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CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

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Issued 2017 - NEW!

Abstract

Objective: To provide an update to "Surviving Sepsis Campaign Guidelines for Management of Sepsis and Septic Shock: 2012".

Design: A consensus committee of 55 international experts representing 25 international organizations was convened. Nominal groups were assembled at key international meetings (for those committee members attending the conference). A formal conflict-of-interest (COI) policy was developed at the onset of the process and enforced throughout. A stand-alone meeting was held for all panel members in December 2015. Teleconferences and electronic-based discussion among subgroups and among the entire committee served as an integral part of the development.

Methods: The panel consisted of five sections: hemodynamics, infection, adjunctive therapies, metabolic, and ventilation. Population, intervention, comparison, and outcomes (PICO) questions were reviewed and updated as needed, and evidence profiles were generated. Each subgroup generated a list of questions, searched for best available evidence, and then followed the principles of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to assess the quality of evidence from high to very low, and to formulate recommendations as strong or weak, or best practice statement when applicable.

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Results: The Surviving Sepsis Guideline panel provided 93 statements on early management and resuscitation of patients with sepsis or septic shock. Overall, 32 were strong recommendations, 39 were weak recommendations, and 18 were best-practice statements. No recommendation was provided for four questions.

Conclusions: Substantial agreement exists among a large cohort of international experts regarding many strong recommendations for the best care of patients with sepsis. Although a significant number of aspects of care have relatively weak support, evidence-based recommendations regarding the acute management of sepsis and septic shock are the foundation of improved outcomes for these critically ill patients with high mortality.

Keywords: Evidence-based medicine, Grading of Recommendations Assessment, Development, and Evaluation criteria, Guidelines, Infection, Sepsis, Sepsis bundles, Sepsis syndrome, Septic shock, Surviving Sepsis Campaign

Sepsis – definition !!!

- **Sepsis** is now defined as **life-threatening organ dysfunction** caused by a **dysregulated host response to infection**

- **Septic shock** is a **subset** of sepsis with
  - **circulatory** and
  - **cellular/metabolic dysfunction**

  associated with a higher risk of **mortality**.

Rhodes, A., Evans, L.E., Alhazzani, W. et al. Intensive Care Med (2017). doi:10.1007/s00134-017-4683-6
Singer M et al: The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) JAMA. 2016;315(8):801-810.

SOFA-score

Points	1	2	3	4
Glasgow Coma Score	13–14	10–12	6–9	<6
Oxygenation index MAP (mmHg)	<400	<300	<200	<100
Catecholamine doses (µg/kg/min)	<70	Dopamine <5 or Dobutamine (whatever dose)	Dopamine >5 or Adrenaline <0.1 or Noradrenaline <0.1	Dopamine >15 or Adrenaline >0.1 or Noradrenaline >0.1
Blood creatinine (µmol/L) or diuresis (ml/L)	110–170	171–299	300–440 or <500	>440 or <200
Platelets (10^9/L)	<150	<100	<50	<20
Blood bilirubin (µmol/L)	20–32	33–101	102–204	>204

Vincent JL, et al. Intensive Care Med 1996; 22: 707-710.

qSOFA (Quick SOFA) criteria

H Systolic blood pressure <100 mmHg **H**ypotension

A **A**ltered mentation

T Respiratory rate >22/min **T**achypnea

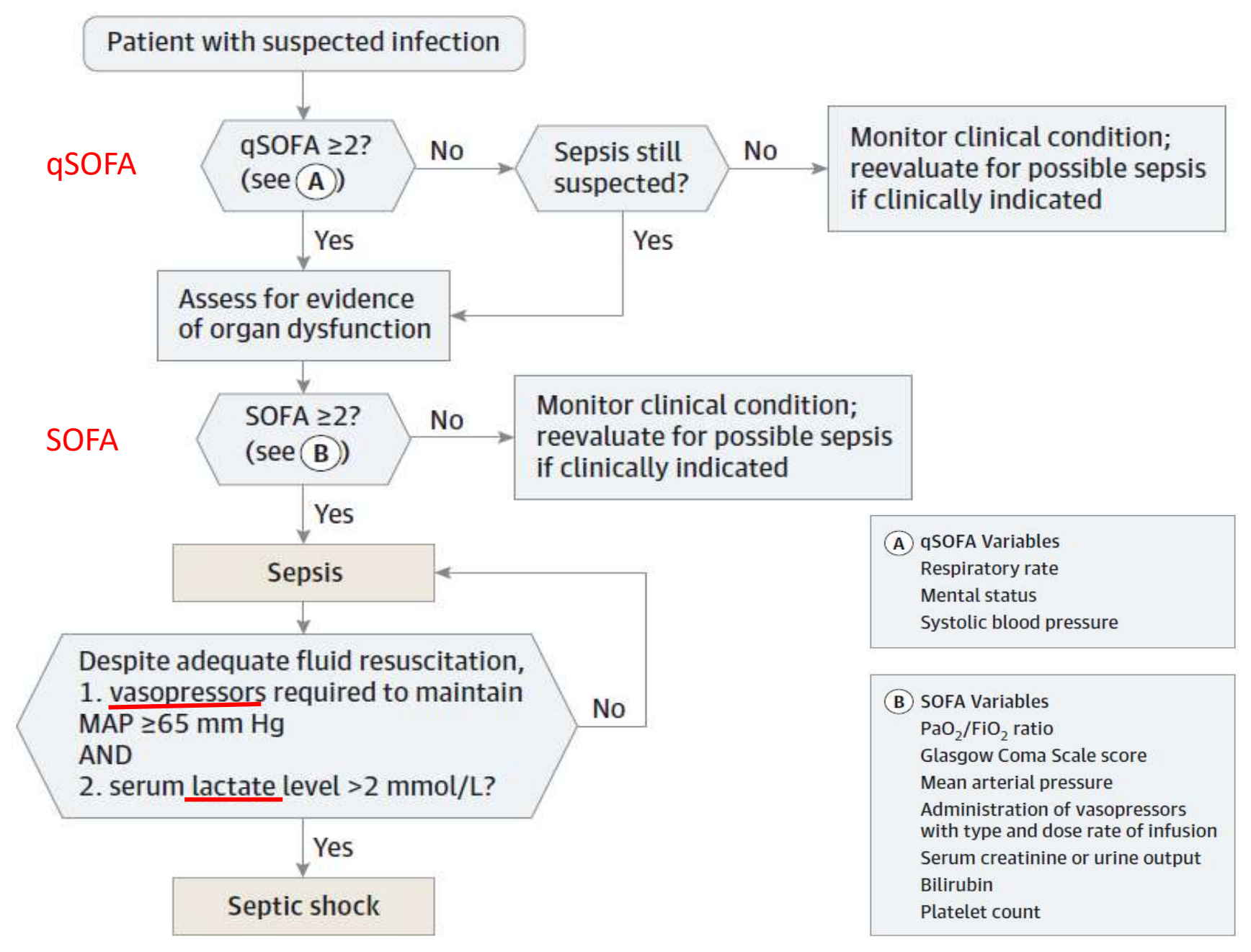
Singer M et al: The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) JAMA. 2016;315(8):801-810.

New definitions...

