sepsis

- **Sepsis**: The systemic response to infection. Manifested by two or more of the following:
  - Temp >38 or <36
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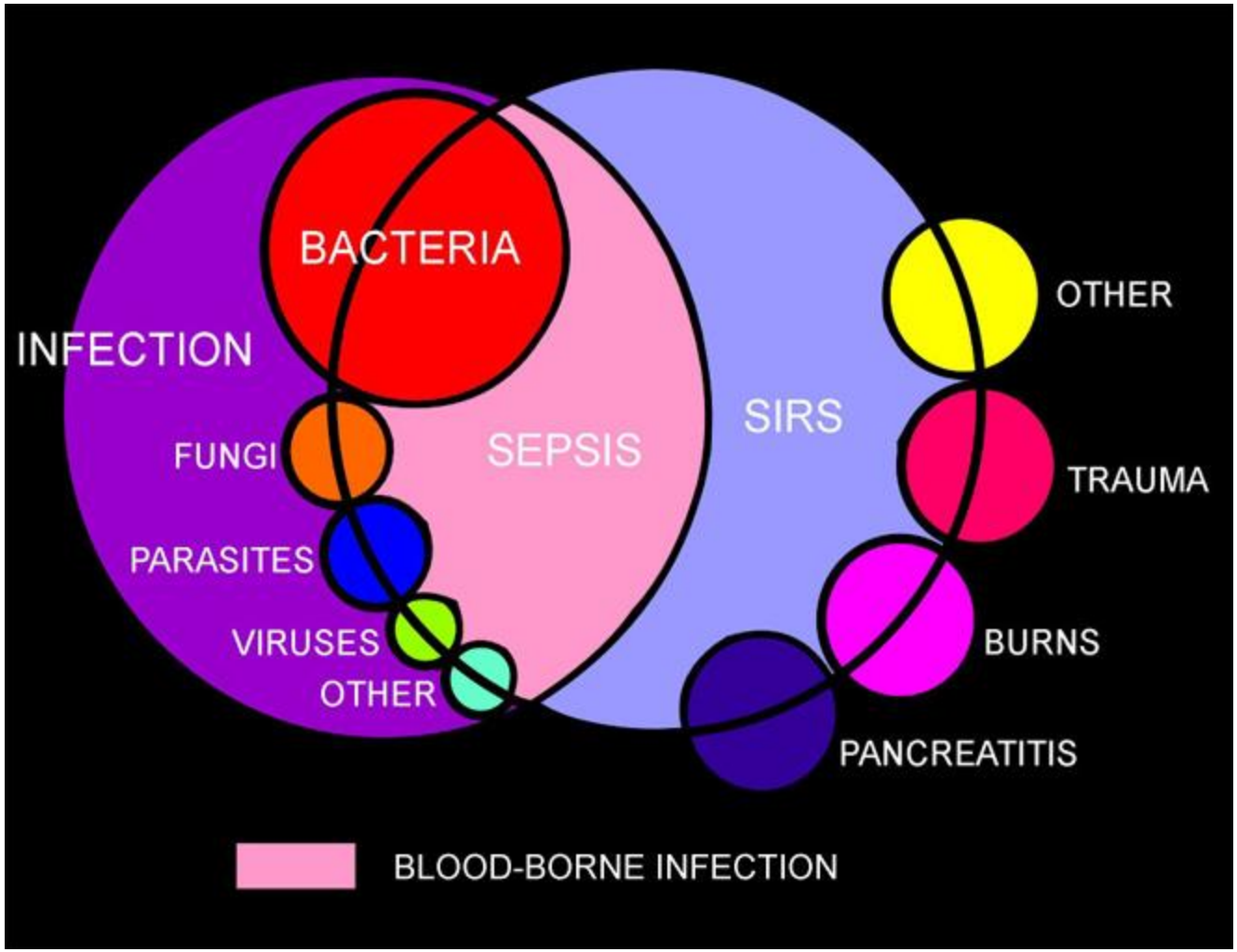
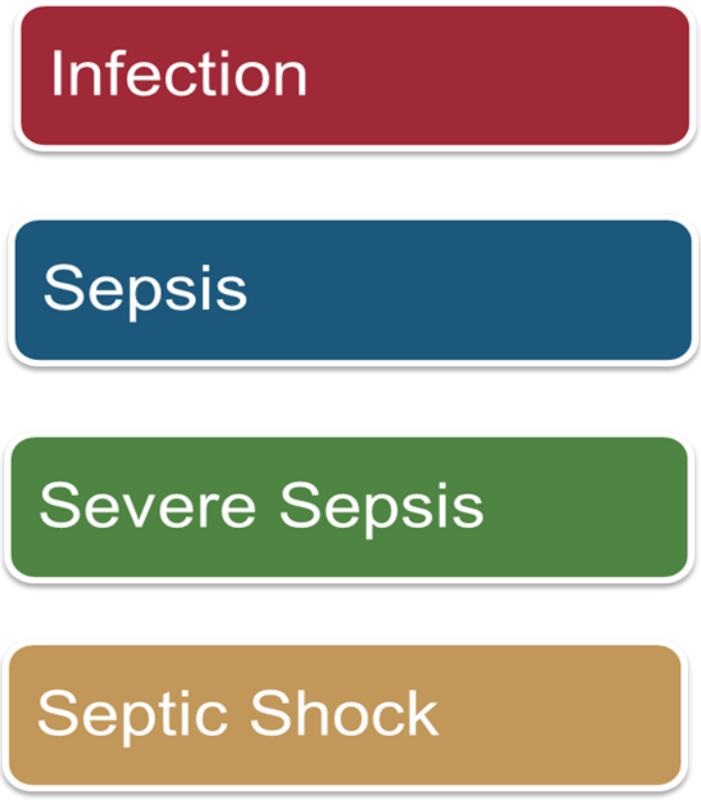

