Sistemic bacterial infections

Classical Definition of Sepsis

Focus

↓

Dissemination of bacteria

↓

Systemic response

Schottmüller

Burden of Severe Sepsis in Europe

Up to 340,000 patients with severe sepsis are treated in ICU each year

Up to 148,500 deaths associated with severe sepsis in ICU

(~44% of all patients)

Up to 7.8 billion Euros in ICU costs alone

(~23,000 Euros per patient)

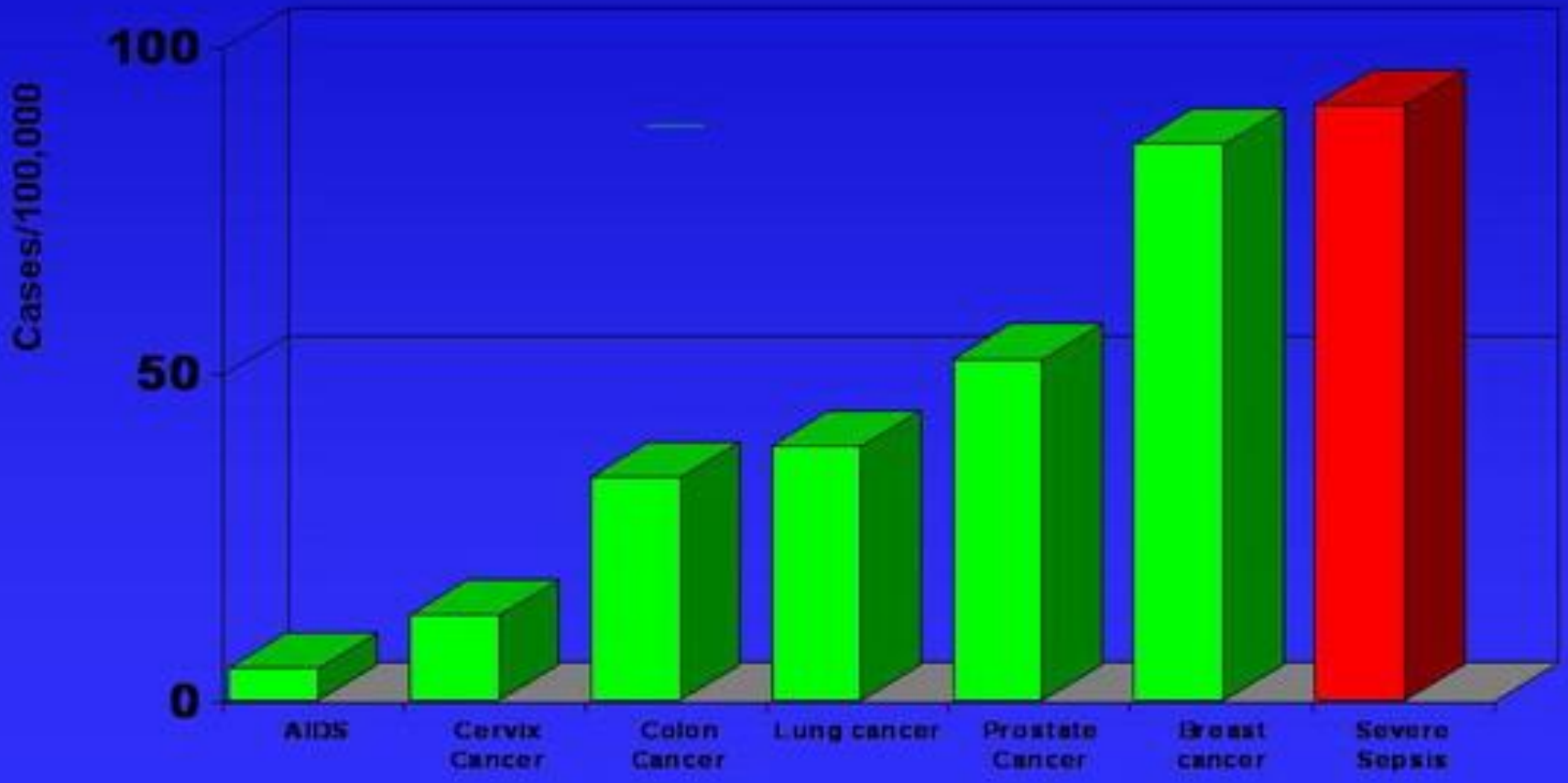
‡Davies A, Intensive Care Medicine 2001; 27 (suppl 2) #581.
Plus updated data in press

- In the United States sepsis is the second-leading cause of death in non-coronary Intensive Care Unit (ICU) patients, and the tenth-most-common cause of death overall according to data from the Centers for Disease Control and Prevention (the first being heart disease).
- Sepsis is common and also more dangerous in elderly, immunocompromised, and critically ill patients. It occurs in 1–2% of all hospitalizations and accounts for as much as 25% of ICU bed utilization. It is a major cause of death in intensive-care units worldwide, with mortality rates that range from 20% for sepsis, through 40% for severe sepsis, to over 60% for septic shock.

SEPSIS

- Each year more than 750.000 people in the US will develop sepsis
  215.000 will die from the condition
- Treating patients with severe sepsis will cost 17 billion dollars a year
- Mortality remains at 28-50 %

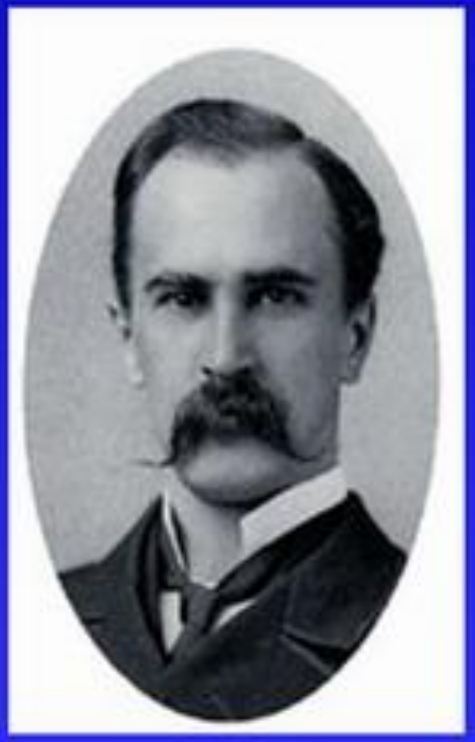
Incidence of Severe Sepsis in the EU



‡ Davies A, Intensive Care Medicine 2001; 27 (suppl 2) #581. OECD HEALTH DATA 2001

- **Sepsis** (/ˈsɛpsɨs/ from *Gr.* σῆψις: the state of putrefaction or decay) is a potentially deadly medical condition that is characterized by a whole-body inflammatory state (called a systemic inflammatory response syndrome or SIRS) and the presence of a known or suspected infection. The body may develop this inflammatory response by the immune system to microbes in the blood, urine, lungs, skin, or other tissues. A lay term for sepsis is **blood poisoning**, also used to describe septicaemia. Severe sepsis is the systemic inflammatory response, plus infection, plus the presence of organ dysfunction.
- **Septicemia** (also **septicaemia** or **septicæmia** [ˌsɛp.tə.ˈsi.miə],) is a related medical term referring to the presence of pathogenic organisms in the bloodstream, leading to sepsis.The term has not been sharply defined. It has been inconsistently used in the past by medical professionals, for example as a synonym of bacteremia, causing some confusion.

- History
- Severe systemic toxicity has been recognised since before the dawn of history but it was only in the 19th century that a spefic term - sepsis- was coined for this condition. By the end of the 19th century, it was widely believed that microbes produced substances that could injure the mammalian host and that soluble toxins released during infection caused the fever and shock that were commonplace during severe infections.
- Pfeiffer coined the term endotoxin at the beginning of the 20th century to denote the pyrogenic principle associated with *Vibrio cholera*. It was soon realised that endotoxins were expressed by most and perhaps all Gram negative organisms.



