Sepsis Guidelines

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Thank you!!!!

SEPSIS

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Institute of Medicine: Six Aims for Improvement

- **Safe:** “First, do no harm”. Avoid injuries to patients from the care that is intended to help them.
- **Effective:** Provide services based on scientific knowledge to all who could benefit and refrain from providing services to those not likely to benefit (avoiding underuse and overuse).
- **Patient-centered:** Provide care that is respectful and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions.
- **Timely:** Reduce wait and harmful delay for both those who receive and those who give care.
- **Efficient:** Avoid waste, in particular waste of equipment, supplies, ideas, and energy.
- **Equitable:** Provide care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographical location, and socioeconomic status.

IoM; Crossing the Quality Chasm: A New Health System for the 21st Century, 2001

What is quality?

- Quality is appropriateness (providing the right treatments at the right times) with successful outcomes plus excellent service (treating patients with respect and dignity, keeping them informed, etc.) from which unnecessary, wasteful steps and processes have been eliminated.

G. Kaplan, CEO, Quality care begins with appropriate care. Virginia Mason Health Systems, Chair, IHI, 24th July 2013

The effect of practice variation on quality and cost

- Wide variations in practice patterns have implications for quality of care.
- Inappropriate hospitalization and medical treatments or surgical procedures clearly represent poor quality of medical care.
- Variation in the way a treatment is applied may also affect quality.

James & Stephenson, Clinical Practice Improvement 1994

Initiatives to reduce variation and generate valid information

Three major initiatives are now under way to address the interrelated problems of practice variation, cost, and medical outcomes:

- Outcomes management
- Practice guidelines
- Traditional clinical research

Definition of Guidelines

- "Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (Institute of Medicine, 1990).
- They define the role of specific diagnostic and treatment modalities in the diagnosis and management of patients.
- The statements contain recommendations that are based on evidence from a rigorous systematic review and synthesis of the published medical literature.

www.nhlbi.nih.gov/guidelines

Purpose of Guidelines

- The purpose of guidelines is to help clinicians and patients make appropriate decisions about health care. Guidelines attempt to do this by:
  - Describing a range of generally accepted approaches for the diagnosis, management, or prevention of specific diseases or conditions.
  - Defining practices that meet the needs of most patients in most circumstances.
- The recommendations are not fixed protocols that must be followed. Responsible clinician's judgment on the management of patients remains paramount. Clinicians and patients need to develop individual treatment plans that are tailored to the specific needs and circumstances of the patient.

www.nhlbi.nih.gov/guidelines

Definition of a Bundle

- A small set of evidence-based interventions for a defined patient segment/population and care setting that, when implemented together, will result in significantly better outcomes than when implemented individually.

Using Care Bundles to Improve Health Care Quality, 2012 www.ihi.org

Bundle Design

- The bundle has three to five interventions (elements), with strong clinician agreement.
- Each bundle element is relatively independent.
- The bundle is used with a defined patient population in one location.
- The multidisciplinary care team develops the bundle.
- Bundle elements should be descriptive rather than prescriptive, to allow for local customization and appropriate clinical judgment.
- Compliance with bundles is measured using all-or-none measurement, with a goal of 95 percent or greater.

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Severe Sepsis and Septic Shock

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N Engl J Med 2013;369:840-51.
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SEPSIS IS ONE OF THE OLDEST AND MOST ELUSIVE SYNDROMES IN MEDICINE. Hippocrates claimed that sepsis (´) was the process by which flesh rots, swamps generate foul airs, and wounds fester.[1] Galen later considered sepsis a laudable event, necessary for wound healing.[2] With the confirmation of germ theory by Semmelweis, Pasteur, and others, sepsis was recast as a systemic infection, often described as "blood poisoning," and assumed to be the result of the host's invasion by pathogenic organisms that then spread in the bloodstream. However, with the advent of modern antibiotics, germ theory did not fully explain the pathogenesis of sepsis: many patients with sepsis died despite successful eradication of the inciting pathogen. Thus, researchers suggested that it was the host, not the germ, that drove the pathogenesis of sepsis.[3]

In 1992, an international consensus panel defined sepsis as a systemic inflammatory response to infection, noting that sepsis could arise in response to multiple infectious causes and that septicemia was neither a necessary condition nor a helpful term.[4] Instead, the panel proposed the term "severe sepsis" to describe instances in which sepsis is complicated by acute organ dysfunction, and they codified "septic shock" as sepsis complicated by either hypotension that is refractory to fluid resuscitation or by hyperlactatemia. In 2003, a second consensus panel endorsed most of these concepts, with the caveat that signs of a systemic inflammatory response, such as tachycardia or an elevated white-cell count, occur in many infectious and noninfectious conditions and therefore are not helpful in distinguishing sepsis from other conditions.[5] Thus, "severe sepsis" and "sepsis" are sometimes used interchangeably to describe the syndrome of infection complicated by acute organ dysfunction.