BACTERIA
INFECTION
FUNGI
PARASITES
VIRUSES
OTHER
SEPSIS
SIRS
OTHER
TRAUMA
BURNS
PANCREATITIS
BLOOD-BORNE INFECTION

Defining Sepsis

- The American College of Chest Physicians and the Society of Critical Care Medicine developed four phases for the progression of the septic process



Definitions: Severe Sepsis

- Severe Sepsis refers to sepsis plus at least one sign of hypo-perfusion or organ dysfunction:
  - Areas of mottled skin
  - Capillary refilling requires $\geq$ 3 seconds
  - Urine output $<$ 0.5 mL/kg/hour
  - Lactate $>$ 2 mmol/L
  - Abrupt change in mental status
  - Platelet count $<$100,000
  - Acute respiratory distress
  - Cardiac dysfunction as defined by echo or measurement of the cardiac index

Definitions: Septic Shock

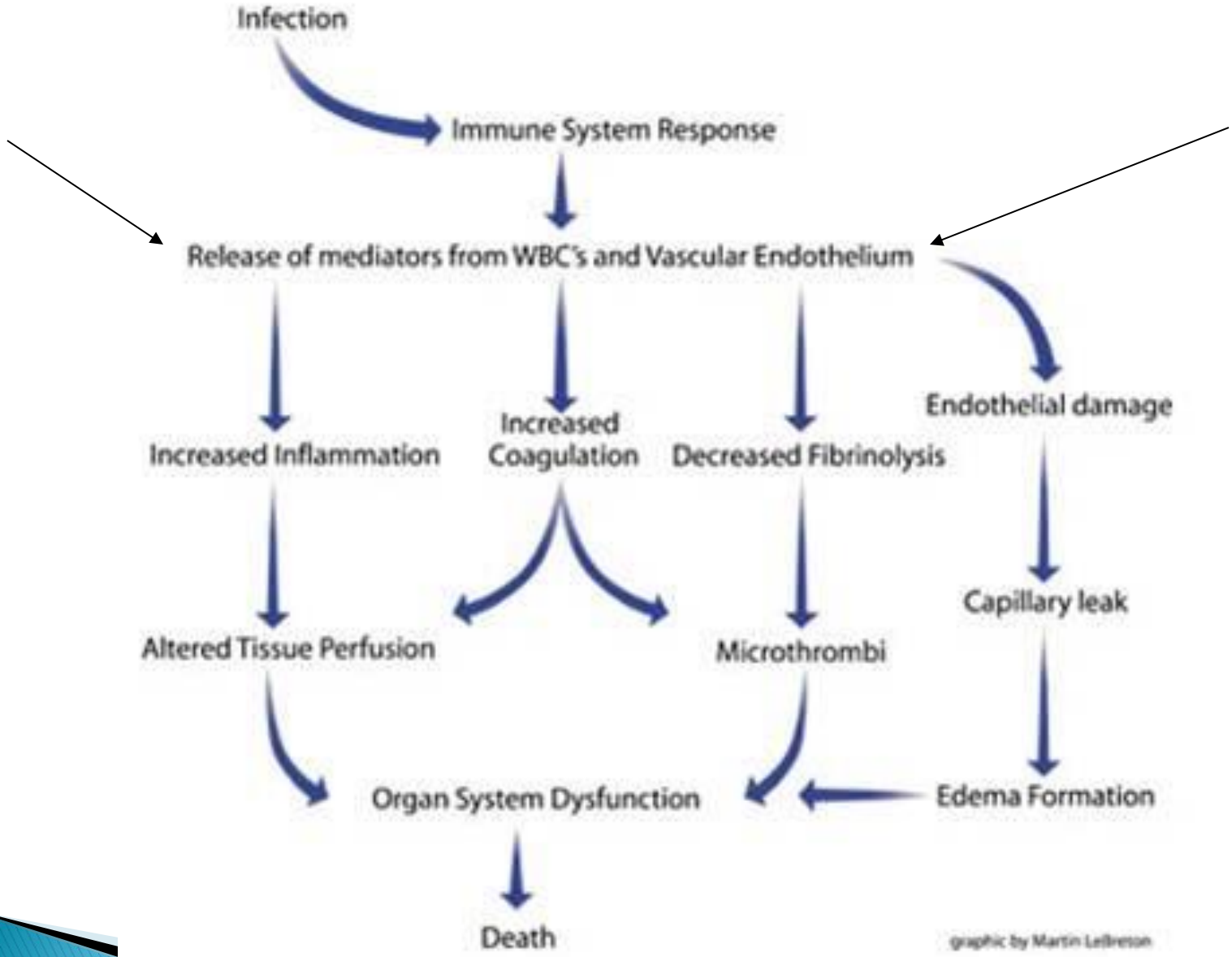
- **Septic Shock**: Severe sepsis plus hypotension despite adequate fluid resuscitation, which is defined as 30 mL/kg of saline, or PCWP 12-20, or CVP 8-12.