"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."

Sir William Osler – 1904

The Evolution of Modern Medicine

- **Bacteremia** is the presence of viable bacteria in the bloodstream. Likewise, the terms viremia and fungemia simply refer to viruses and fungi in the bloodstream. These terms say nothing about the consequences this has on the body. For example, bacteria can be introduced into the bloodstream during toothbrushing. This form of bacteremia almost never causes problems in normal individuals. However, bacteremia associated with certain dental procedures can cause bacterial infection of the heart valves (known as endocarditis) in high-risk patients. Conversely, a systemic inflammatory response syndrome can occur in patients without the presence of infection, for example in those with burns, polytrauma, or the initial state in pancreatitis and chemical pneumonitis.

- According to the American College of Chest Physicians and the Society of Critical Care Medicine, there are different levels of sepsis:
- **Systemic inflammatory response syndrome** (SIRS). Defined by the presence of two or more of the following findings:
  - Body temperature< 36 °C (97 °F) or >38 °C (100 °F) (hypothermia or fever).
  - Heart rate > 90 beats per minute.
  - Respiratory rate > 20 breaths per minute or, on blood gas, a $PaCO_2$ less than 32 mm Hg (4.3 kPa) (tachypnea or hypocapnia due to hyperventilation).
  - White blood cell count < 4,000 cells/mm3 or > 12,000 cells/mm3 (< 4 × 109 or > 12 × 109 cells/L), or greater than 10% band forms (immature white blood cells). (leukopenia, leukocytosis, or bandemia).

SEPSIS – CLINICAL MANIFESTATION

- Sepsis is defined as a systemic inflammatory response syndrome (SIRS) resulting from bacterial or fungal infection
- SIRS includes the presence of:
  - Temperature > 38°C or < 36°C
  - Heart rate > 90 beats/min
  - Tachypnea RR > 20 breaths/min
  - Alteration of white blood cell count and/or C-reactive protein
- Severe sepsis – at least one organ dysfunction

SIRS

SIRS is present with any 2 of the following conditions[1]:

- Temperature > 38.0°C or < 36.0°C;
- Heart rate > 90 beats per minute;
- Respiratory rate > 20 breaths per minute:
- Partial pressure of carbon dioxide (PCO2) < 32 mm Hg;
- Leukopenia (WBC count < 4G/l); and
- Normal WBC count with > 10% immature forms.

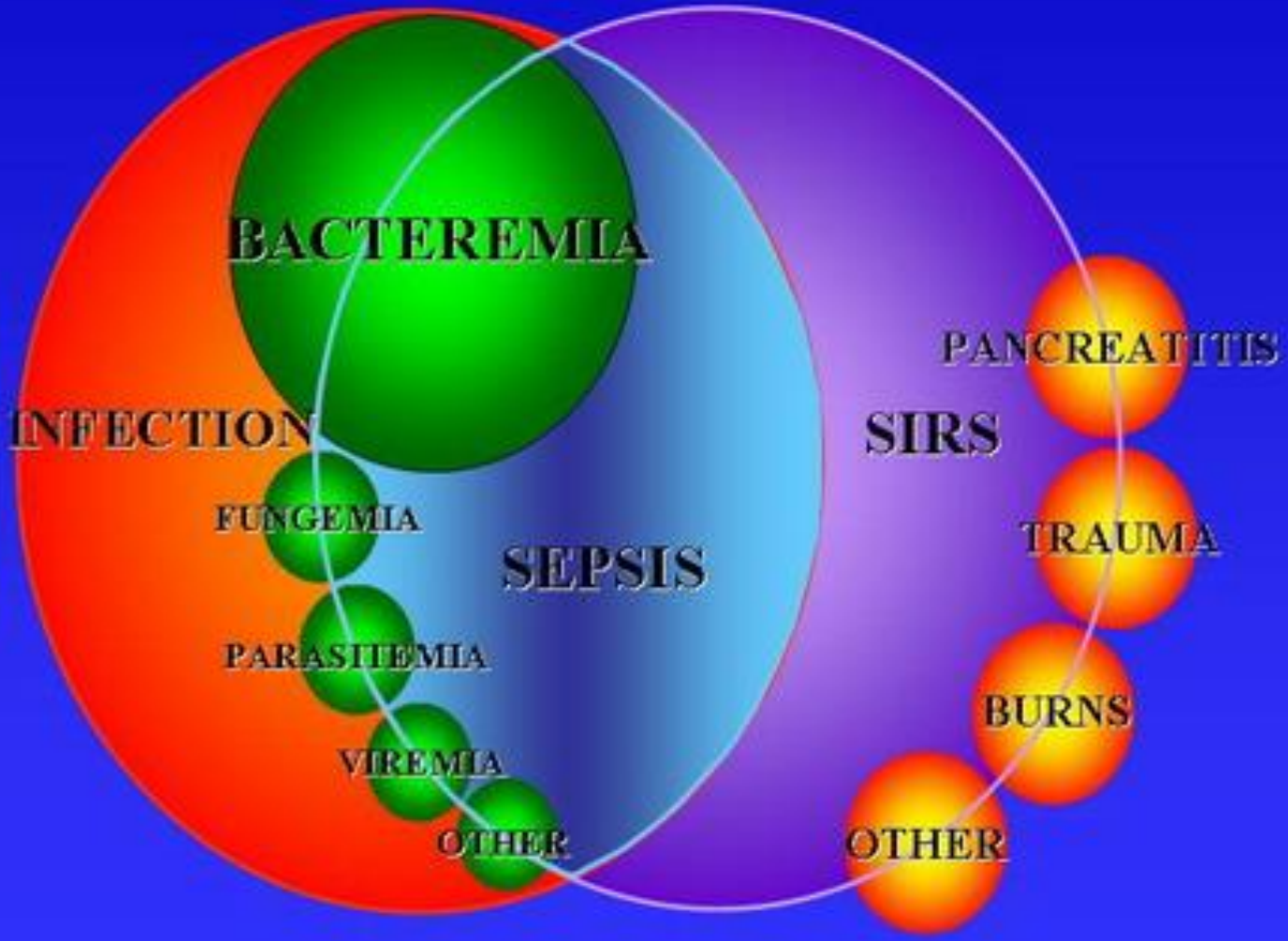
SIRS 2002

- Significant edema or positive fluid balance (>20 mL/kg over 24 hours);
- Hyperglycemia (plasma glucose > 120 mg/dL) in the absence of diabetes;
- Imflammatory variable: plasma C-reactive protein > 2 SD above the normal value or plasma
- Mixed venous oxygen saturation (SVO2) > 70%; and
- Cardiac index > 3.5 L min^{-1} M^{-23}

Sepsis has been defined as infection-induced organ dysfunction or hypoperfusion with 2 or more SIRS Criteria.[1]

In 2002, the definition was broadened to define sepsis as documented or suspected with any of the SIRS criteria or 1 or more of the following[2]:

Relationship Of SIRS, Sepsis, and Infection



The ACCP/SCCM Consensus Conference Committee. *Chest*. 1992;101:1644-1655.

of infection	Pathogens to be covered	Antibiotics
(hospital acquired)	*Pseudomonas aeruginosa*	Cefepime, or ticarcillin–clavulanate
	Enterobacter	Piperacillin–tazobactam, plus aminoglycoside
omen or pelvis	Gram-negative rods	Ticarcillin–clavulanate, or piperacillin–tazobactam, plus aminoglycoside
	Anaerobes	Imipenem, meropenem, or doripenem
ary tract	*Escherichia coli*	Ciprofloxacin
	Klebsiella	Ceftriaxone
	Proteus	
	Staphylococcus aureus	Oxacillin, Vancomycin or ceftaroline
	Streptococcus pyogenes	Ticarcillin–clavulanate
	Mixed aerobic/anaerobic (necrotizing fasciitis)	Piperacillin–tazobactam
		Imipenem, meropenem, or doripenem
remia of unknown source pital acquired)	Methicillin-resistant *S. aureus (MRSA)*	Cefepime, plus vancomycin or ceftarolin
	Gram negative rods	
eremia of unknown source mmunity acquired)	*S. aureus*	Vancomycin, plus ceftriaxone or cefepim
	Strep. pneumoniae	
	E. coli	
	Klebsiella	