	OLD	NEW
SEPSIS	SIRS + Suspected Infection	**SUSPECTED/DOCUMENTED INFECTION** + **H A T** **2 or 3 on qSOFA** (HAT): Hypotension (SBP ≤100 mmHg) AMS (GCS ≤13) Tachypnea (≥22/min) OR Rise in SOFA score by 2 or more
SEVERE SEPSIS	Sepsis + SBP <90 mmHg or MAP < 65 mmHg lactate > 2.0 mmol/L INR >1.5 or a PTT >60 s Bilirubin >34 µmol/L Urine output <0.5 mL/kg/h for 2 h Creatinine >177 µmol/L Platelets <100 ×109/L SpO2 <90% on room air	———
SEPTIC SHOCK	SEPSIS + HYPOTENSION after adequate fluid resuscitation	**SEPSIS** + **VASOPRESSORS needed for MAP >65 mmHg** + **LACTATE >2 mmol/L** after adequate fluid resuscitation

Singer M, Deutschman CS, Seymour CW, et al: The Sepsis Definitions Task Force The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810.

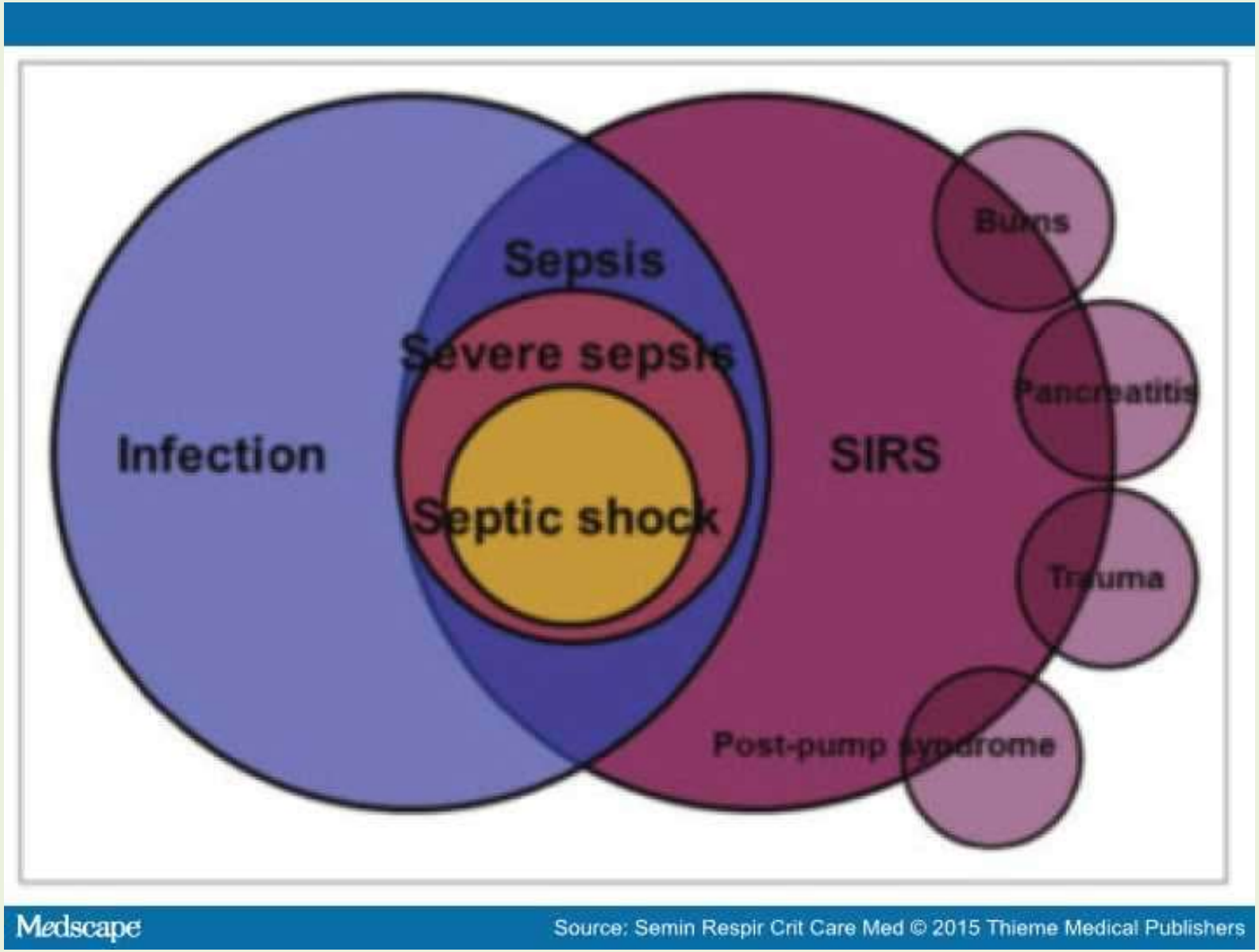
Clinical Criteria Identifying Patients With Sepsis and Septic Shock



CLINICAL SYNDROMES - OLD

- **SIRS** = fever + leukocytosis
- **Sepsis** = SIRS + infection
- ~~**Severe sepsis**~~ = sepsis + MODS (MSOF)
- **Septic shock** = severe sepsis + refractory hypotension

Kerr G. E.: Some current concepts and strategies in critical care. PGA55



http://www.medscape.com/viewarticle/839504_11?nlid=78644_530

Best practice statements (BPSs)

- A number of best practice statements (**BPSs**) appear throughout the document;
- these statements represent **ungraded strong recommendations** and are used under strict criteria.
- A BPS **would be appropriate**, for example, when the **benefit or harm is unequivocal**, but the evidence is **hard** to summarize or assess using **GRADE methodology**.

Comparison of 2016 grading terminology with previous 2012 alphanumeric descriptors