INCIDENCE AND CAUSES

The incidence of severe sepsis depends on how acute organ dysfunction is defined and on whether that dysfunction is attributed to an underlying infection. Organ dysfunction is often defined by the provision of supportive therapy (e.g., mechanical ventilation), and epidemiologic studies thus count the "treated incidence" rather than the actual incidence. In the United States, severe sepsis is recorded in 2% of patients admitted to the hospital. Of these patients, half are treated in the intensive care unit (ICU), representing 10% of all ICU admissions.[6,7] The number of cases in the United States exceeds 750,000 per year[7] and was recently reported to be rising.[8] However, several factors — new *International Classification of Diseases, 9th Revision* (ICD-9) coding rules, confusion over the distinction between septicemia and severe sepsis, the increasing capacity to provide intensive care, and increased awareness and surveillance — confound the interpretation of temporal trends.

Studies from other high-income countries show similar rates of sepsis in the ICU.[9] The incidence of severe sepsis outside modern ICUs, especially in parts of

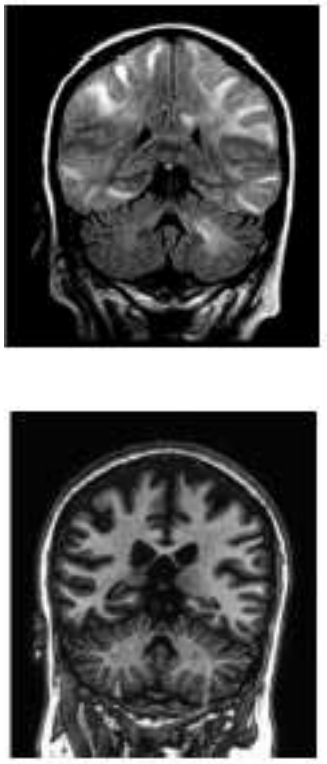
Incidence and Outcomes of Severe Sepsis

- Incidence
  - 2% of patients admitted to the hospital in the USA
  - 10% of all ICU admissions
  - 750000/year in the USA
  - Estimated up to 19 million cases worldwide/year (extrapolating the rates in the USA)
- Outcomes
  - Mortality 20-30%
  - Increased risk for death after hospital discharge
  - Impaired physical and neurocognitive functioning, mood disorders, and low quality of life.