Definitions: Hypotension

- **Hypotension**:
  - Systolic blood pressure <90mmHg
    (or decrease of >40 from normal if hypertensive)
  - Mean arterial pressure <70 mmHg

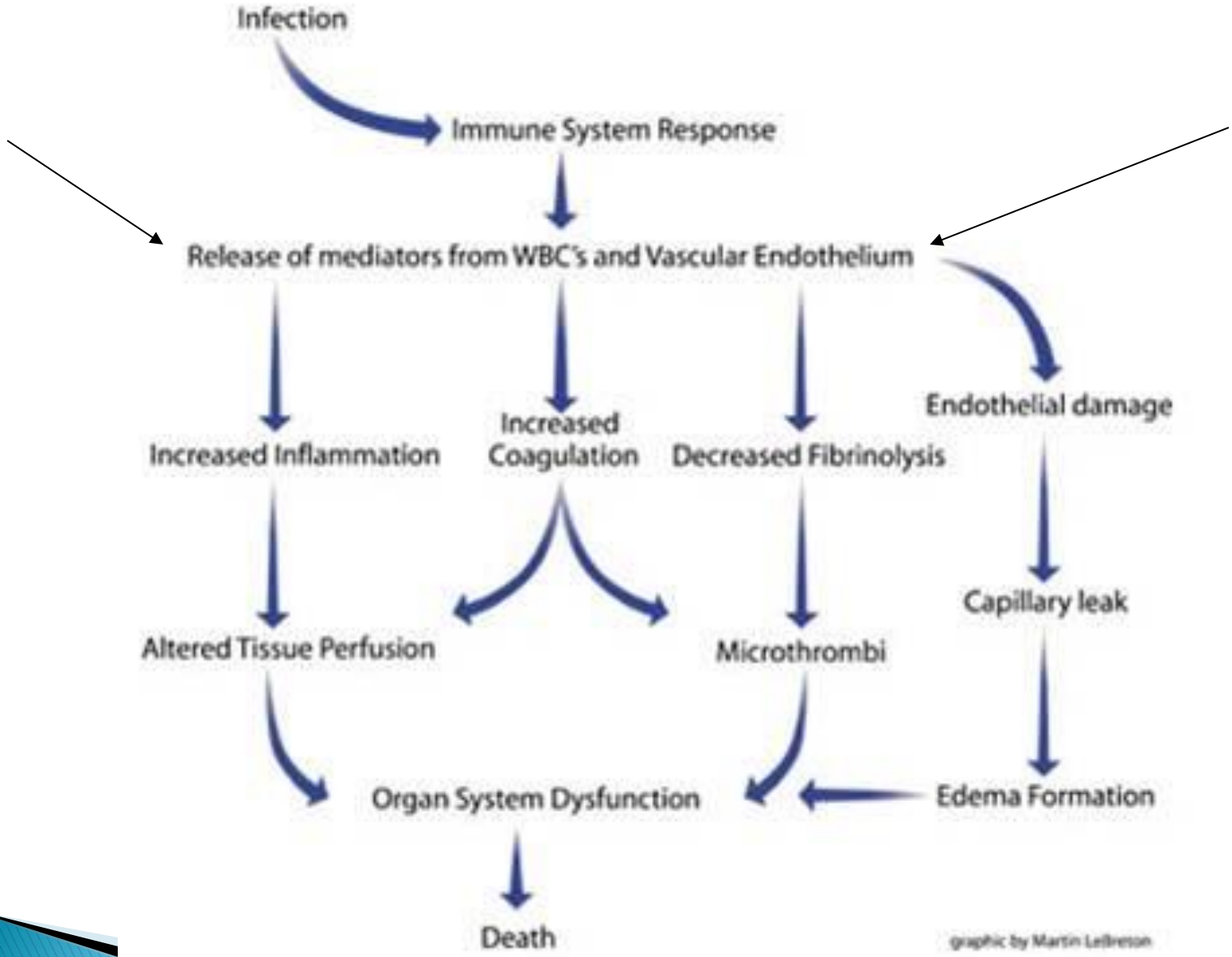
Risk Factors for Developing Sepsis

- Advanced age (≥65 years)
- Immunosuppression: cancer, renal failure, liver failure, AIDS, and immunosuppressant medications
- Community acquired pneumonia


Infection
Immune System Response
Release of mediators from WBC's and Vascular Endothelium
Increased Inflammation
Increased Coagulation
Decreased Fibrinolysis
Endothelial damage
Altered Tissue Perfusion
Microthrombi
Capillary leak
Organ System Dysfunction
Edema Formation
Death
graphic by Martin LeBreton