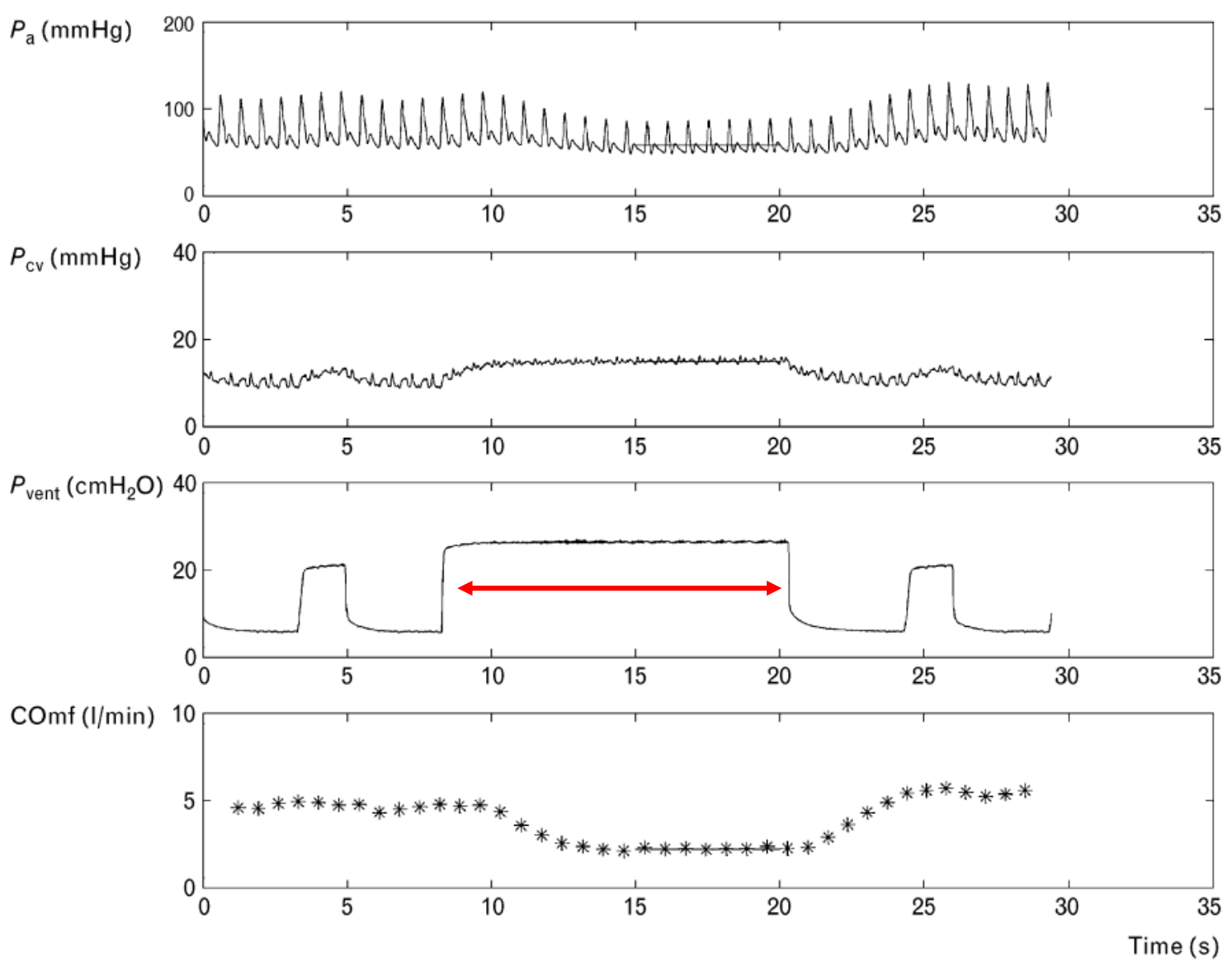
	2016 Descriptor	2012 Descriptor
Strength	Strong	1
	Weak	2
Quality	High	A
	Moderate	B
	Low	C
	Very Low	D
Ungraded strong recommendation	Best Practice Statement	Ungraded

A. INITIAL RESUSCITATION

1. Sepsis and septic shock are **medical emergencies**, and we recommend that **treatment and resuscitation begin immediately** (BPS).
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at **least 30 mL/kg** of IV **crystalloid** fluid be given within the **first 3 h** (strong recommendation, low quality of evidence).
3. We recommend that, following initial fluid resuscitation, **additional fluids** be guided by **frequent reassessment of hemodynamic** status (BPS).

Remarks: Reassessment should include a thorough clinical examination and evaluation of available physiologic variables (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and others, as available) as well as other noninvasive or invasive monitoring, as available.

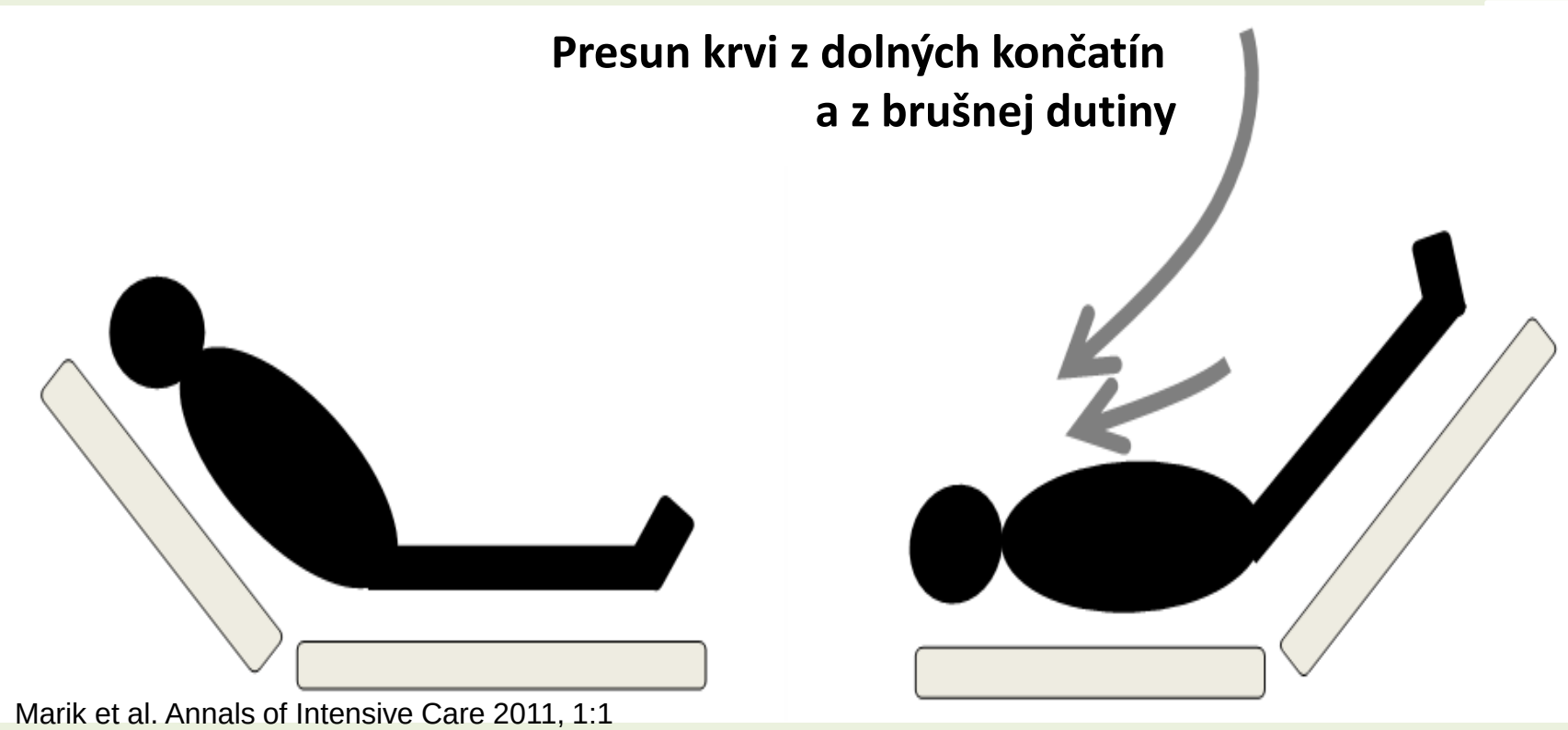
Effects of an inspiratory hold maneuver on arterial pressure (Pa), central venous pressure (Pcv), airway pressure (Pvent) and beat-to-beat cardiac output (COmf)



Jansen JRC, Maas JJ, Pinsky MR: Bedside assessment of mean systemic filling pressure. Current Opinion in Critical Care 2010, 16:231–236

Passive leg raising test (PLRT)

- The passive leg raising test consists in measuring the hemodynamic effects of a leg elevation up to 45°.
- A simple way to perform the postural maneuver is to transfer the patient from the semirecumbent posture to the passive leg raising position by using the automatic motion of the bed.