- In addition to symptoms related to the provoking infection, sepsis is characterized by presence of acute inflammation present throughout the entire body, and is, therefore, frequently associated with fever and elevated white blood cell count (leukocytosis) or low white blood cell count and lower-than-average temperature.
- The modern concept of sepsis is that the host's immune response to the infection causes most of the symptoms of sepsis, resulting in hemodynamic consequences and damage to organs.
- This host response has been termed systemic inflammatory response syndrome (SIRS) and is characterized by an elevated heart rate (above 90 beats per minute), high respiratory rate (above 20 breaths per minute or a partial pressure of carbon dioxide in the blood of less than 32), abnormal white blood cell count (above 12,000, lower than 4,000, or greater than 10% band forms) and elevated or lowered body temperature, i.e. under 36 °C (97 °F) or over 38 °C (100 °F).
- Sepsis is differentiated from SIRS by the presence of a known or suspected pathogen. For example SIRS and a positive blood culture for a pathogen indicates the presence of sepsis. However, in many cases of sepsis no specific pathogen is identified.

SEVERE SEPSIS

Severe sepsis is defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension.[1] The organ-dysfunction variables include:

- Arterial hypoxemia (PaO2/fraction of inspired oxygen [FiO2] ratio of < 300 torr);
- Acute oliguria (urine output < .5 mL kg^{-1} $hour^{-1}$ or 45 mmol/L for at least hours);
- Creatinine > 2.0 mg/dL;

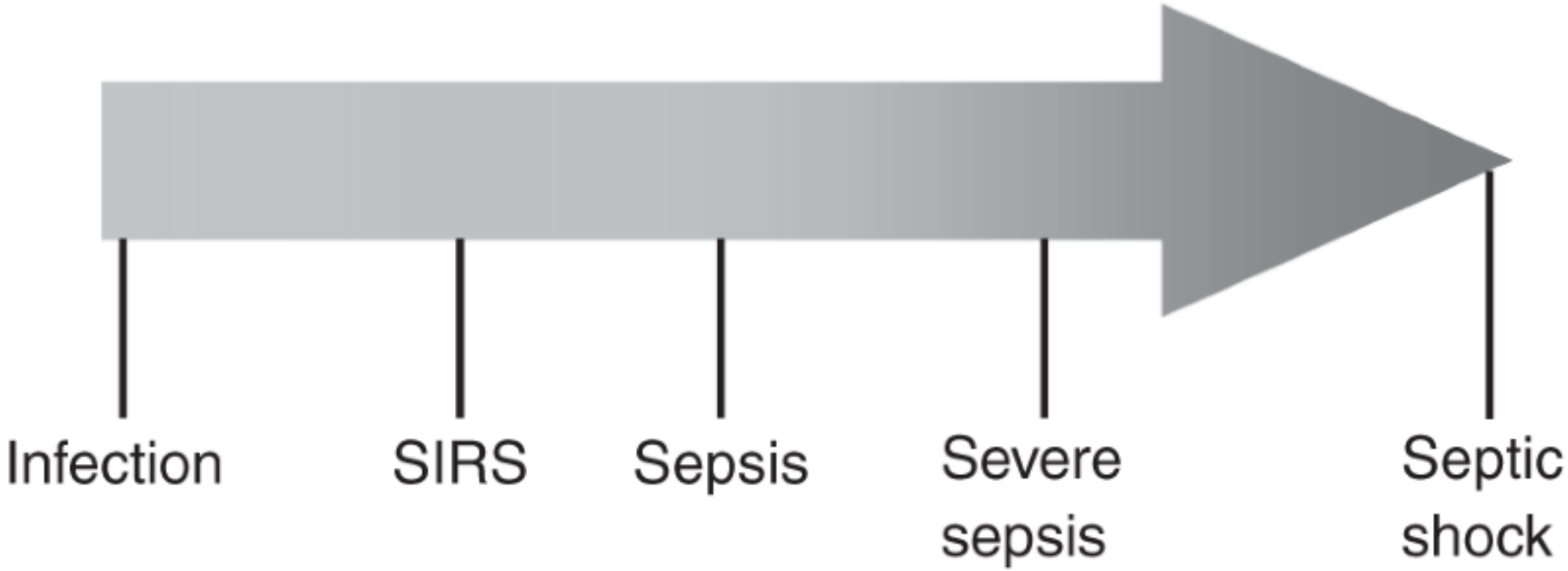
SEVERE SEPSIS

- Coagulation abnormalities (international normalized ratio > 1.5 or activated partial thromboplastin time > 60 seconds);
- Thrombocytopenia (platelet count < 100,000 mcL^{-1});
- Tissue-perfusion variable: hyperlactatemia (> 2 mmol/L); and
- Hemodynamic variable: arterial hypotension, mean arterial pressure [MAP] < 70 mm Hg, or SBP decrease > 40 mmHg).

- **Sepsis**. Defined as SIRS in response to a confirmed infectious process. Infection can be suspected or proven (by culture, stain, or PCR), or a clinical syndrome pathognomonic for infection. Specific evidence for infection includes WBCs in normally sterile fluid (such as urine or cerebrospinal fluid (CSF)); evidence of a perforated viscus (free air on abdominal x-ray or CT scan; signs of acute peritonitis); abnormal chest x-ray (CXR) consistent with pneumonia (with focal opacification); or petechiae,purpura, or purpura fulminans.
- **Severe sepsis**. Defined as sepsis with organ dysfunction, hypoperfusion, or hypotension.

- Examples of end-organ dysfunction include the following:
- Lungs:acute lung injury (ALI) ($PaO_2/FiO_2 < 300$) or acute respiratory distress syndrome (ARDS) ($PaO_2/FiO_2 < 200$)
- Brain: encephalopathy symptoms: agitation, confusion, coma; cause: ischemia, hemorrhage, microthrombi, microabscesses, multifocal necrotizing leukoencephalopathy
- Liver: disruption of protein synthetic function: manifests acutely as progressive coagulopathy due to inability to synthesize clotting factors, disruption of metabolic functions: manifests as cessation of bilirubin metabolism, resulting in elevated unconjugated serum bilirubin levels (indirect bilirubin)
- Kidney: oliguria and anuria, electrolyte abnormalities, volume overload
- Heart: systolic and diastolic heart failure, likely due to cytokines that depress myocyte function, cellular damage, manifest as atroponin leak (although not necessarily ischemic in nature)

- **Septic shock**. Defined as sepsis with refractory arterial hypotension or hypoperfusion abnormalities in spite of adequate fluid resuscitation. Signs of systemic hypoperfusion may be either end-organ dysfunction or serum lactate greater than 4 mmol/L. Other signs include oliguria and altered mental status. Patients are defined as having septic shock if they have sepsis plus hypotension after aggressive fluid resuscitation (typically upwards of 6 liters or 40 ml/kg of crystalloid solution).


Infection
SIRS
Sepsis
Severe sepsis
Septic shock


ICU
STAPH
1991
DEFINITIONS FOR SEPSIS AND ORGAN FAILVRE
2001
INTER-NATIONAL SEPSIS DEFINITIONS CONFERENCE
2016
3RD INTER-NATIONAL CONSENSUS DEFINITIONS FOR SEPSIS AND SEPTIC SHOCK
2:01

Topic

Critical Care Congress 2016

nd AKI After Cardiac Surgery
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efinitions for Sepsis and Septic Shock
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e for Management of High Blood Pressure
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Zika Pandemic (53,215 views)

Current Highlights

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Theme Issue: Critical Care and Sepsis

Special Communication

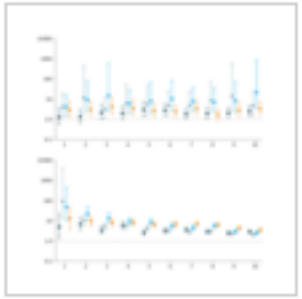
Special Communication | February 22, 2016 FREE

Consensus Definitions for Sepsis and Septic Shock

This article presents updated definitions of and clinical criteria for sepsis and septic shock based on recommendations from an exp force.