Mediators of Endothelial Damage in Sepsis

- Tumor necrosis factor
- Interleukins
- Platelet activating factor
- Leukotrienes
- Thromboxane A2
- Prostaglandins
- Prostacyclin
- Interferon
- Complement fragment
- Adhesion molecules
- Platelets
- Bradykinin
- Thrombin
- Myocardial depressant
- B-endorphin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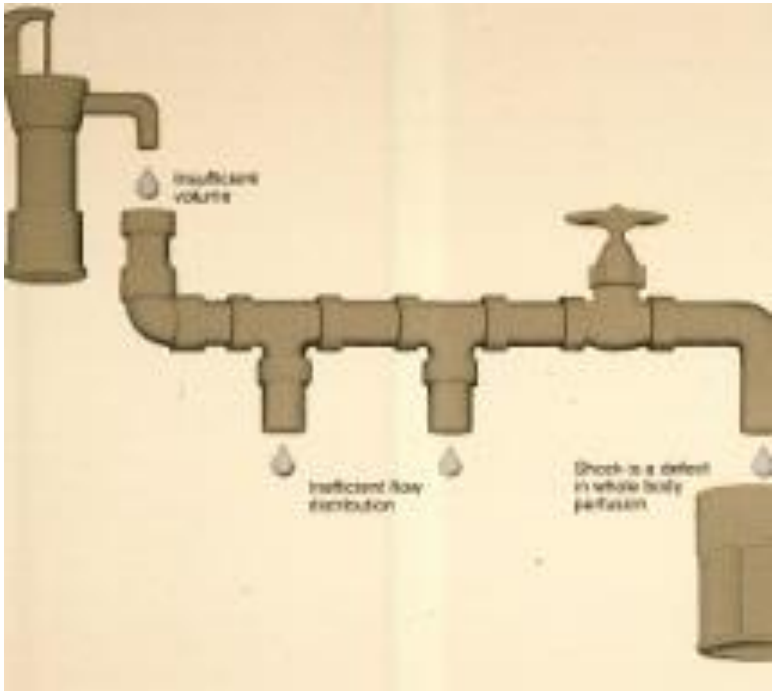
Progression of Septic Shock

- Myocardial depression due to sepsis.
- Inadequate volume due to vasodilation and ↑ permeability.
- ↓ tissue perfusion leads to Multiple Organ Dysfunction Syndrome



Clinical Manifestations of Sepsis: Early/Warm Phase

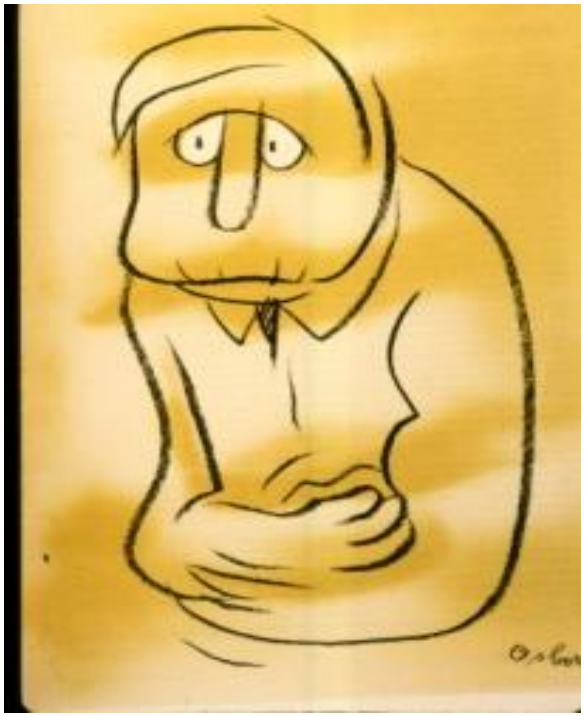
- Cardiovascular:
  - Heart rate: >90
  - Blood pressure <90 systolic or decrease of >40
  - Temp >38 or <36, skin warm and dry
  - Cardiac output normal or increased.

Clinical Manifestations of Early Sepsis

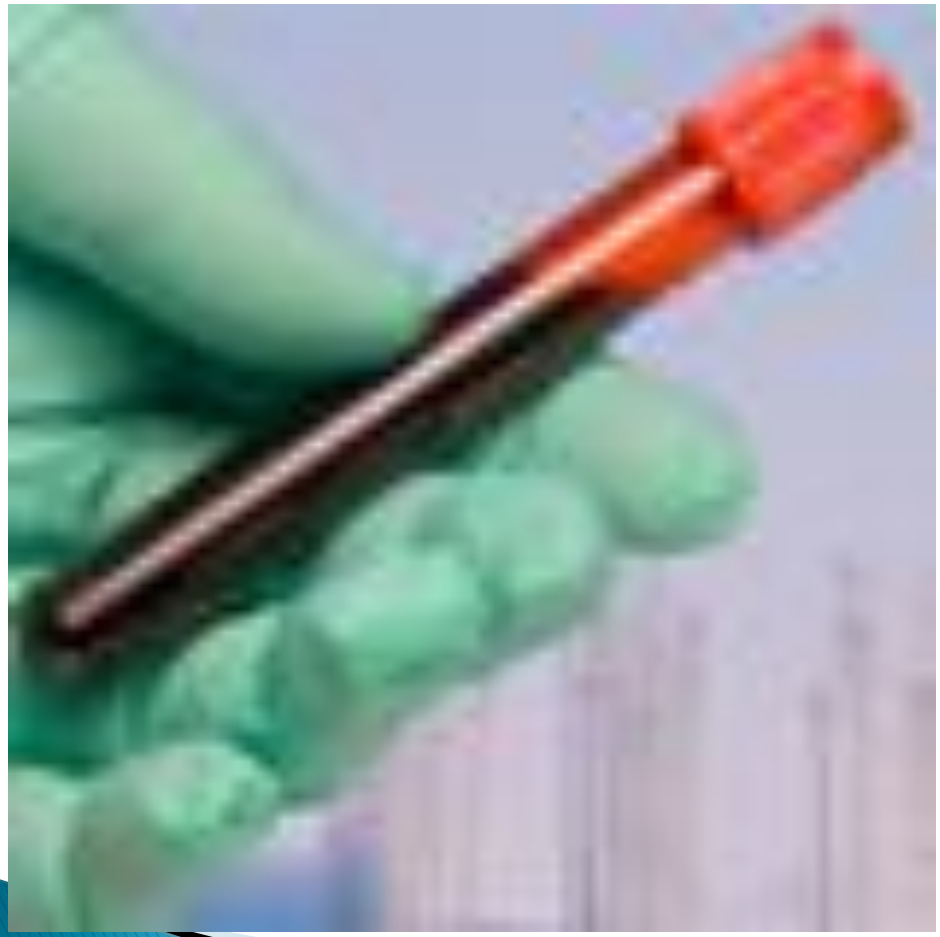
- Pulmonary
  - Respiratory rate >20
  - Arterial blood gases: pC02 decreased
- Neurologic
  - Restless
  - Disoriented
  - Personality Change