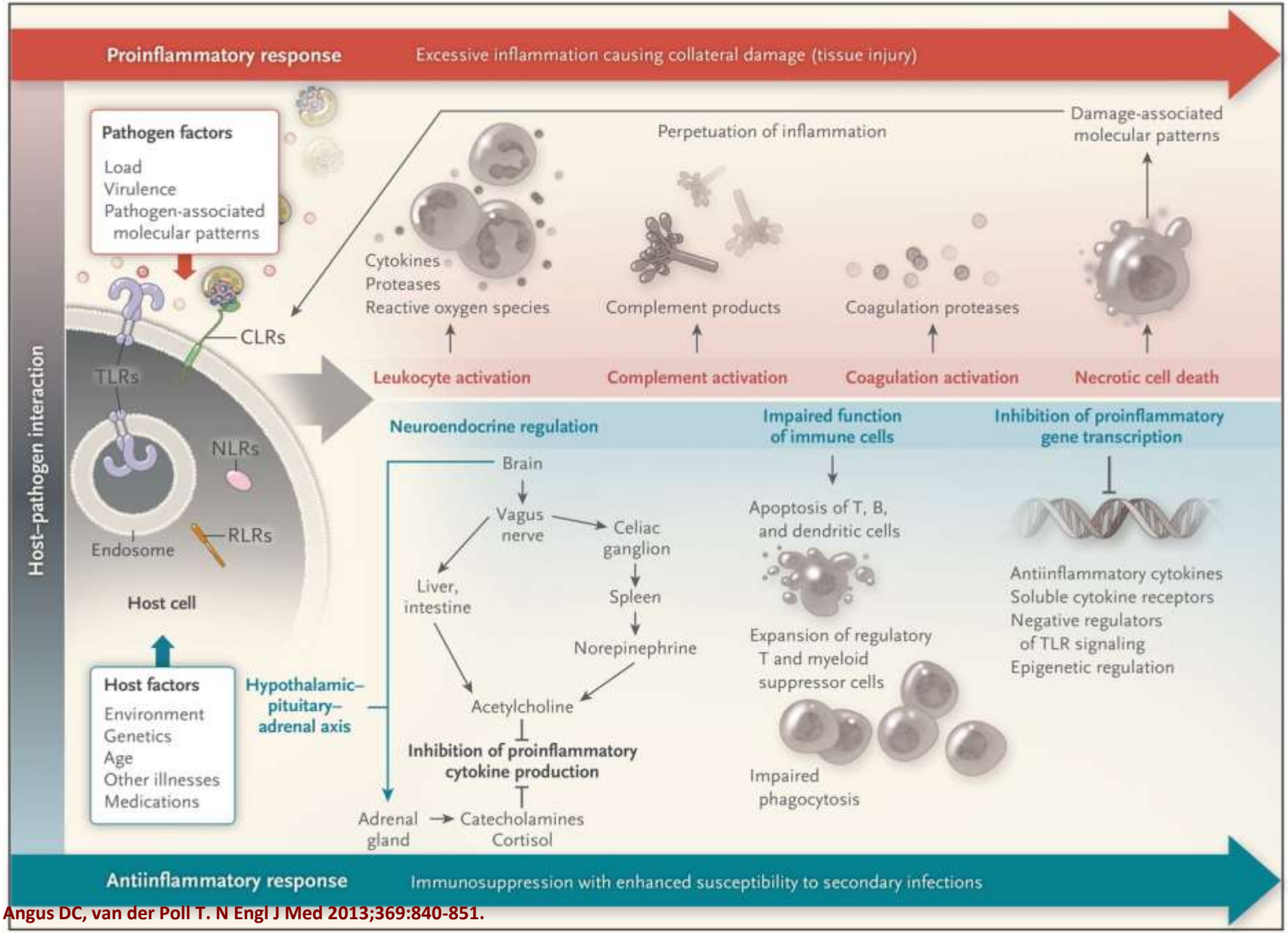
Angus DC, van der Poll T. N Engl J Med 2013;369:840-851.

IMPACT

- High mortality
- Economical impact
- Low quality of life after discharge
  - Functional and cognitive dysfunction
    - Long term cognitive dysfunction in more than 50% of sepsis survivors