Editorial

Research



Original Investigation | February 22, 2016 FREE

Assessment of Clinical Criteria for Sepsis

This cohort study uses health system and research cohort data to the ability of existing vs new clinical criteria for sepsis to identify int unit patients with suspected infection at higher mortality risk.

Original Investigation | February 22, 2016 FREE

New Definition and Criteria for Septic Shock

This article describes the results of a meta-analysis of criteria use

CTION

CHANGE IN:

SEPSIS-RELATED
ORGAN
FAILURE
ASSESSMENT

FiO_2

HYPOTENSION OR VASOPRESSORS

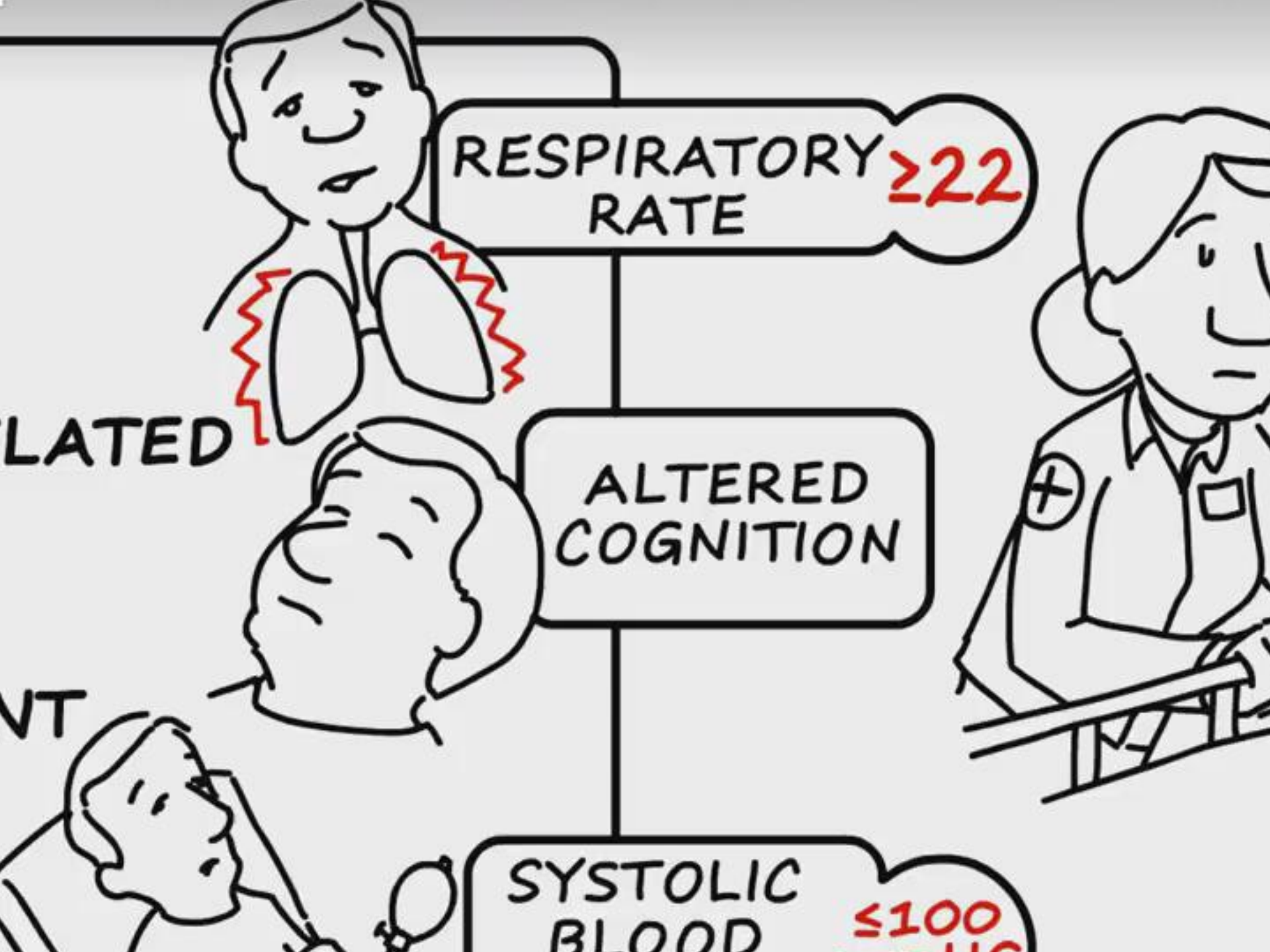
GOW
A SCALE

BILIRUBIN

Scorul SOFA

Calcul du score SOFA	0 point	1 point	2 points	3 points	4 points
PaO_2/FiO_2	>400	301-400	201-300	101-200 et VA	≤ 100 et VA
Plaquettes $x10^3/mm^3$	>150	101-150	51-100	21-50	≤20
Bilirubine, mg/L (mmol/L)	<12 (<20)	12-19 (20-32)	20-59 (33-101)	60-119 (102-204)	>120 (>204)
Hypotension	PAM ≥70mmHG	PAM < 70mmHG	Dopamine ≤ 5 ou dobutamine (toute dose)	Dopa > 5 ou adrénaline ≤ 0,1 ou noradré ≤ 0,1	Dopamine > 15 ou adré > 0,1 ou noradré > 0,1
Score de Glasgow	15	13-14	10-12	6-9	<6
Créatinine, mg/L (µmol/L) ou diurèse	<12 (<110)	12-19 (110-170)	20-34 (171-299)	35-49 (300-440) ou <500mL/j	>50 (>440) ou <200mL/j

VA : ventilation assistée. PAM : pression artérielle moyenne [estimée par (PAS + 2 x PAD) / 3]. Amines : dose en γ/kg/mn


RESPIRATORY RATE ≥22
LATED
ALTERED COGNITION
NT
SYSTOLIC BLOOD ≤100

SEPTIC SHOCK

EPSIS

+

VASOPRESSO
TO MAINTAIN
≥65 mmHG

AND

SERUM LACTA
LEVEL
≥18 mg/dL

Sepsis: Defining a Disease Continuum

Infection or Trauma → SIRS → **Sepsis** → **Severe Sepsis**

Sepsis with ≥ 1 sign of organ dysfunction, for example:

- Cardiovascular (refractory hypotension)
- Renal
- Respiratory
- Hepatic
- Hematologic
- CNS
- Unexplained metabolic acidosis

→ **Shock**

Adapted from Bone et al. *Chest.* 1992;101:1644; Wheeler and Bernard. *N Engl J Med.* 1999;340:207.