Marik et al. Annals of Intensive Care 2011, 1:1

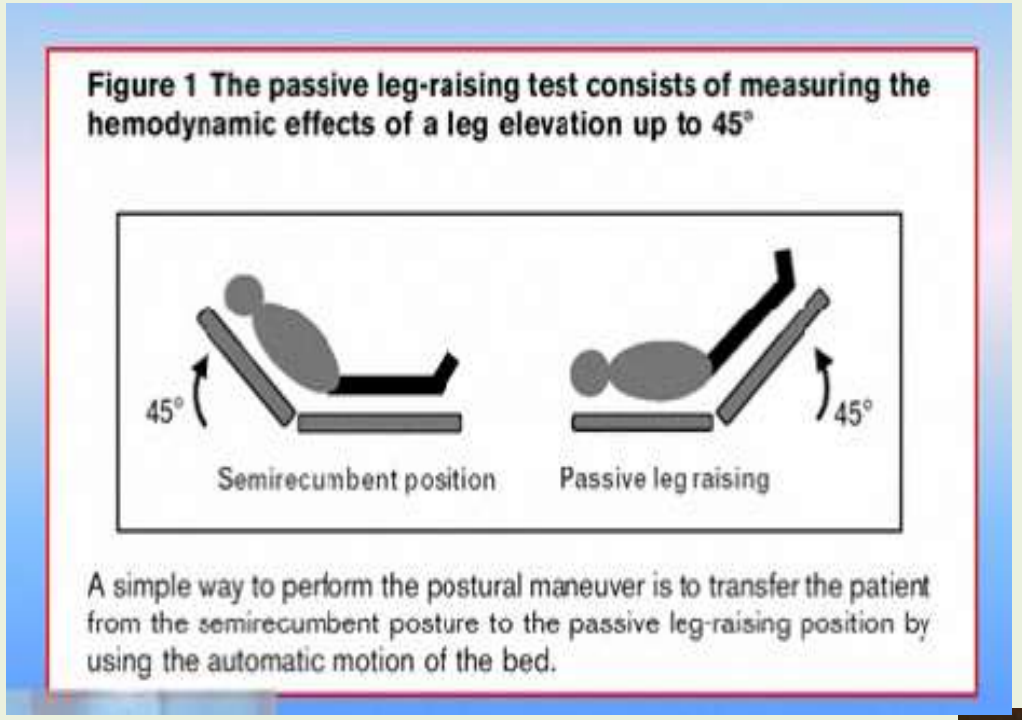
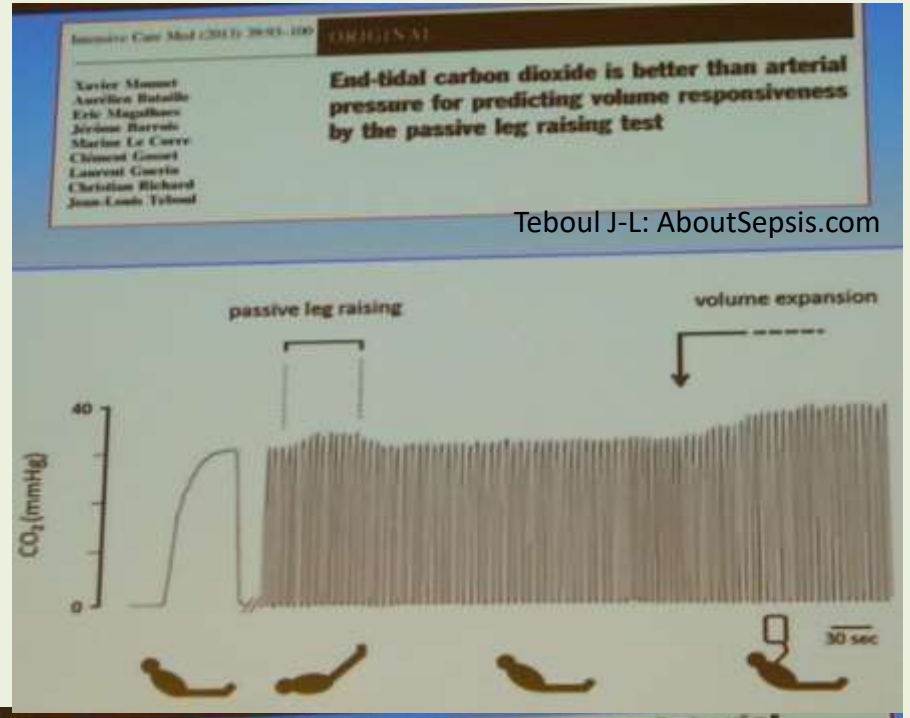
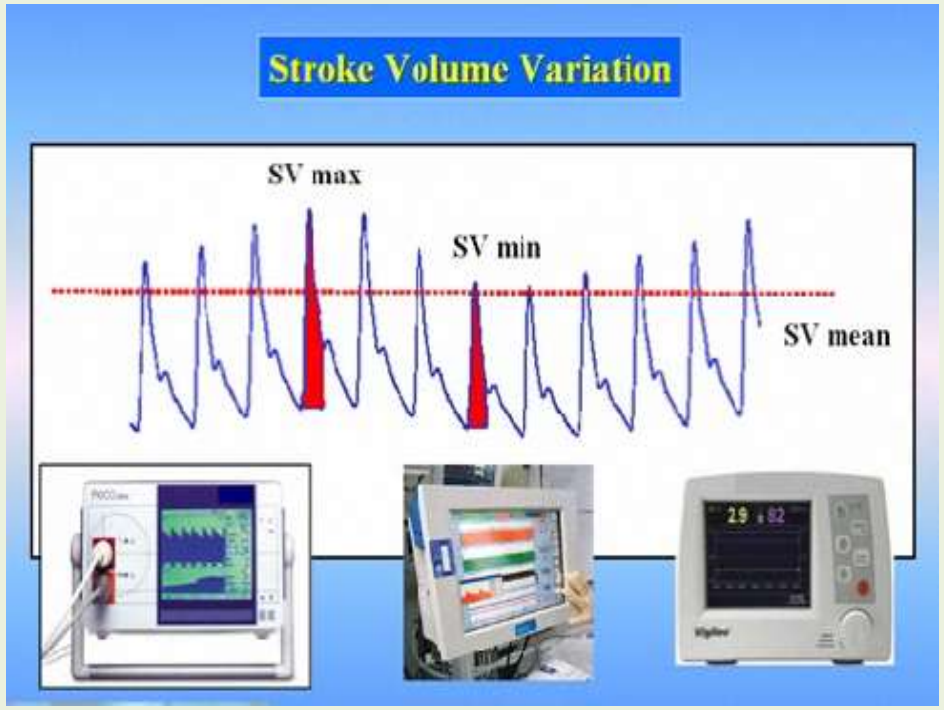
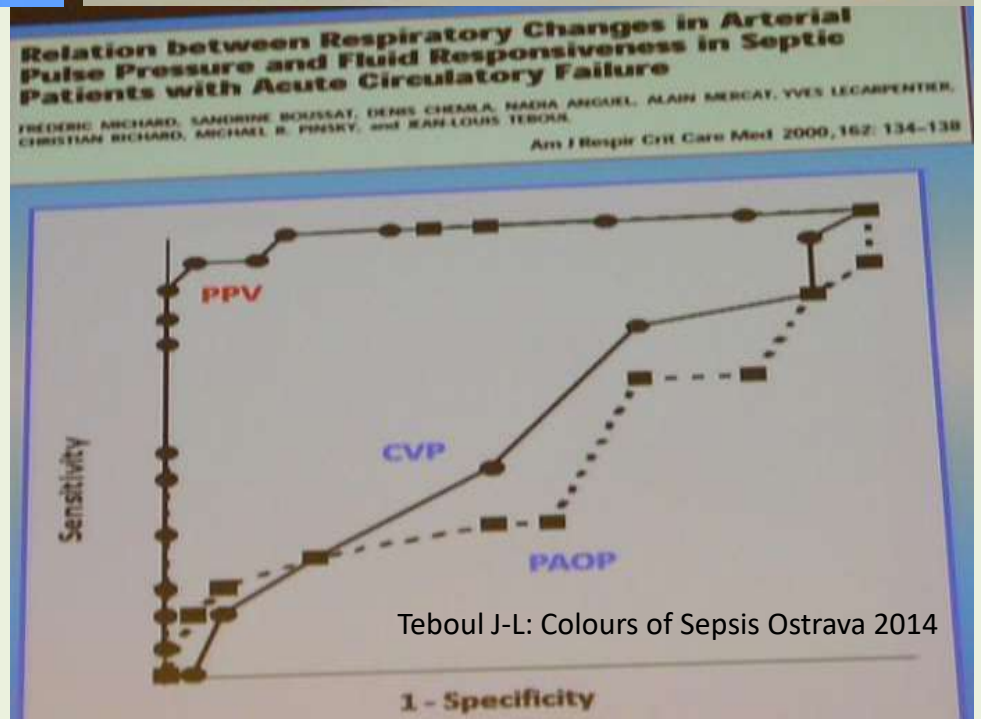