Clinical Manifestations of Early Sepsis

- Gastrointestinal
  - Nausea
  - Vomiting
  - Diarrhea
  - Ileus



Labs in early sepsis



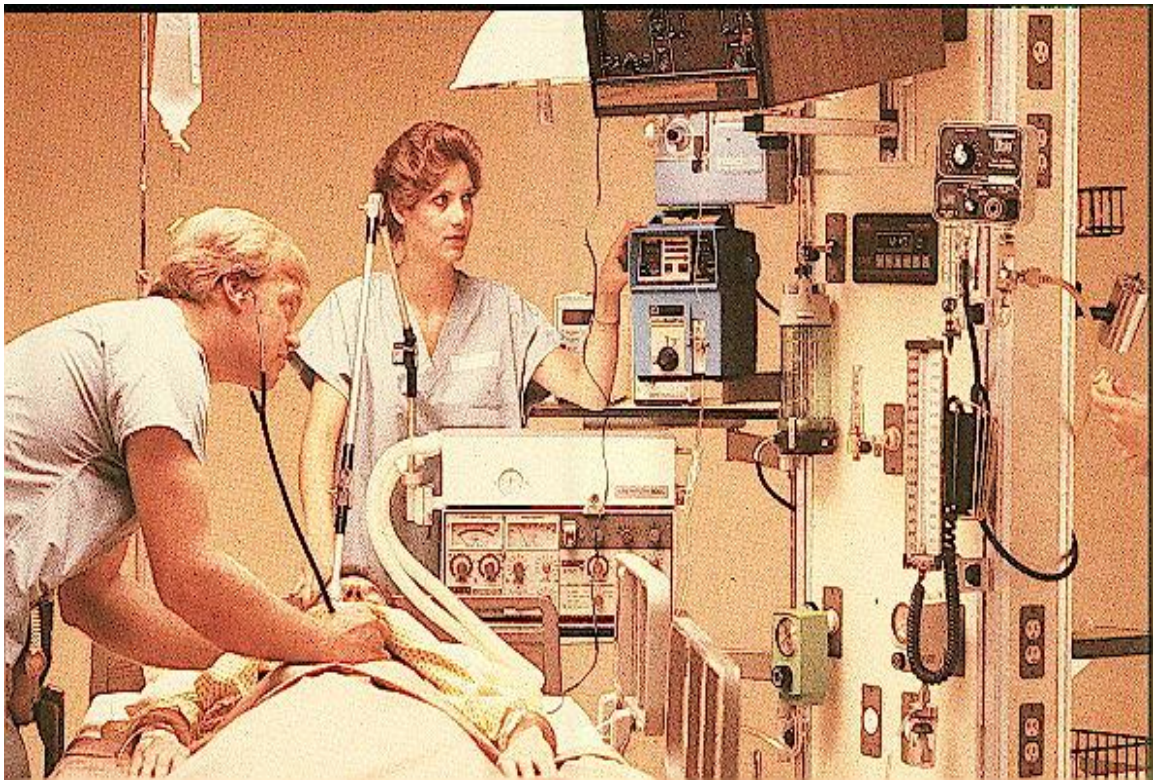
- Blood sugar increased
- ↓WBC <4000 or ↑ WBC >12,000
- Increased lactate, metabolic acidosis
- Clotting factors decreased

Clinical Manifestations of Late/Cool Phase of Septic Shock

- Cardiovascular
  - Heart rate >120
  - Blood Pressure: unresponsive to treatment
  - Temperature: subnormal, cool extremities
  - Cardiac output: decreased
    - PWP increased
    - SVR increased

Clinical Manifestations of Late Septic Shock

- Pulmonary:
  - Severe respiratory distress
  - Hypoxemia



Clinical Manifestations of Late/Cool Phase of Septic Shock

- Renal
  - Urine output decreased
- Neurologic
  - Stuporous, comatose

- Decreased blood sugar
- Acidosis (respiratory and metabolic), ↑Lactate >4
- Elevated liver enzymes and bilirubin
- Elevated BUN, Creatinine

Multiple Organ Dysfunction Syndrome

- Acute respiratory distress syndrome (ARDS)
- Disseminated intravascular coagulation (DIC)
- Renal failure
- Liver failure

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012

SurvivingSepsis.org

RP Dellinger, MM Levy, A Rhodes, et al: Critical Care Medicine 2013; 41: 580-637

"The potential to save lives is enormous. Assuming that the reduction in mortality seen to date can be sustained and 10,000 hospitals comply with the Campaign recommendations, we could save 400,000 lives *if we treat only half* of the eligible patients with the Surviving Sepsis Campaign Bundles."