SIGNS AND TEST OF SEPSIS

- Blood gases revealing low oxygen concentrations and acidosis
- Low blood pressure
- Blood tests detecting poor organ function and organ failure
- Blood cultures

IDENTIFYING AT – RISK PATIENTS

- ICU patients receiving anti-infectives
- Severe CAP
- Intra-abdominal surgery
- Meningitis
- Chronic diseases
- Compromised immune states
- Cellulites
- Urinary tract infections

Pseudosepsis – Conditions that mimic the clinical and hemodynamic parameters of sepsis

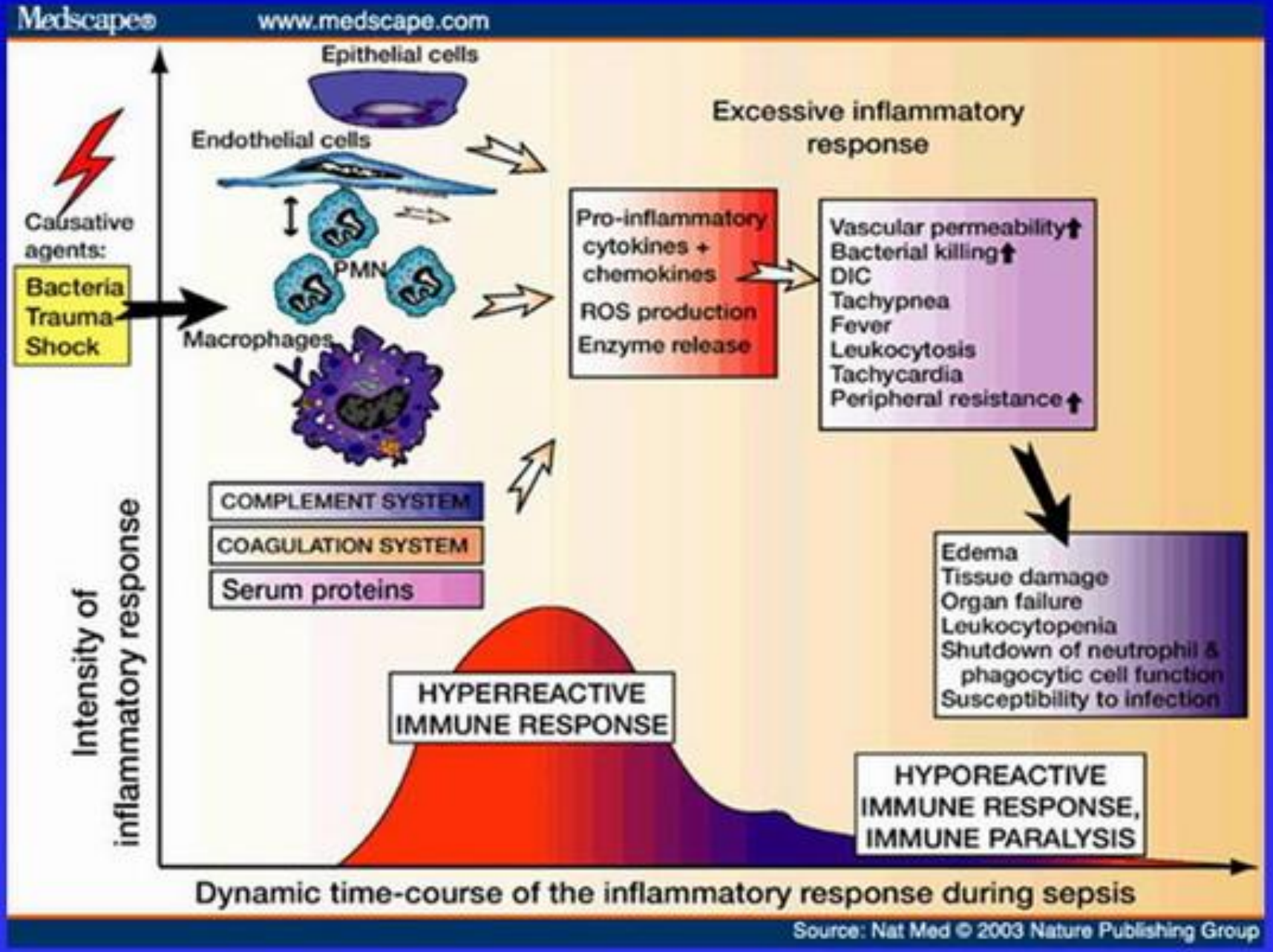
- Gastrointestinal hemorrhage
- Pulmonary embolism
- Acute myocarolial infarction
- Acute pancrealitis
- Diuretic induced hypovolemia
- Relative adrenal insufficency
- Anaphylaxis

SEPSIS PATHOPHYSIOLOGY

- Severe sepsis results from the body's systemic over-response to infection
- Deranged microcirculatory function results in organ failure
- Anti-infectives, resuscitation and supportive care do not necessarily prevent the progressive organ dysfunctive

- This immunological response causes widespread activation of acute-phase proteins, affecting the complement system and the coagulation pathways, which then cause damage to the vasculature as well as to the organs. Various neuroendocrine counter-regulatory systems are then activated as well, often compounding the problem. Even with immediate and aggressive treatment, this may progress to multiple organ dysfunction syndrome and eventually death.

- Pathophysiology
- Systemic inflammatory response syndrome or SIRS is evidence of the body's ongoing inflammatory response. When SIRS is suspected or known to be caused by an infection, this is sepsis. Severe sepsis occurs when sepsis leads to organ dysfunction, such as trouble breathing, coagulation or other blood abnormalities, decreased urine production, or altered mental status. If the organ dysfunction of severe sepsis is low blood pressure (hypotension), or insufficient blood flow (hypoperfusion) to one or more organs (causing, for example,lactic acidosis), this is septic shock.
- Sepsis can lead to multiple organ dysfunction syndrome (MODS) (formerly known as multiple organ failure), and death. Organ dysfunction results from local changes in blood flow, from sepsis-induced hypotension (< 90 mmHg or a reduction of ≥ 40 mmHg from baseline) and from diffuse intravascular coagulation, among other things.
- Sepsis can be defined as the body's response to an infection. An infection is caused by microorganisms or bacteria invading the body and can be limited to a particular body region or can be widespread in the bloodstream. Sepsis is acquired quickest with infections developed in surgery and physical contact with someone with sepsis.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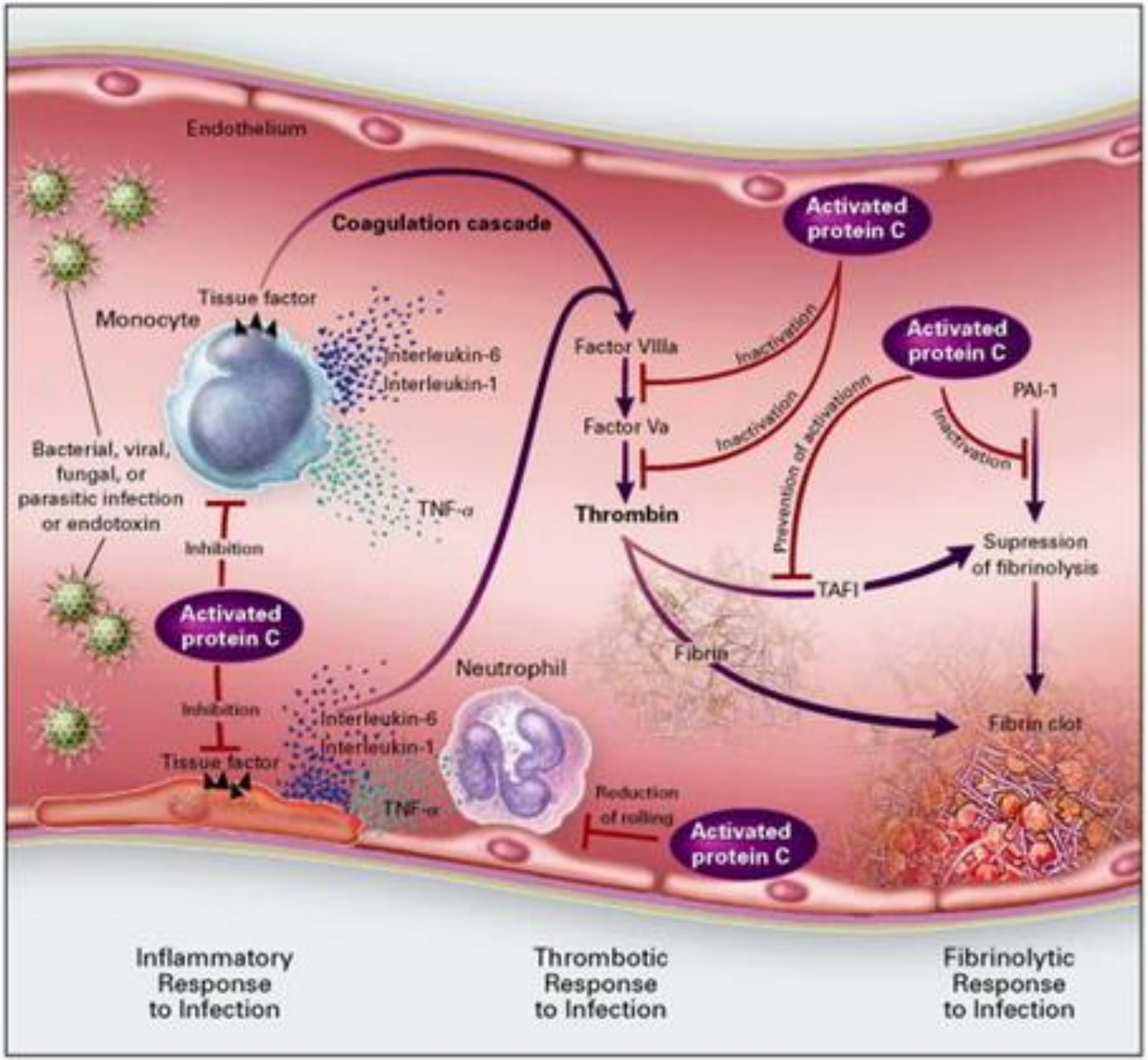
Pro-inflammatory cytokines + chemokines
ROS production
Enzyme release
Vascular permeability↑
Bacterial killing↑
DIC
Tachypnea
Fever
Leukocytosis
Tachycardia
Peripheral resistance↑
COMPLEMENT SYSTEM
COAGULATION SYSTEM
Serum proteins
Edema
Tissue damage
Organ failure
Leukocytopenia
Shutdown of neutrophil & phagocytic cell function
Susceptibility to infection
HYPERREACTIVE IMMUNE RESPONSE
HYPOREACTIVE IMMUNE RESPONSE, IMMUNE PARALYSIS
Intensity of inflammatory response
Dynamic time-course of the inflammatory response during sepsis
Source: Nat Med © 2003 Nature Publishing Group