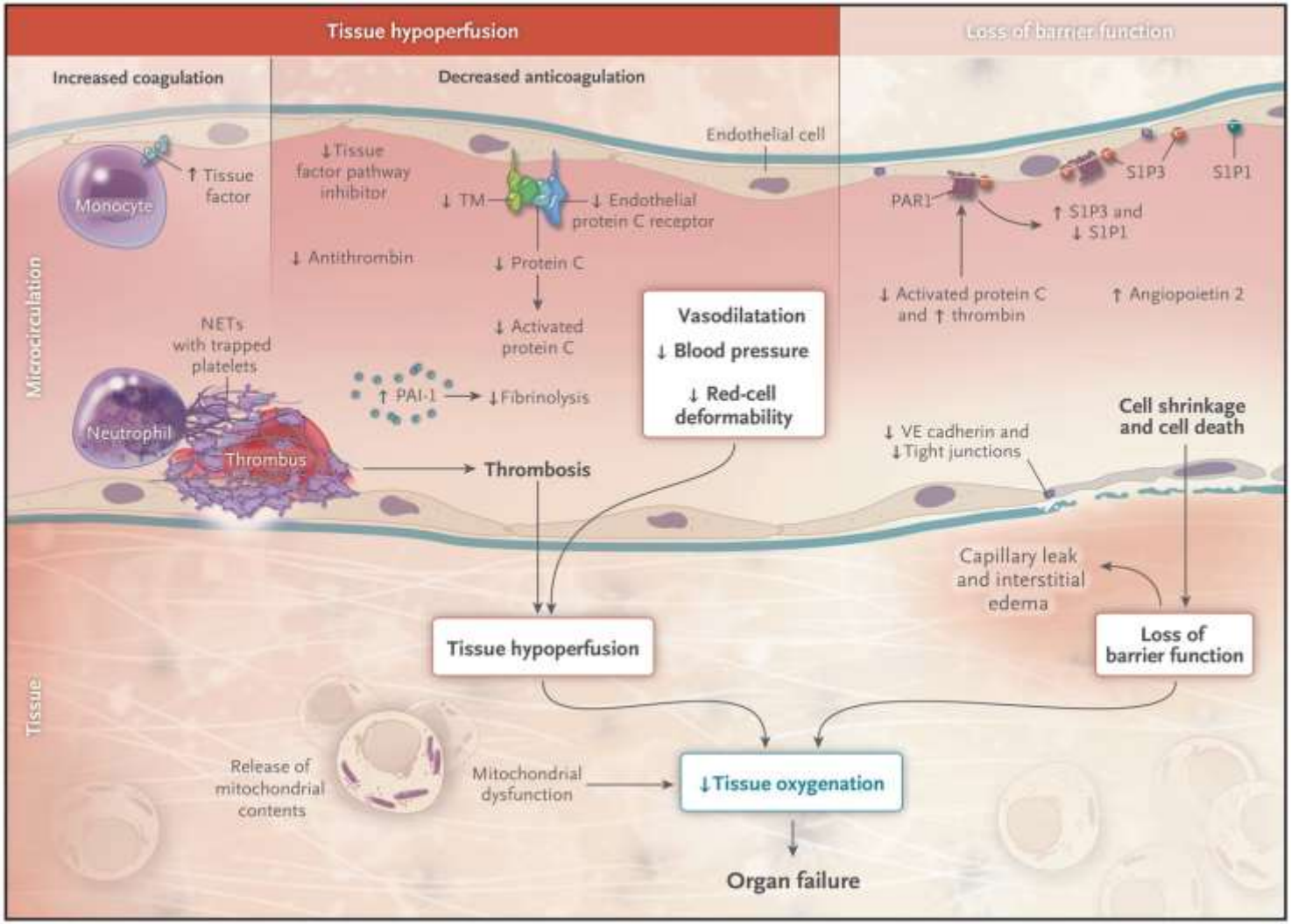


The Host Response in Severe Sepsis



Angus DC, van der Poll T. N Engl J Med 2013;369:840-851.

Organ Failure in Severe Sepsis and Dysfunction of the Vascular Endothelium and Mitochondria



Angus DC, van der Poll T. N Engl J Med 2013;369:840-851.

Table 1. Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.*

Sepsis (documented or suspected infection plus ≥1 of the following)†
General variables
Fever (core temperature, >38.3°C)
Hypothermia (core temperature, <36°C)
Elevated heart rate (>90 beats per min or >2 SD above the upper limit of the normal range for age)
Tachypnea
Altered mental status
Substantial edema or positive fluid balance (>20 ml/kg of body weight over a 24-hr period)
Hyperglycemia (plasma glucose, >120 mg/dl [6.7 mmol/liter]) in the absence of diabetes
Inflammatory variables
Leukocytosis (white-cell count, >12,000/mm^3)
Leukopenia (white-cell count, <4000/mm^3)
Normal white-cell count with >10% immature forms
Elevated plasma C-reactive protein (>2 SD above the upper limit of the normal range)
Elevated plasma procalcitonin (>2 SD above the upper limit of the normal range)
Hemodynamic variables
Arterial hypotension (systolic pressure, <90 mm Hg; mean arterial pressure, <70 mm Hg; or decrease in systolic pressure of >40 mm Hg in adults or to >2 SD below the lower limit of the normal range for age)
Elevated mixed venous oxygen saturation (>70%)‡
Elevated cardiac index (>3.5 liters/min/square meter of body-surface area)§
Organ-dysfunction variables
Arterial hypoxemia (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, <300)
Acute oliguria (urine output, <0.5 ml/kg/hr or 45 ml/hr for at least 2 hr)
Increase in creatinine level of >0.5 mg/dl (>44 μmol/liter)
Coagulation abnormalities (international normalized ratio, >1.5; or activated partial-thromboplastin time, >60 sec)
Paralytic ileus (absence of bowel sounds)
Thrombocytopenia (platelet count, <100,000/mm^3)
Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 μmol/liter])
Tissue-perfusion variables
Hyperlactatemia (lactate, >1 mmol/liter)
Decreased capillary refill or mottling
Severe sepsis (sepsis plus organ dysfunction)
Septic shock (sepsis plus either hypotension [refractory to intravenous fluids] or hyperlactatemia)¶

* Data are adapted from Levy et al.[3]

† In children, diagnostic criteria for sepsis are signs and symptoms of inflammation plus infection with hyperthermia or hypothermia (rectal temperature, >38.5°C or <35°C, respectively), tachycardia (may be absent with hypothermia), and at least one of the following indications of altered organ function: altered mental status, hypoxemia, increased serum lactate level, or bounding pulses.

‡ A mixed venous oxygen saturation level of more than 70% is normal in newborns and children (pediatric range, 75 to 80%).