Figure 1 The passive leg-raising test consists of measuring the hemodynamic effects of a leg elevation up to 45°
45°
45°
Semirecumbent position
Passive leg raising
A simple way to perform the postural maneuver is to transfer the patient from the semirecumbent posture to the passive leg-raising position by using the automatic motion of the bed.


End-tidal carbon dioxide is better than arterial pressure for predicting volume responsiveness by the passive leg raising test
Teboul J-L: AboutSepsis.com
passive leg raising
volume expansion
40
0
CO_2 (mmHg)
30 sec


Stroke Volume Variation
SV max
SV min
SV mean


Relation between Respiratory Changes in Arterial Pulse Pressure and Fluid Responsiveness in Septic Patients with Acute Circulatory Failure
Am J Respir Crit Care Med 2000, 162: 134–138
PPV
CVP
PAOP
Sensitivity
1 - Specificity
Teboul J-L: Colours of Sepsis Ostrava 2014

Parallax MAP 65 mmHg & initial steps in shock

- **MAP increase from 65 mmHg to 85 mmHg after administration NA** did not significantly affect the metabolism of O_2, the microcirculation of the skin, diuresis or splanchnic perfusion.
- Rise to 85 mmHg from 65 mmHg **is not a significant indicator of recovery**. It is a picture of **macro**circulation (eg. under the influence of NA) **micro**circulation can still be closed and **shock may persist**!
- But **fell to 65 mmHg** from normal pressure is **an important indicator of deterioration!**

MAP 65 mmHg!!!

LeDoux D et al: Effects of perfusion pressure on tissue perfusion in septic shock. Crit Care Med. 2000, 28(8):2729-32.
Rhodes, A et al: Surviving Sepsis Campaign: International guidelines for Management of Severe Sepsis and Septic Shock: 2016, 2017, 45, 3,

Initial resuscitation of septic shock - lactate

- It serves as a **more objective** indicator of tissue perfusion than **clinical** examination or **diuresis**
- Significantly reduce mortality in **septic shock resuscitation by lactate levels** compared with resuscitation without monitoring of lactate

Rhodes, A et al: Surviving Sepsis Campaign: International guidelines for Management of Severe Sepsis and Septic Shock: 2016, 2017, 45, 3,

B. SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT

1. We recommend that **hospitals** and hospital systems have a **performance improvement program for sepsis**, including sepsis **screening** for acutely ill, high-risk patients (BPS).

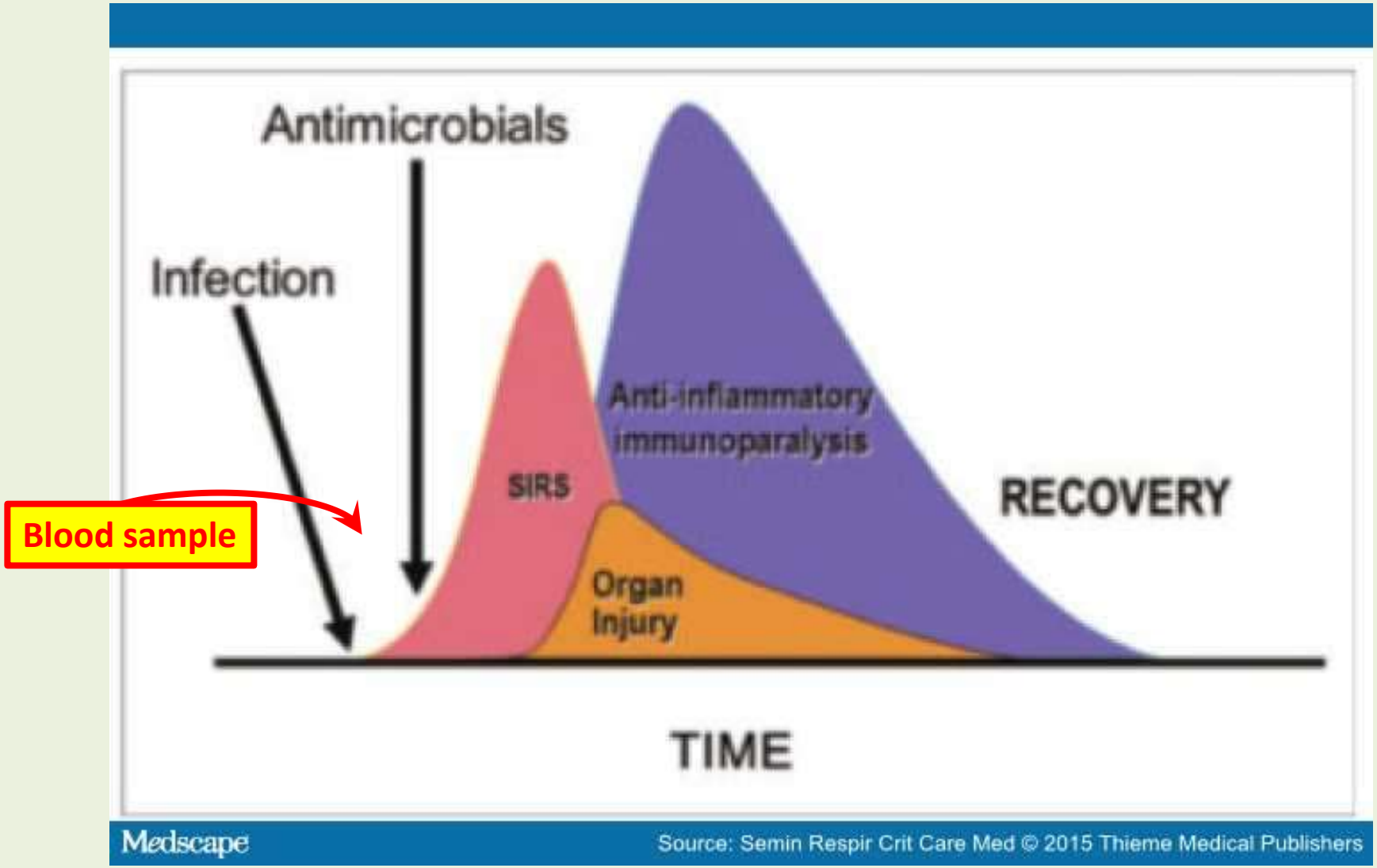
RRT, MET...