Endothelium
Coagulation cascade
Activated protein C
Tissue factor
Monocyte
Interleukin-6
Interleukin-1
Factor VIIIa
Inactivation
Activated protein C
Factor Va
Inactivation
PAI-1
Bacterial, viral, fungal, or parasitic infection or endotoxin
TNF-α
Thrombin
Prevention of activation
Inactivation
Inhibition
Supression of fibrinolysis
TAFI
Activated protein C
Fibrin
Neutrophil
Inhibition
Interleukin-6
Interleukin-1
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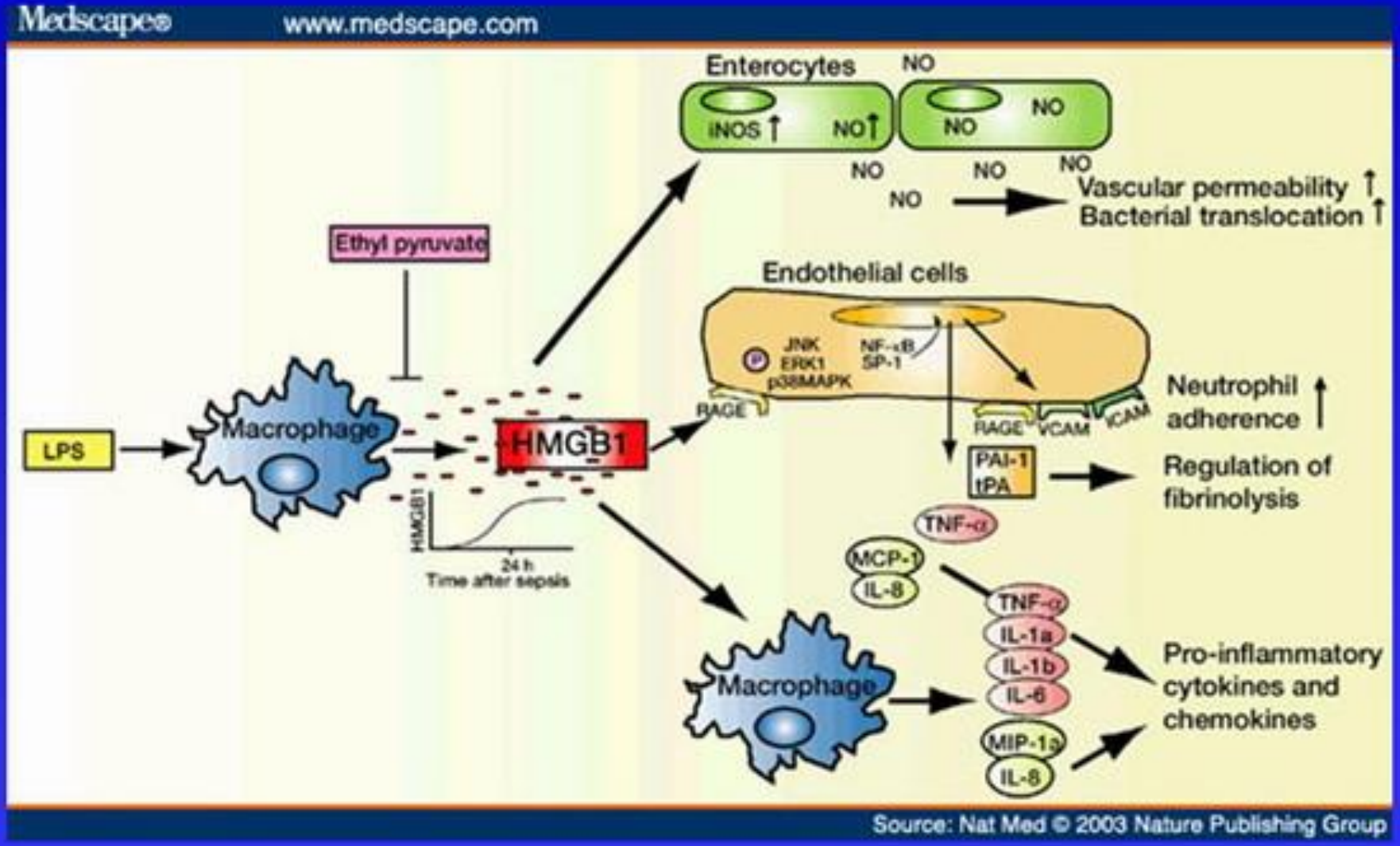
Tissue factor
TNF-α
Reduction of rolling
Activated protein C
Inflammatory Response to Infection
Thrombotic Response to Infection
Fibrinolytic Response to Infection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Endothelial cells
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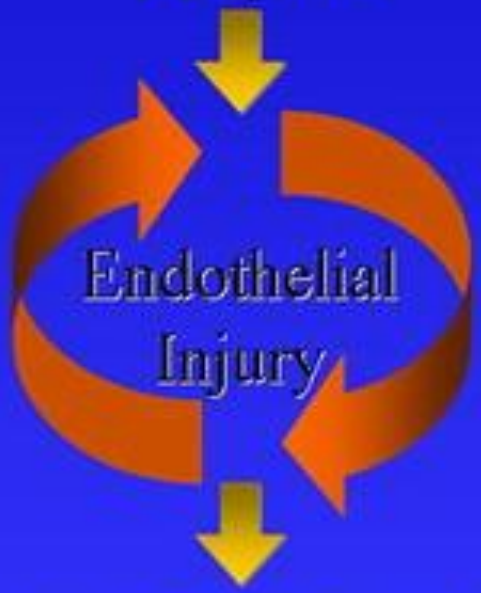
ERK1
p38MAPK
NF-κB
SP-1
RAGE
RAGE
VCAM
ICAM
Neutrophil adherence ↑
LPS
Macrophage
HMGB1
PAI-1
tPA
Regulation of fibrinolysis
HMGB1
24 h
Time after sepsis
TNF-α
MCP-1
IL-8
TNF-α
IL-1a
IL-1b
IL-6
Macrophage
MIP-1a
IL-8
Pro-inflammatory cytokines and chemokines
Source: Nat Med © 2003 Nature Publishing Group