§ A cardiac index ranging from 3.5 to 5.5 liters per minute per square meter is normal in children.

¶ Refractory hypotension is either persistent hypotension or a requirement for vasopressors after the administration of an intravenous fluid bolus.

Angus DC, van der Poll T. N Engl J Med 2013;369:840-851.

DEFINITIONS

Heart rate > 90/min

Respiratory rate >20/min or pCO2 <32%

Body temperature >38° C or <36° C

White blood cell> 12,000/mm^3 or < 4,000/mm^3 or >10%band

Suspected or confirmed infection

Organ dysfunction

Hypotension refractory to fluid resuscitation

DEFINITIONS

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

Suspected or confirmed infection

Organ dysfunction

Hypotension refractory to fluid resuscitation

DEFINITIONS

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

SEPSIS

Organ dysfunction

Hypotension refractory to fluid resuscitation

DEFINITIONS

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

SEPSIS

SEVERE SEPSIS

Hypotension refractory to fluid resuscitation

DEFINITIONS

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

SEPSIS

SEVERE SEPSIS

SEPTIC SHOCK

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
Sepsis-induced hypotension
Lactate above upper limits laboratory normal
Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
Acute lung injury with Pao_2/Fio_2 < 250 in the absence of pneumonia as infection source
Acute lung injury with Pao_2/Fio_2 < 200 in the presence of pneumonia as infection source
Creatinine > 2.0 mg/dL (176.8 μmol/L)
Bilirubin > 2 mg/dL (34.2 μmol/L)
Platelet count < 100,000 μL
Coagulopathy (international normalized ratio > 1.5)

Adapted from Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003; 31: 1250–1256.