C. DIAGNOSIS

1. We recommend that appropriate routine **microbiologic cultures** (including blood) be obtained **before starting antimicrobial therapy** in patients with suspected sepsis or septic shock if doing so results in no substantial delay in the start of antimicrobials (BPS).

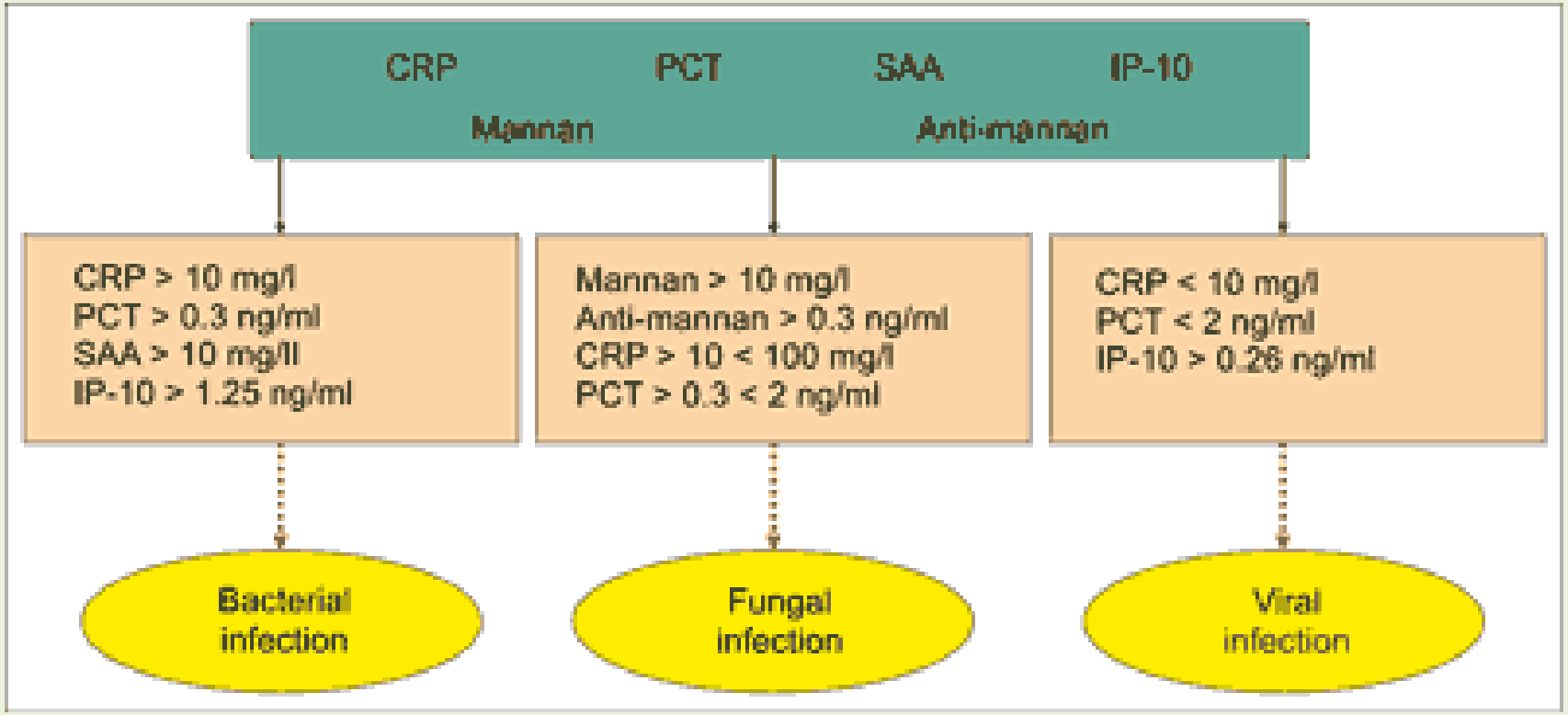
Remarks: Appropriate routine microbiologic cultures always include **at least two sets of blood cultures** (aerobic and anaerobic).

Immunologic view of sepsis and septic shock. SIRS - systemic inflammatory response syndrome