Surviving Sepsis Campaign

Surviving Sepsis Campaign Bundles

To Be Completed Within 3 Hours

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30 ml/kg crystalloid for hypotension or lactate $\geq$4mmol/L

Surviving Sepsis Campaign Bundles
To Be Completed Within 6 Hours

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a MAP ≥65 mmHg

6. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4:

    1. -Measure central venous pressure (CVP). Goal ≥8
    2. -Measure central venous oxygen saturation (Scv02). Goal ≥70

7. Re-measure lactate if initial lactate was elevated

Goals of Initial Resuscitation

- Mean Arterial Pressure (MAP) ≥ 65 mmHg
- Central Venous Pressure (CVP) 8-12 mmHg
- Urine Output ≥ 0.5 mL/kg/hour
- Central venous (superior vena cava) oxygen saturation ≥ 70% or mixed venous oxygen saturation > 65%

Serum Lactate

- Lactate levels are elevated in patients with severe sepsis or septic shock secondary to anaerobic metabolism due to hypoperfusion.
- Obtaining a lactate level is essential to identifying tissue hypoperfusion in patients who are not yet hypotensive but are at risk for septic shock.
- Patients with an elevated lactate (>4 mmol/L) should receive early goal-directed therapy of the sepsis bundle, regardless of blood pressure.

Diagnosis

- Obtain appropriate cultures before starting antibiotics, provided this does not significantly delay antimicrobial administration.
- Perform imaging studies promptly in order to confirm and sample any source of infection, if safe to do so.

Prior to Antibiotic Therapy

- Blood Cultures
  - Minimum of 2
  - 1 percutaneous
  - 1 from each vascular access device in >48 hours (if suspect cath related infection)
- Other sites as indicated
  - Urine culture/urinalysis
  - Sputum culture
  - Wound culture

Antibiotic Therapy

- Begin IV antibiotics as early as possible, and always within the 1st hour of recognizing severe sepsis and septic shock. (One hour delay increases mortality by 7.6%)
- Broad-spectrum
- Reassess daily
- Duration of therapy typically 7-10 days
- Stop antimicrobial therapy if cause is found to be non-infectious.

Fluid Therapy

- Fluid-resuscitate to target of CVP of ≥8 (≥12 if mechanically ventilated)
- Give 1000mL over 30 minutes, then 500 mL every 30 minutes. (Monitor closely for pulmonary complications.)
- Use albumin as needed.
- Goal: 30 mL/kg (100kg patient = 3000 mL)

Vasopressors

- Goal: Maintain MAP $\geq$ 65
- Norepinephrine centrally administered is the initial vasopressor of choice.
- Alternative agents when BP is poorly responsive to norepinephrine:
  - Epinephrine
  - Vasopressin
  - Dopamine (if low heart rate)

Achieve CVP of >8 mmHg

- Do not delay fluid resuscitation for central line placement.
- In addition to fluid challenges, give red blood cells when hemoglobin decreases to <9.

Tissue Oxygenation: Scv02>70% or Sv02 >65%

- Fluid resuscitation
- Vasopressors
- Red blood cells
- Inotropes: Use dobutamine in patients with myocardial dysfunction (elevated cardiac filling pressures and low cardiac output)
- Oxygen and/or mechanical ventilation

Steroids

- IV hydrocortisone only when BP responds poorly to adequate fluid resuscitation and vasopressors

Glycemic Control

Use IV insulin to maintain blood glucose <150 mg/dL

Timing Critical to Reduce Sepsis Variation

Prevent Severe Sepsis and Shock to Decrease Mortality and Cost

1 Hour
Delay in Antimicrobials

→

7.6%
Increase in Mortality

Crimson Data Reveals Breakdowns in Sepsis Care

47% Sepsis cases in which clinicians failed to order lactate with blood culture

External Literature Points to Costly Delays

50% Septic shock patients who did not receive antibiotics within six hours of documented hypotension

Source: Kumar A. et al., "Duration of Hypotension Before Initiation of Effective Anti-Microbial Therapy Is the Critical Determinant of Survival in Human Septic Shock," *Critical Care Medicine*, 34, no. 6 (2006): 1589-1596; Physician Executive Council, *10 Imperatives for Reducing Sepsis Mortality*; Washington, DC; The Advisory Board Company, 2013; Crimson Continuum of Care data and analysis.

CMS Core Measures for Sepsis

- Effective **October 1, 2015** CMS implemented new core measures for Sepsis, because:
  - Sepsis is common,
  - Wide variation in clinical practices and outcomes, and
  - Care is expensive
- **Goal**: Early recognition and early, aggressive, standardized management of sepsis.
  - Reduces mortality & disability/morbidity
  - Produces reproducible and more consistent outcomes
  - Reduces length of stay and cost per case

Presence of Severe Sepsis

- If no inclusion terms are contained in physician/APN/PA documentation, review the record to determine if severe sepsis was present.
- In order to establish the presence of severe sepsis, there are three criteria, all three of which must **be met within 6 hours of each other.**

I. Documentation of a suspected source of clinical infection.

There may be reference to "possible infection from xx", "suspect infection from xx", or similar reference in progress notes, consult notes, or similar physician/APN/PA documentation