Hypoperfusion

Hypotension that is refractory to first trial of fluid challange

Blood lactate concentration > 4 mmol/L

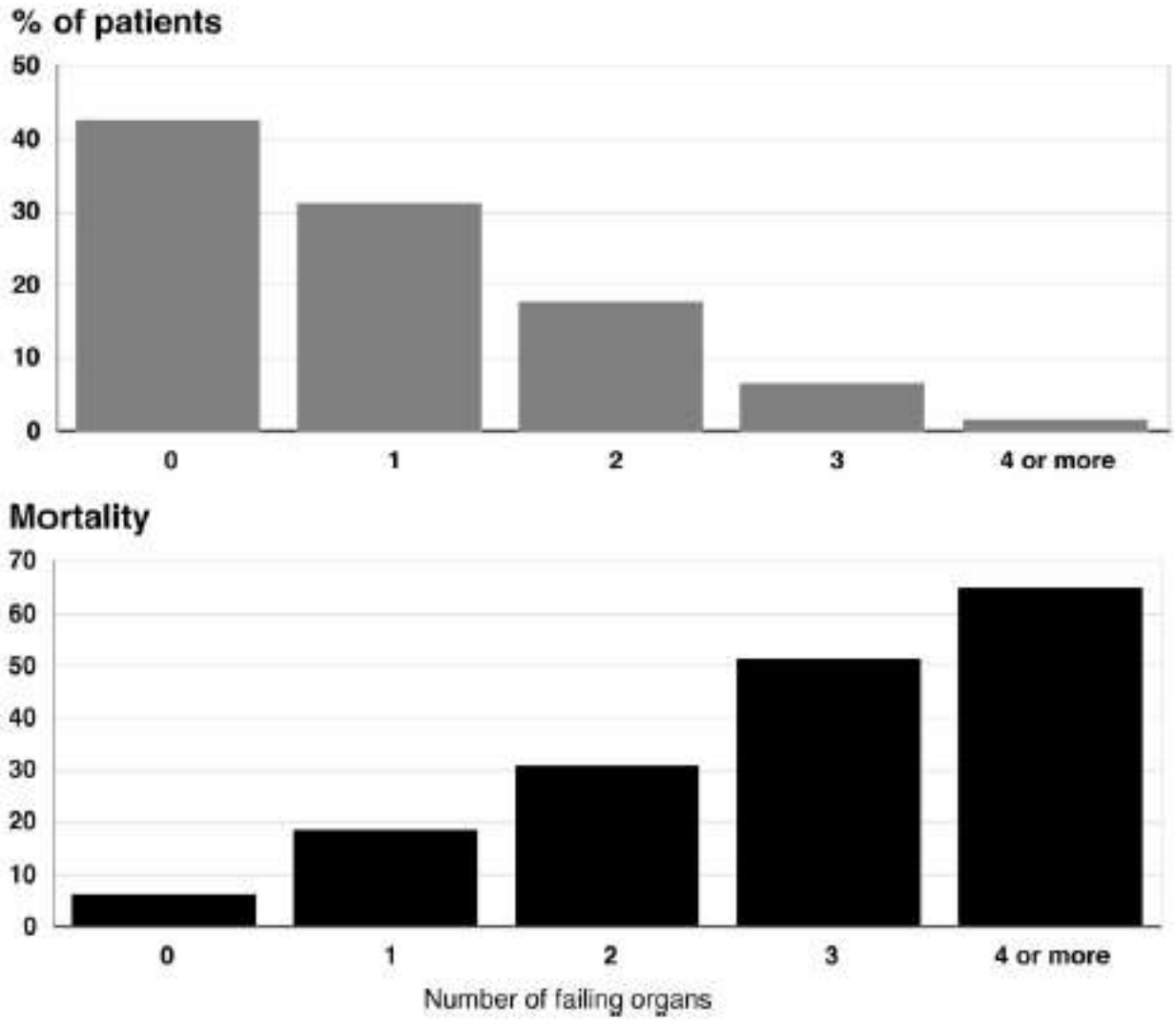


Figure 3. Frequency of organ failure on admission and corresponding intensive care unit mortality.

Vincent JL et al. SOAP. Crit Care Med 2006;34:344-353

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

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Objective: To provide an update to the "Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock," last published in 2008.

Design: A consensus committee of 68 international experts representing 30 international organizations was convened. Nominal groups were assembled at key international meetings (for those committee members attending the conference). A formal conflict of interest policy was developed at the onset of the process and enforced throughout. The entire guidelines process was conducted independent of any industry funding. A stand-alone meeting was held for all subgroup heads, co- and vice-chairs, and selected individuals. Teleconferences and electronic-based discussion among subgroups and among the entire committee served as an integral part of the development.

Methods: The authors were advised to follow the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to guide assessment of quality of evidence from high (A) to very low (D) and to determine the strength of recommendations as strong (1) or weak (2). The potential drawbacks of making strong recommendations in the presence of low-quality evidence were emphasized. Some recommendations were ungraded (UG). Recommendations were classified into three groups: 1) those directly targeting severe sepsis; 2) those targeting general care of the critically ill patient and considered high priority in severe sepsis; and 3) pediatric considerations.

Results: Key recommendations and suggestions, listed by category, include: early quantitative resuscitation of the septic patient during the first 6 hrs after recognition (1C); blood cultures

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* Members of the 2012 SSC Guidelines Committee and Pediatric Subgroup are listed in **Appendix A** at the end of this article.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this on the journal's Web site (http://journals.lww.com/ccmjournal).

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CRITICAL HOURS

- **Pathophysiological changes:**
  - **Hypovolemia**
  - **Vasoplegia**
  - **Cardiac dysfunction**

"Golden window"

Aim is to improve the circulation and tissue perfusion as soon as possible

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

Crit Care Med 2013; 41:580–637

Goal-directed therapy-2012

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 ≥4mmol/L

TO BE COMPLETED WITHIN 6 HOURS:

5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation ($Scvo_2$)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, $Scvo_2$ of ≥70%, and normalization of lactate.

Initial resuscitation

- Quantitative resuscitation
  - Central venous pressure 8-12 mmHg (up to 15 if ventilated)
  - Mean arterial pressure ≥ 65 mmHg
  - Urinary output ≥ 0.5 mL/kg/hr
  - Central venous O_2 sat 70%

    Mixed venous O_2 sat 65% (1C)
- The aim should be to decrease the lactate level if elevated at the beginning

Crit Care Med 2013; 41:580–637

Diagnosis

- Cultures should be obtained before antibiotic treatment (if this won't lead to a delay in antibiotic initiation >45 min) (1C)
  - ≥ 2 blood culture set (aerobic and anaerobic)
  - ≥ 1 percutanous blood culture
  - Blood culture from catheters that are present ≥ 48 hours (1C)
- 1,3 beta-D-glucan (2B), mannan, anti-mannan antibody (2C)*
- Appropriate imaging, if safe!