http://www.medscape.com/viewarticle/839504_11?nlid=78644_530

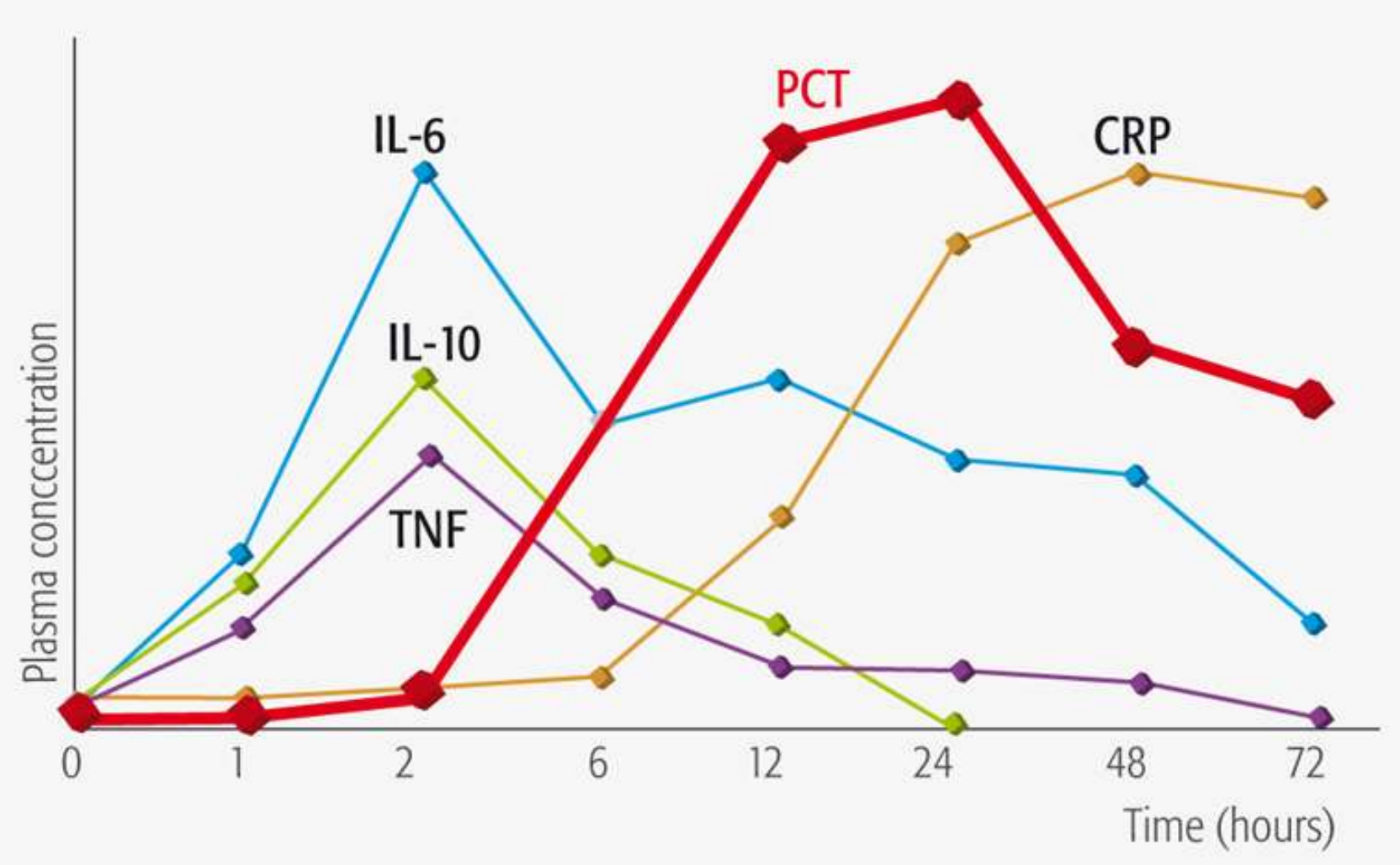
Biomarkers used in diagnosis of sepsis



CRP – C reactive protein, PCT – prokalcitonin, SAA – serum amyloid A,
IP-10 – IFN-γ inducible protein-10

Chan T, Gu F: Early Diagnosis of Using Serum Biomarkers. Expert Rev Mol Diagn 2011; 11, 5: 487-496.
http://www.czytelniamedyczna.pl/4792,diagnostyka-laboratoryjna-sepsy-biomarkery.html

Kinetic profiles of different biomarkers of bacterial infection



Meisner *et al*., Crit Care 1999, 3:45-50
http://www.biomerieux-diagnostics.com/vidas-brahms-pct

D. ANTIMICROBIAL THERAPY

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and **within 1 h** for both **sepsis** and **septic shock** (strong recommendation, moderate quality of evidence; grade applies **to both conditions**).
2. We recommend **empiric broad-spectrum therapy with one or more antimicrobials** for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage) (strong recommendation, moderate quality of evidence).
3. We recommend that empiric antimicrobial therapy be **narrowed** once pathogen identification and **sensitivities** are established and/or adequate clinical **improvement** is noted (BPS).

Several factors must be assessed and used in determining the appropriate antimicrobial regimen

a) The **anatomic site** of infection with respect to the typical **pathogen** profile and to the properties of individual antimicrobials to **penetrate** that site.

b) **Prevalent pathogens** within the community, hospital, and even hospital ward.

c) The **resistance** patterns of those prevalent pathogens.

d) The presence of specific **immune defects** such as neutropenia, splenectomy, poorly controlled HIV infection and acquired or congenital defects of immunoglobulin, complement or leukocyte function or production.

e) **Age** and patient **comorbidities** including chronic illness (e.g., diabetes) and chronic **organ dysfunction** (e.g., liver or renal failure), the presence of **invasive devices** (e.g., central venous lines or urinary catheter) that compromise the defense to infection.

E. SOURCE CONTROL

1. We recommend that a **specific anatomic diagnosis of infection** requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock, and that any required **source control intervention** be implemented **as soon as** medically and logistically practical after the diagnosis is made (BPS).
2. We recommend **prompt removal of intravascular access devices** that are a **possible source** of sepsis or septic shock after other vascular access has been established (BPS).

F. FLUID THERAPY

1. We recommend that a **fluid challenge** technique be applied where fluid administration is continued as long as **hemodynamic factors** continue to **improve** (BPS).
2. We recommend **crystalloids** as the fluid of choice for **initial** resuscitation and **subsequent** intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).
3. We suggest using either **balanced crystalloids or saline** for fluid resuscitation of patients with sepsis or septic shock (weak recommendation, low quality of evidence).

F. FLUID THERAPY

4. We suggest using **albumin in addition to crystalloids** for **initial** resuscitation and **subsequent** intravascular volume replacement in patients with sepsis and septic shock **when patients require substantial amounts of crystalloids** (weak recommendation, low quality of evidence).
5. We recommend **against using hydroxyethyl starches** (HESs) for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence).
6. We suggest using **crystalloids over gelatins** when resuscitating patients with sepsis or septic shock (weak recommendation, low quality of evidence).

G. VASOACTIVE MEDICATIONS

1. We recommend **norepinephrine as the first choice** vasopressor (strong recommendation, moderate quality of evidence).
2. We suggest **adding either vasopressin** (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) or **epinephrine** (weak recommendation, low quality of evidence) to norepinephrine with the intent of raising **MAP to target**, or adding vasopressin (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) to **decrease norepinephrine** dosage.
3. We suggest using **dopamine** as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with **low risk of tachyarrhythmias** and absolute or relative **bradycardia**) (weak recommendation, low quality of evidence).

Inotrope or Vasoactive	Dose	Mechanism of Action	HR	Systolic Function	Diastolic Function	Myocardial O2 demand	SVR	PVR
Dopamine	1-5 mcg/kg/min	Dopaminergic agonist	↑	↑	No Change	Mild Increase	Renal artery dilation	No Change
	6-10 mcg/kg/min	β1 Agonist	↑	↑	No Change	↑	↑	No Change
	11-20 mcg/kg/min	α-1 agonist	↑	↑	No Change	↑	↑↑	↑
Dobutamine	1-10 mcg/kg/min	β1 Agonist β2 Agonist	↑↑	↑↑	No Change	↑	↓	Minimal ↓
Epinephrine	0.01-0.05 mcg/kg/min	β1 Agonist β2 Agonist	↑↑	↑↑	No Change	↑	↓	No Change
	0.06-1 mcg/kg/min	α-1 agonist	↑	↑	No Change	↑	↑	↑
Norepinephrine	0.01-1 mcg/kg/min	α-1 agonist>> β1 Agonist	↑	↑	No Change	↑	↑↑	↑
Milrinone	0.3-0.7 mcg/kg/min	PDE3 inhibitor	No Change	↑	↑	No Change	↓	↓
Phenylephrine	0.1-2 mcg/kg/min	α-1 agonist	No Change	No Change	No Change	No Change	↑↑	No Change
Vasopressin	0.0003-0.008 u/kg/min	V1 receptor agonist	No Change	No Change	No Change	No Change	↑↑	No Change

http://www.learnpicu.com/Sepsis

H. CORTICOSTEROIDS

1. We suggest **against using IV hydrocortisone** to treat septic shock patients **if** adequate **fluid** resuscitation and **vasopressor** therapy are **able** to restore hemodynamic stability. If this is not achievable, we suggest **IV hydrocortisone at a dose of 200 mg per day** (weak recommendation, low quality of evidence).