A New Understanding of Sepsis Pathophysiology

Sepsis

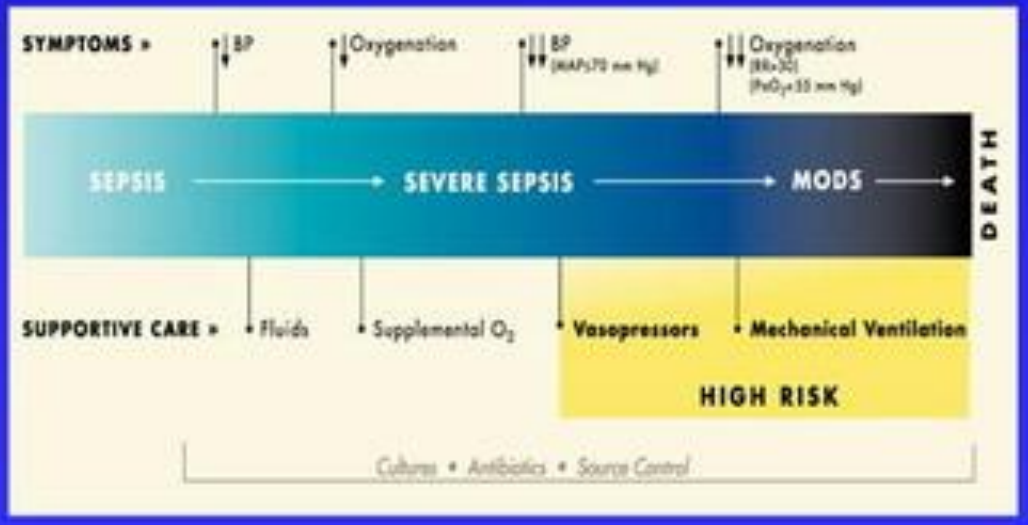


•Organ Dysfunction

Death

A severe sepsis patient identification initiative enables early intervention to positively early intervention to positively **impact** clinical outcomes.

- **Despite treatment with standard-of-care therapies, patients often**
- **progress to severe sepsis.**
- • Periodic assessment of at-risk patients will help ensure early disease recognition.



IDENTIFICATION OF THE INFECTOUS SOURCE

Identifying the source of the infection helps to determine what antibiotic therapy should be used and may revealan infected
site that can be drained. This process requires:

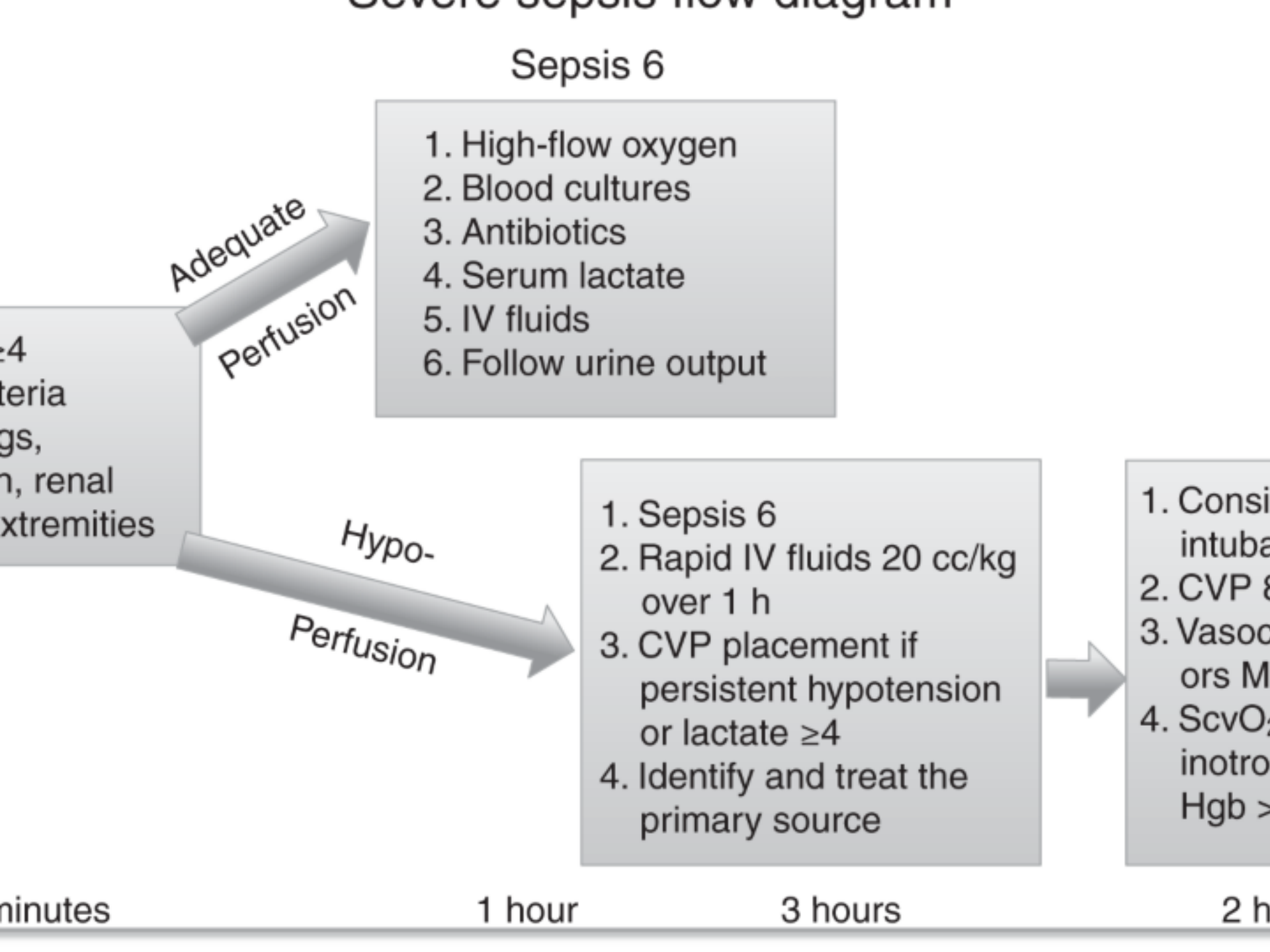
- Careful clinical examination
- Procedures such as chest X-rays, CT scans, urine analysis,
  etc.

SYMPTOMS OF SEPSIS

- High or very low temperature, chills
- Light headedness
- Shortness of breath
- Cool, pale extremities
- Restlessness, agitation, lethargy or confusion
- Low urinary output, low blood pressure
- Rapid heart rate

Management

- The therapy of sepsis rests on antibiotics, surgical drainage of infected fluid collections, fluid replacement and appropriate support for organ dysfunction. This may include hemodialysis in kidney failure, mechanical ventilation in pulmonary dysfunction, transfusion of blood products, and drug and fluid therapy for circulatory failure. Ensuring adequate nutrition—preferably by enteral feeding, but if necessary by parenteral nutrition—is important during prolonged illness.
- **A problem in the adequate management of septic patients has been the delay in administering therapy after sepsis has been recognized. Published studies have demonstrated that for every hour delay in the administration of appropriate antibiotic therapy there is an associated 7% rise in mortality.**


Severe sepsis flow diagram
Sepsis 6
1. High-flow oxygen
2. Blood cultures
3. Antibiotics
4. Serum lactate
5. IV fluids
6. Follow urine output
Adequate
Perfusion
≥4
teria
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Hypo-
Perfusion
1. Sepsis 6
2. Rapid IV fluids 20 cc/kg over 1 h
3. CVP placement if persistent hypotension or lactate ≥4
4. Identify and treat the primary source
1. Consi
intuba
2. CVP 8
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ors M
4. ScvO
inotro
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minutes
1 hour
3 hours
2 h