Crit Care Med 2013; 41:580–637

Antimicrobial therapy

- Start within 1 hour
- Broad spectrum, empirically
- Review everyday for de-escalation (1B)
- Low procalcitonin stops empirical therapy (2C)*
- Empirical combicanation therapy for high risk patients (2B)- 3-5 days
- Hard to treat infections for 7-10 day (abscess, immune deficiency) (2C)
- Antiviral treatment (2C)
- Infectious focus control within 12 hours (1C)

Crit Care Med 2013; 41:580–637

Fluid treatment in severe sepsis

- Crystalloids (1B)*
- Don’t use hydoxy ethyl starch- acute kidney injury risk (1B)*
- Use albumine if high volume crystalloid required (2C)*
- Fluid challenge
  - 30 mL/kg* crystalloid should be given before declaring that the patient is refractory to fluid challenge (1C)
  - Always use bolus, don’t infuse
- Continue fluid as long as the peripheral perfusion gets better

Crit Care Med 2013; 41:580–637

Vasopressors

- Aim mean arterial pressure ≥65 mmHg
- First choice norepinephrine (1B)*
  - 0.5-30 µg/min
- Second choice (or in addition) epinephrine (2B)
  - 0.5-1.0 µg/min → 10 µg/min
- Vazopressine 0.03 units/min may be added to norepinephrine

Crit Care Med 2013; 41:580–637

Vasopressors

- Dopamine only in selected patients (in whom there is no risk of tachyarrhythmia) (2C)
- NEVER use low dose dopamine for renal protection (1A)
  - Intermediate dose 5-10 µg/kg/min, high dose > 10 ug/kg/min
- Intraarterial blood pressure monitorization is required if vasopressor given

Crit Care Med 2013; 41:580–637

Inotropic therapy

- If myocardial dysfunction or refractory hypoperfusion (1C)
  - 2.5 µg/kg/min→ 20 µg/kg/min
- Never aim supranormal cardiac output (1B)

Crit Care Med 2013; 41:580–637

Corticosteroids

- Consider if refractory shock despite adequate fluid therapy and vasopressors
  - Hydrocortisone 200 mg/day *(2C)
- ACTH stimulation test not recommended (2B)
- Taper and stop when vasopressors are discontinued*
- Continous infusion over 24 hours *(2D)*

Crit Care Med 2013; 41:580–637

Transfusion

- Aim a hemoglobin level of 7-9 gr/dl, if below 7 gr/dL (1B)

  – In case of significant hypoxemia, myocardial ischemia, acute bleeding, lactic acidosis higher threshold may be set.

Crit Care Med 2013; 41:580–637

Glucose control

- If two subsequent glucose > 180 mg/dL → Aim < 180 mg/dL according to a protocol*(1A)
- Intensive glucose lowering not recommended anymore

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Deep vein thrombosis prophylaxis

- Low molecular weight heparin*
- Dalteparin or unfractionated heparin if creatinine clearance < 30 mL/min (1A)
- Both pharmacological and mechanical treatment when possible (2C)

Crit Care Med 2013; 41:580–637

Stress ulcer prophylaxis

- H2 receptor blocker or proton pump inhibitor* (1B)

Crit Care Med 2013; 41:580–637

Nutrition*

- Oral or enteral nutrition during the first 48 hours (2C)
- Low calorie feeding during the first week (up to 500 cal), increase when tolerated (2B)
- Enteral feeding + iv glucose (2B)
- Don’t use immune modulators (2C)

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Not recommended

- Immunoglobuline (2B)
- Selenium (2C)
- Recombinant activated protein C

Recommended

- Discuss end of life issues and chronic care

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SURVIVING SEPSIS CAMPAIGN BUNDLES

SAINT JOSEPH MERCY HEALTH SYSTEM
A Member of Trinity Health

Initial Resuscitation Bundle

To Be Completed in 3 hours:

1) Measure lactate level
2) Obtain cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30ml/kg crystalloid for hypotension or lactate greater than or equal to 4mmol/kg

Septic Shock Bundle

To be Completed Within 6 Hours:

1) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) greater than or equal to 65mmHg
2) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate greater than or equal to 4mmol/L
   a. Measure central venous pressure (CVP)*
   b. Measure central venous oxygen saturation (ScvO2)*
3) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP greater than or equal to 8mmHg, ScvO2 greater than or equal to 70% and normalization of lactate