M. MECHANICAL VENTILATION

1. We recommend using a **target tidal volume of 6 mL/kg** predicted body weight compared with 12 mL/kg in adult patients with sepsis-induced acute respiratory distress syndrome (**ARDS**) (strong recommendation, high quality of evidence).
2. We recommend using an **upper limit goal for plateau pressures of 30 cmH_2O** over higher plateau pressures in adult patients with sepsis-induced severe **ARDS** (strong recommendation, moderate quality of evidence).
3. We suggest using **higher positive end-expiratory pressure (PEEP)** over lower PEEP in adult patients with sepsis-induced moderate to severe **ARDS** (weak recommendation, moderate quality of evidence).
4. We suggest using **recruitment maneuvers** in adult patients with sepsis-induced, severe **ARDS** (weak recommendation, moderate quality of evidence).
5. We recommend using **prone over supine position** in adult patients with sepsis-induced **ARDS** and a **PaO_2/FIO_2 ratio < 150** (strong recommendation, moderate quality of evidence).

R. VENOUS THROMBOEMBOLISM PROPHYLAXIS

1. We recommend pharmacologic prophylaxis (unfractionated heparin [**UFH**] or low-molecular-weight heparin [**LMWH**]) **against venous thromboembolism (VTE)** in the absence of contraindications to the use of these agents (strong recommendation, moderate quality of evidence).
2. We recommend **LMWH rather than UFH** for VTE prophylaxis in the absence of contraindications to the use of LMWH (strong recommendation, moderate quality of evidence).
3. We suggest **combination pharmacologic VTE prophylaxis and mechanical prophylaxis**, whenever possible (weak recommendation, low quality of evidence).
4. We suggest **mechanical VTE prophylaxis** when pharmacologic VTE is contraindicated (weak recommendation, low quality of evidence).

T. NUTRITION

1. We recommend **against the administraon of early parenteral** nutrition alone or parenteral nutrion in combination with enteral feedings (but rather **initiate early enteral** nutrition) in critically ill patients with sepsis or septic shock who **can be fed enterally** (strong recommendation, moderate quality of evidence).
2. We recommend **against the administration of parenteral nutrition alone** or in combination with enteral feeds (but rather to iniate IV glucose and advance enteral feeds as tolerated) over the first 7 days in crically ill patients with sepsis or septic shock for whom early enteral feeding is not feasible (strong recommendation, moderate quality of evidence).
3. We suggest the **early initiation of enteral feeding** rather than a complete fast or only IV glucose in crically ill paents with sepsis or sepc shock who can be fed enterally (weak recommendation, low quality of evidence).
4. We suggest either **early trophic/hypocaloric or early full enteral feeding** in crically ill patients with sepsis or septic shock; if trophic/hypocaloric feeding is the inial strategy, then feeds should be advanced according to patient tolerance (weak recommendation, moderate quality of evidence).

U. SETTING GOALS OF CARE

1. We recommend that **goals of care and prognosis be discussed** with patients and families (BPS).
2. We recommend that goals of care be **incorporated into treatment** and **end-of-life care** planning, utilizing palliative care principles where appropriate (strong recommendation, moderate quality of evidence).
3. We suggest that goals of care be **addressed as early as feasible**, but **no later than within 72 hours** of ICU admission (weak recommendation, low quality of evidence).

End of Life Decisions

a. **Withholding** = refusal or no initiation of the treatment or specific treatment step, no further escalation of the treatment or specific treatment step
b. **Withdrawing** = decision to stop or remove treatment or specific treatment step after it has begun
c. **Euthanasia** = administration of a medication with intentional ending of a patient`s life according to wishes of the patient
d. **Assisted suicide** = the patient administers the lethal agent themselves with health care member`s assistance
e. **Double effect** = giving medication for pain relief on one side can speed up dying process on the other side

Hour-1 Surviving Sepsis Campaign Bundle of Care

- Measure lactate level. Remeasure if initial lactate is >2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate ≥4 mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg.

**"Time zero" or "time of presentation" is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of sepsis (formerly severe sepsis) or septic shock ascertained through chart review.*

Levy MM, Evans LE, Rhodes A: The Surviving Sepsis Campaign Bundle: 2018 update. *Intensive Care Med.* https://doi.org/10.1007/s00134-018-5085-0

Bundle elements with strength of recommendations and under-pinning quality of evidence

Bundle element	Grade of recommendation and level of evidence
Measure lactate level. Re-measure if initial lactate is > 2 mmol/L	Weak recommendation, low quality of evidence
Obtain blood cultures prior to administration of antibiotics	Best practice statement
Administer broad-spectrum antibiotics	Strong recommendation, moderate quality of evidence
Rapidly administer 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L	Strong recommendation, low quality of evidence
Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg	Strong recommendation, moderate quality of evidence

Levy MM, Evans LE, Rhodes A: The Surviving Sepsis Campaign Bundle: 2018 update. *Intensive Care Med.* https://doi.org/10.1007/s00134-018-5085-0

Surviving Sepsis Campaign

A. INITIAL RESUSCITATION
B. SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT
C. DIAGNOSIS
D. ANTIMICROBIAL THERAPY
E. SOURCE CONTROL
F. FLUID THERAPY
G. VASOACTIVE MEDICATIONS
H. CORTICOSTEROIDS
I. BLOOD PRODUCTS
J. IMMUNOGLOBULINS
L. ANTICOAGULANTS
M. MECHANICAL VENTILATION
N. SEDATION AND ANALGESIA
O. GLUCOSE CONTROL
P. RENAL REPLACEMENT THERAPY
Q. BICARBONATE THERAPY
R. VENOUS TE PROPHYLAXIS
S. STRESS ULCER PROPHYLAXIS
T. NUTRITION
U. SETTING GOALS OF CARE

Rhodes, A., Evans, L.E., Alhazzani, W. et al. Intensive Care Med (2017). doi:10.1007/s00134-017-4683-6

UNIVERZITA PAVLA JOZEFA ŠAFÁRIKA V KOŠICIACH

Lekárska fakulta

CONTROL TEST

Anaesthesiology & Intensive Medicine

March 03 2020 (Tuesday)

At 17:30 (AULA)

40 questions, one – the best answer

The test will be based on lectures
(understanding the content of lectures is mandatory for the test)

https://www.upjs.sk/en/faculty-of-medicine/clinic/anaesthesiology/teaching/lectures/