TREATMENTS OPTIONS OF SEPSIS

- Anti-infectives and source control
- Supportive care
- Cardiovascular support
- Respiratory support
- Renal replacement therapy
- Glucose control

- Severe sepsis is usually treated in the intensive care unit with intravenous fluids and antibiotics. If fluid replacement isn't sufficient to maintain blood pressure, specific vasopressor medications can be used. Mechanical ventilation and dialysis may be needed to support the function of the lungs and kidneys, respectively. To guide therapy, a central venous catheter and an arterial catheter may be placed; measurement of other hemodynamic variables (such as cardiac output, or mixed venous oxygen saturation) may also be used. Sepsis patients require preventive measures for deep vein thrombosis, stress ulcers and pressure ulcers, unless other conditions prevent this. Some patients might benefit from tight control of blood sugar levels with insulin (targeting stress hyperglycemia), low-dose corticosteroids or activated drotrecogin alfa (recombinant protein C)

EMPIRICAL ANTIMICROBIAL THERAPY

- The microorganisms most likely to cause infection at the suspected site are key to treatment decisions
- Generally broad-spectrum anti-infection are used
- Potential risk of antibiotic resistance

of infection	Pathogens to be covered	Antibiotics
(hospital acquired)	*Pseudomonas aeruginosa*	Cefepime, or ticarcillin–clavulanate
	Enterobacter	Piperacillin–tazobactam, plus aminoglycoside
omen or pelvis	Gram-negative rods	Ticarcillin–clavulanate, or piperacillin–tazobactam, plus aminoglycoside
	Anaerobes	Imipenem, meropenem, or doripenem
ary tract	*Escherichia coli*	Ciprofloxacin
	Klebsiella	Ceftriaxone
	Proteus	
	Staphylococcus aureus	Oxacillin, Vancomycin or ceftaroline
	Streptococcus pyogenes	Ticarcillin–clavulanate
	Mixed aerobic/anaerobic (necrotizing fasciitis)	Piperacillin–tazobactam
		Imipenem, meropenem, or doripenem
remia of unknown source pital acquired)	Methicillin-resistant *S. aureus (MRSA)*	Cefepime, plus vancomycin or ceftarolin
	Gram negative rods	
eremia of unknown source mmunity acquired)	*S. aureus*	Vancomycin, plus ceftriaxone or cefepim
	Strep. pneumoniae	
	E. coli	
	Klebsiella	

EMPIRIC ANTIBIOTICS IN SEPSIS

- IV-line infections
  Flucloxacillin/ Cefuroxime
- Biliary tract infections
  Ampicillin/ Piperacillin/ Ceftriaxone
- Intra-abdominal infections
  Amoxi + Clav/ Cefuroxime + Meto/Penem
- Urosepsis
  Meropenem/ Levofloxacin
- Unknown origin
  Levofloxacin/ Metro
  Meropenem

CARDIOVASCULAR SUPPORT

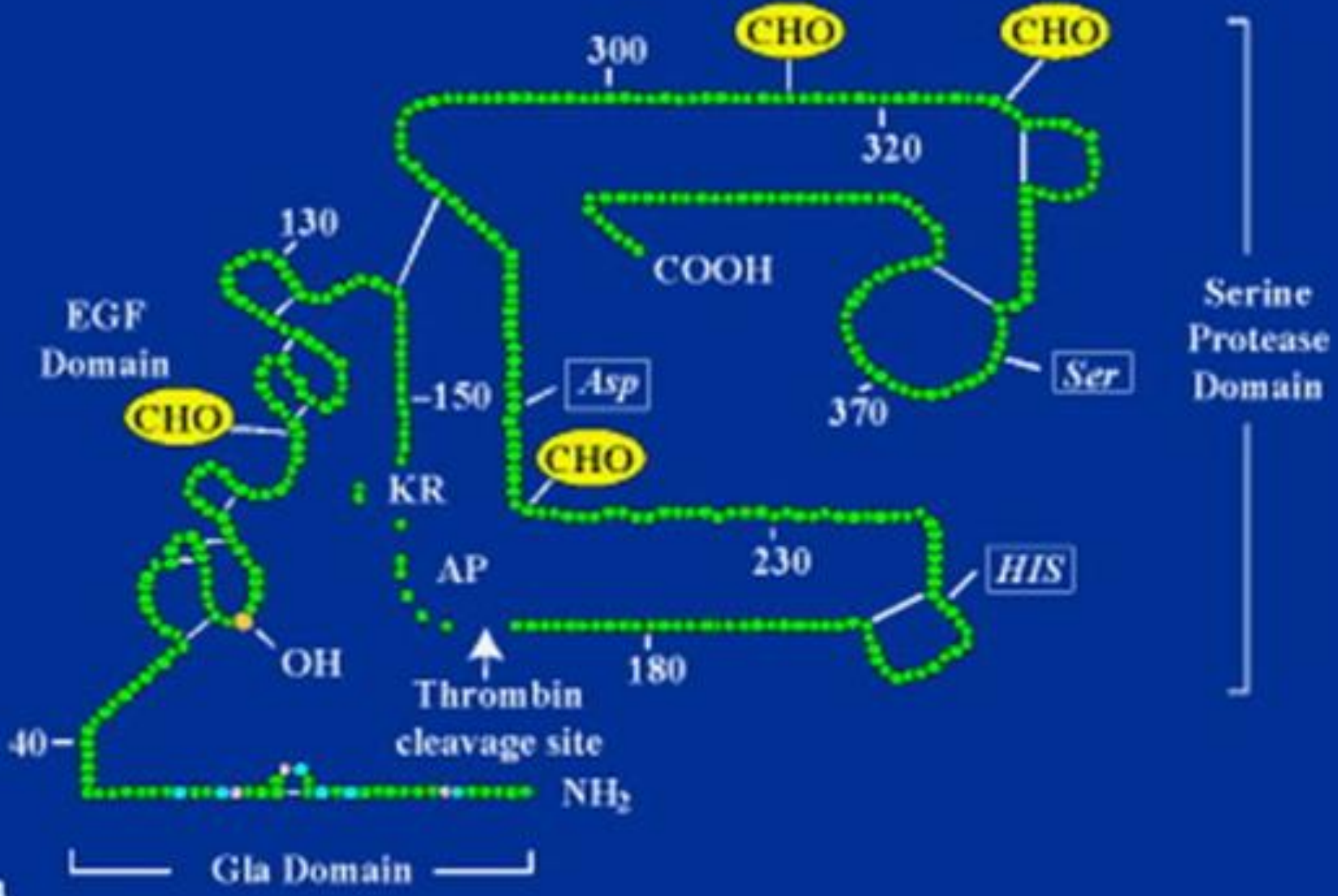
- Hypotension is a hallmark of severe sepsis
- Rapid fluid resuscitation
- Vasopressors
- Low-dose corticosteroids

Treatment of sepsis

- Eradication of focus
- Antimicrobial therapy

- Intensive insulin therapy
- Low dose hydrocortisone

Drotrecogin Alfa (Activated)
Recombinant Human Activated Protein C



Therapy with monoclonal antibodies in sepsis - mortality

	n	Placebo	Verum
Antiendotoxin	2010	35 %	35 %
Anti-TNF	4132	41 %	40 %
Sol. TNF-R	686	38 %	40 %
IL1-RA	1896	35 %	31 %
Anti-PAF	870	50 %	43 %

OTHER SUPPORTIVE MEASURES

- Sedation
- Analgesia
- Deep vein thrombosis prophylaxis
- Stress ulcer prophylaxis
- Blood product administration
- Nutritional support

Prognosis

- Approximately 20–35% of patients with severe sepsis and 40–60% of patients with septic shock die within 30 days. Others die within the ensuing 6 months. Late deaths often result from poorly controlled infection, immunosuppression, complications of intensive care, failure of multiple organs, or the patient's underlying disease.