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SAINT JOSEPH MERCY HEALTH SYSTEM
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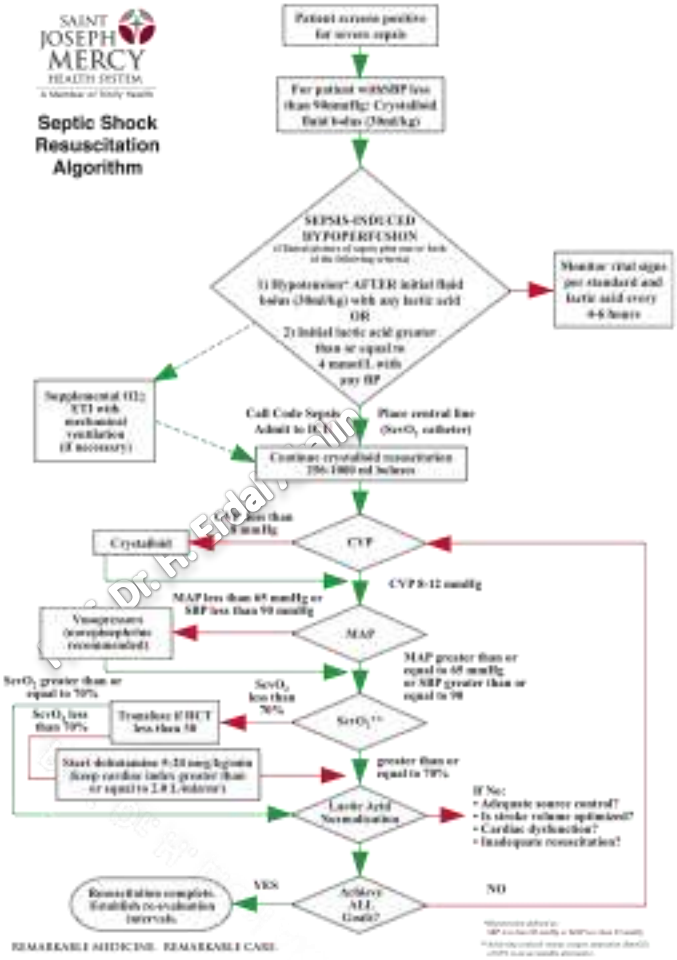
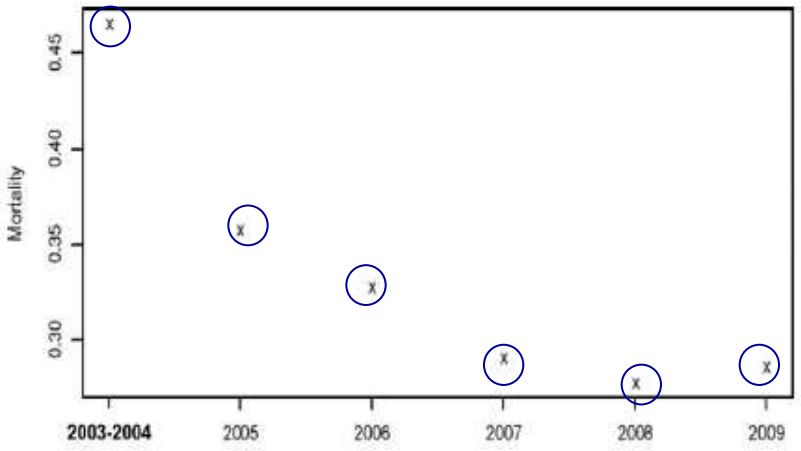
Septic Shock Resuscitation Algorithm



REMARKABLE MEDICINE. REMARKABLE CARE.

GENESIS

- GENeralized Early Sepsis Intervention Strategies
  - Cumulative mortality
  - Organ dysfunction
  - Health resource utilization

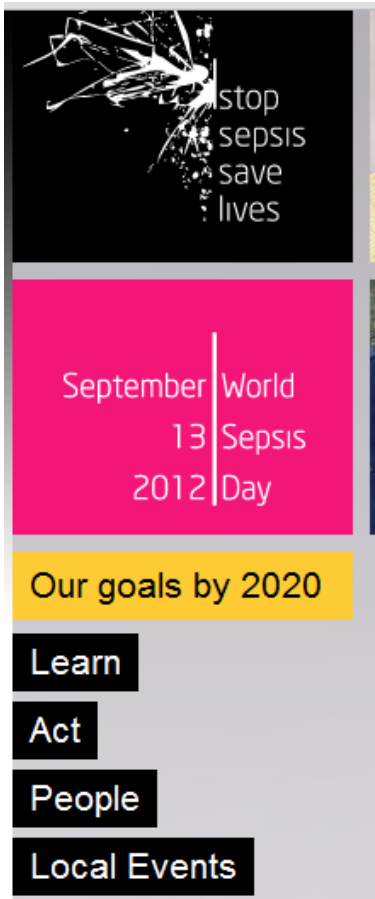


Cannon et al. J Inten Care Med 2012

September 13, 2012 Global Sepsis Alliance–

First World Sepsis Day

- Prevention
- Survival
- Awareness
- Rehabilitation
- Sepsis data bases




stop
sepsis
save
lives

Thank you.