II. Two or more manifestations of systemic infection according to the Systemic Inflammatory Response Syndrome (SIRS) criteria, which are:

i. Temperature > 38.3 C or < 36.0 C

ii. Heart rate (pulse) > 90

iii. Respiration > 20 per minute

iv. White blood cell count > 12,000 or < 4,000 or > 10% bands

III. Organ dysfunction, evidenced by any one of the following:

i. Systolic blood pressure < 90, or mean arterial pressure < 65, or a systolic blood pressure decrease of more than 40 points

ii. Creatinine > 2.0, or urine output < 0.5 mL/kg/hour for 2 hours

iii. Bilirubin > 2 mg/dL (34.2 mmol/L)

iv. Platelet count < 100,000

v. INR > 1.5 or aPTT > 60 sec

vi. Lactate > 2 mmol/L (18.0 mg/dL)

CMS Core Measures for Sepsis

Core measure requirements for **Severe Sepsis** include the following elements :

- within 3 hours of presentation
  - Initial lactate level
  - Broad spectrum or other antibiotics administered
  - Blood cultures drawn prior to antibiotics
- within 6 hours of presentation of severe sepsis
  - Repeat lactate if initial level >2

Presence of Severe Shock

- The criteria for determining that Septic Shock is present are:

There must be documentation of **Severe Sepsis present**.

AND

Tissue hypoperfusion persists after crystalloid fluid administration, evidenced by either

- systolic blood pressure < 90, or
- mean arterial pressure < 65 or
- a decrease in systolic blood pressure by > 40 points

OR

- Lactate level is > 4 mmol/L

CMS Core Measures for Sepsis

In addition to the severe sepsis elements, core measure requirements for **Septic Shock** include the following:

- within 3 hours of presentation
  - Resuscitation with 30 ml/kg of crystalloid fluids (NS or LR)
- within 6 hours of presentation
  - Vasopressors if hypotension persists after fluid administration
  - Volume status / tissue perfusion assessment

- Assessment consists of either:

  A focused exam including:

  - ✓Vital signs, AND
  - ✓Cardiopulmonary exam, AND
  - ✓Capillary Refill evaluation, AND
  - ✓Peripheral pulse evaluation, AND
  - ✓Skin examination

  OR any 2 of the following:

  - ✓Central venous pressure measurement
  - ✓Central venous oxygen measurement
  - ✓Bedside Cardiovascular Ultrasound
  - ✓Passive Leg Raise or Fluid Challenge

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DOCUMENTATION: PHYSICAL EXAM WITHIN 6 HOURS

CAPILLARY REFILL:

- Capillary refill examination is done to assess superficial circulatory status.
- The assessment of circulatory adequacy may include such terms as “capillary refill,” “capillary fill,” “nail bed refill,” “mottled,” or similar terms.

CARDIOPULMONARY EVALUATION:

- Cardiopulmonary evaluation is done to assess the status of the heart and lungs. The notes must include reference to both the heart and lungs.

  Example:

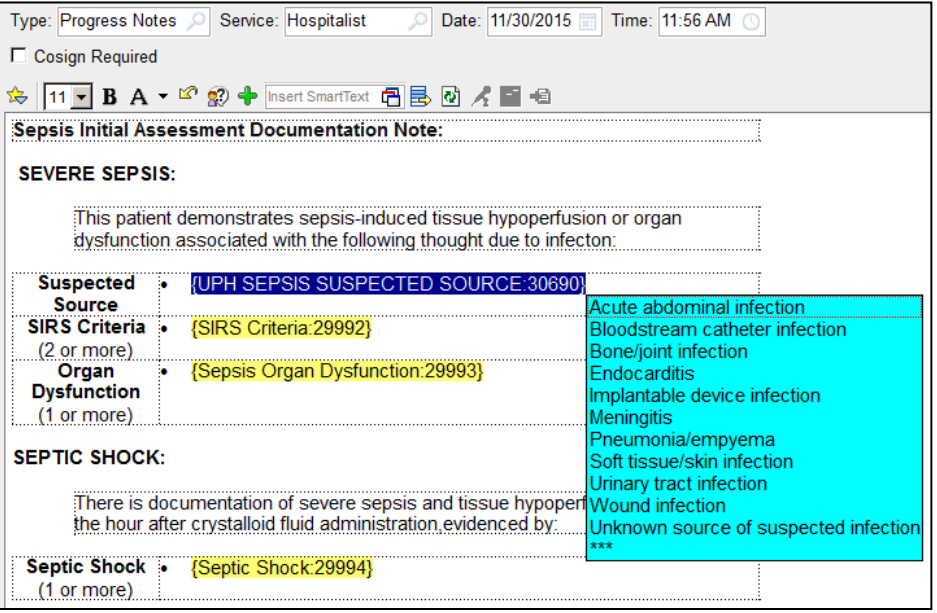
  “Heart: Gallop rhythm noted, lungs crackling at both bases” or “Lungs clear, heart RRR”

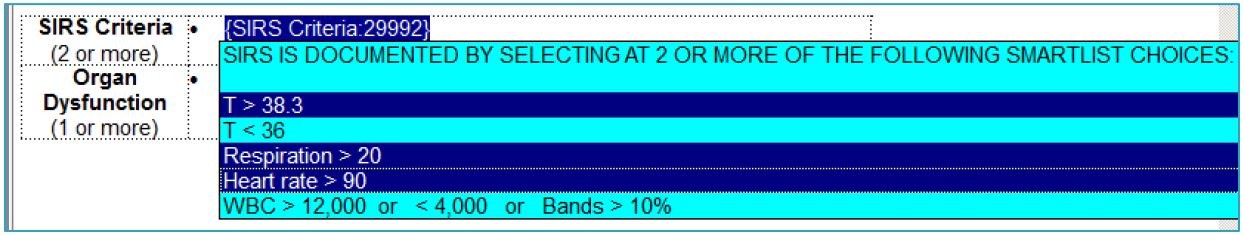
PERIPHERAL PULSE EVALUATION:

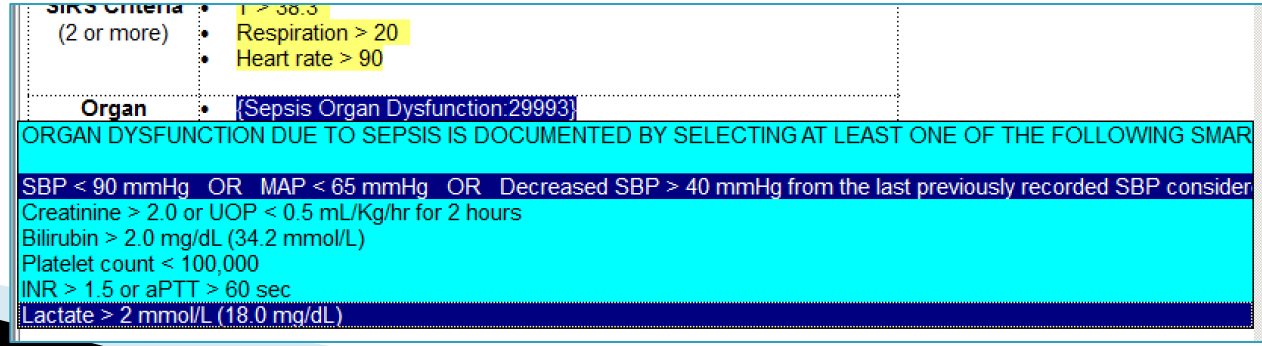
- Peripheral pulse evaluation is done to assess circulatory status and must include reference to either radial pulse, dorsalis pedis (or DP) pulse, or posterior tibialis (or PT) pulse.

SKIN EXAMINATION

- Skin examination is done to assess superficial circulatory status and must include reference to both skin color and circulatory status. These references may include such terms as “nail beds pink with good capillary refill” or “skin over kneecaps purple and mottled.”
- The assessment of skin color may include such terms as “flushed,” “mottled,” “pale,” “pallor,” “pink,” or similar terminology.


Type: Progress Notes
Service: Hospitalist
Date: 11/30/2015
Time: 11:56 AM
Cosign Required
Insert SmartText
Sepsis Initial Assessment Documentation Note:
SEVERE SEPSIS:
This patient demonstrates sepsis-induced tissue hypoperfusion or organ dysfunction associated with the following thought due to infecton:
Suspected Source
{UPH SEPSIS SUSPECTED SOURCE:30690}
SIRS Criteria (2 or more)
{SIRS Criteria:29992}
Organ Dysfunction (1 or more)
{Sepsis Organ Dysfunction:29993}
SEPTIC SHOCK:
There is documentation of severe sepsis and tissue hypoperf
the hour after crystalloid fluid administration,evidenced by:
Septic Shock (1 or more)
{Septic Shock:29994}
Acute abdominal infection
Bloodstream catheter infection
Bone/joint infection
Endocarditis
Implantable device infection
Meningitis
Pneumonia/empyema
Soft tissue/skin infection
Urinary tract infection
Wound infection
Unknown source of suspected infection
***


SIRS Criteria (2 or more)
{SIRS Criteria:29992}
Organ Dysfunction (1 or more)
SIRS IS DOCUMENTED BY SELECTING AT 2 OR MORE OF THE FOLLOWING SMARTLIST CHOICES:
T > 38.3
T < 36
Respiration > 20
Heart rate > 90
WBC > 12,000 or < 4,000 or Bands > 10%


(2 or more)
Respiration > 20
Heart rate > 90
Organ
{Sepsis Organ Dysfunction:29993}
ORGAN DYSFUNCTION DUE TO SEPSIS IS DOCUMENTED BY SELECTING AT LEAST ONE OF THE FOLLOWING SMAR
SBP < 90 mmHg OR MAP < 65 mmHg OR Decreased SBP > 40 mmHg from the last previously recorded SBP consider
Creatinine > 2.0 or UOP < 0.5 mL/Kg/hr for 2 hours
Bilirubin > 2.0 mg/dL (34.2 mmol/L)
Platelet count < 100,000
INR > 1.5 or aPTT > 60 sec
Lactate > 2 mmol/L (18.0 mg/dL)

There are 2 time clocks with this measure.

- Severe Sepsis: 3 hour and 6 hour Counters
- Septic Shock: 3 and 6 Hour Counters

Severe Sepsis Time Clock

- Received within 3 hours of presentation:
  - Initial Lactate Level Measurement
  - Broad Spectrum Antibiotics administered
  - Blood cultures drawn prior to antibiotics
- Within 6 hours of presentation:
  - Repeat lactate level *only if* initial lactate level is elevated.

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Septic Shock Time Clock

- Received within 3 hours of presentation:
  - Resuscitation with 30 ml/kg crystalloid fluids
- Only IF hypotension persist after fluids, received within 6 hours of presentation:
  - Vasopressors
  - Repeat volume status and tissue perfusion assessment