UPDATE SEPSIS AND SEPTIC SHOCK 2016

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Intensive care unit

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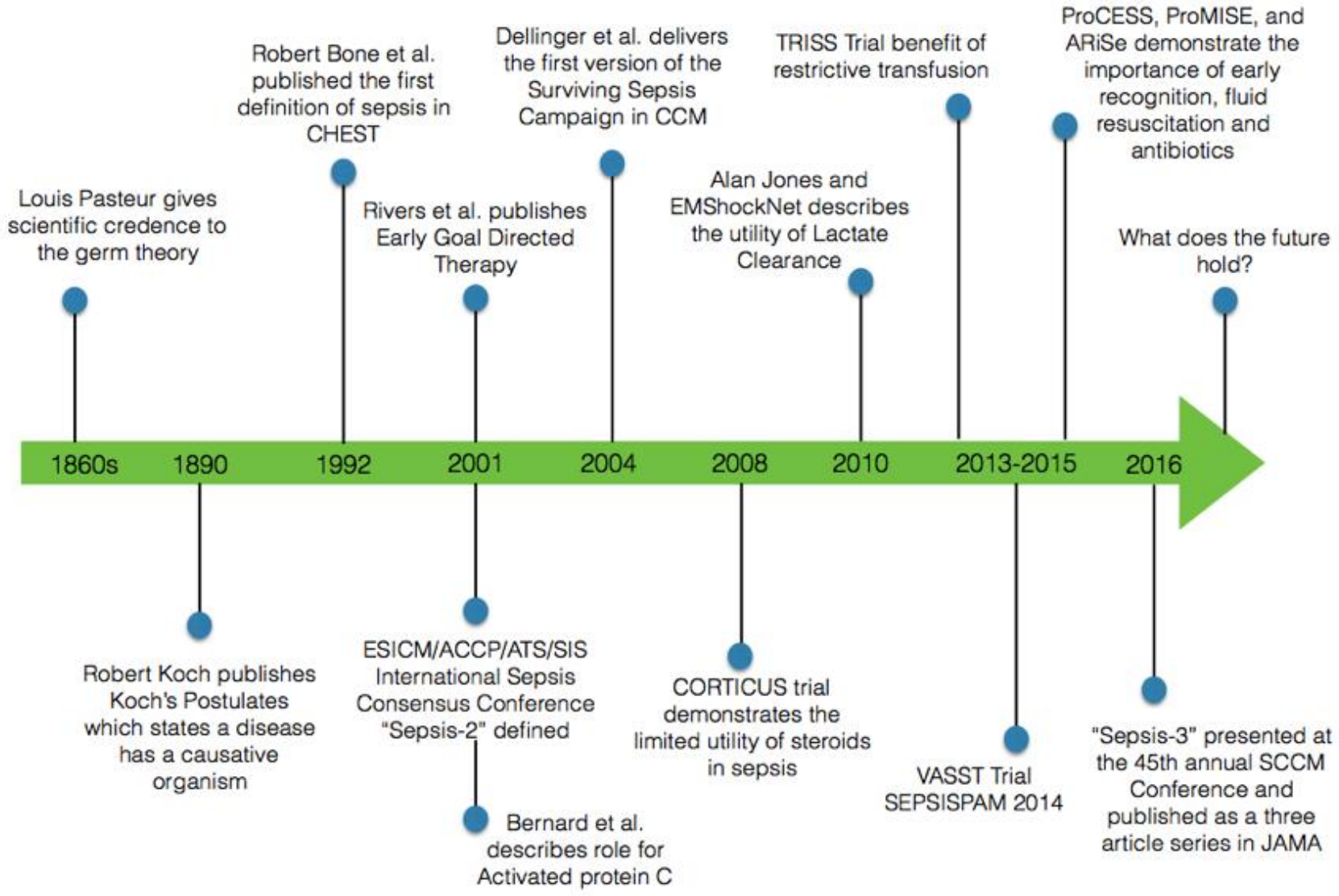
Louis Pasteur gives scientific credence to the germ theory
1860s
Robert Koch publishes Koch's Postulates which states a disease has a causative organism
1890
Robert Bone et al. published the first definition of sepsis in CHEST
1992
Rivers et al. publishes Early Goal Directed Therapy
ESICM/ACCP/ATS/SIS International Sepsis Consensus Conference "Sepsis-2" defined
2001
Bernard et al. describes role for Activated protein C
Dellinger et al. delivers the first version of the Surviving Sepsis Campaign in CCM
2004
Alan Jones and EMShockNet describes the utility of Lactate Clearance
2008
CORTICUS trial demonstrates the limited utility of steroids in sepsis
2010
TRISS Trial benefit of restrictive transfusion
VASST Trial SEPSISPAM 2014
2013-2015
ProCESS, ProMISE, and ARiSe demonstrate the importance of early recognition, fluid resuscitation and antibiotics
What does the future hold?
"Sepsis-3" presented at the 45th annual SCCM Conference and published as a three article series in JAMA
2016

JAMA The Journal of the American Medical Association

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CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) FREE

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DEFINITIONS

Sepsis	Septic shock
Life threatening Organ dysfunction Caused by a dysregulated host response To infection	Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone

CLINICAL CRITERIA

2001 vs 2016 Definitions of Sepsis [1,4]

	OLD	NEW
SEPSIS	SIRS + Suspected Infection	**SUSPECTED/DOCUMENTED INFECTION** + **2 or 3 on qSOFA** (HAT): **H**ypotension (SBP ≤100 mmHg) **A**MS (GCS ≤13) **T**achypnea (≥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

Sepsis Definitions: Old vs. 3.0

The overlap SIRS, infection, sepsis and inflammation

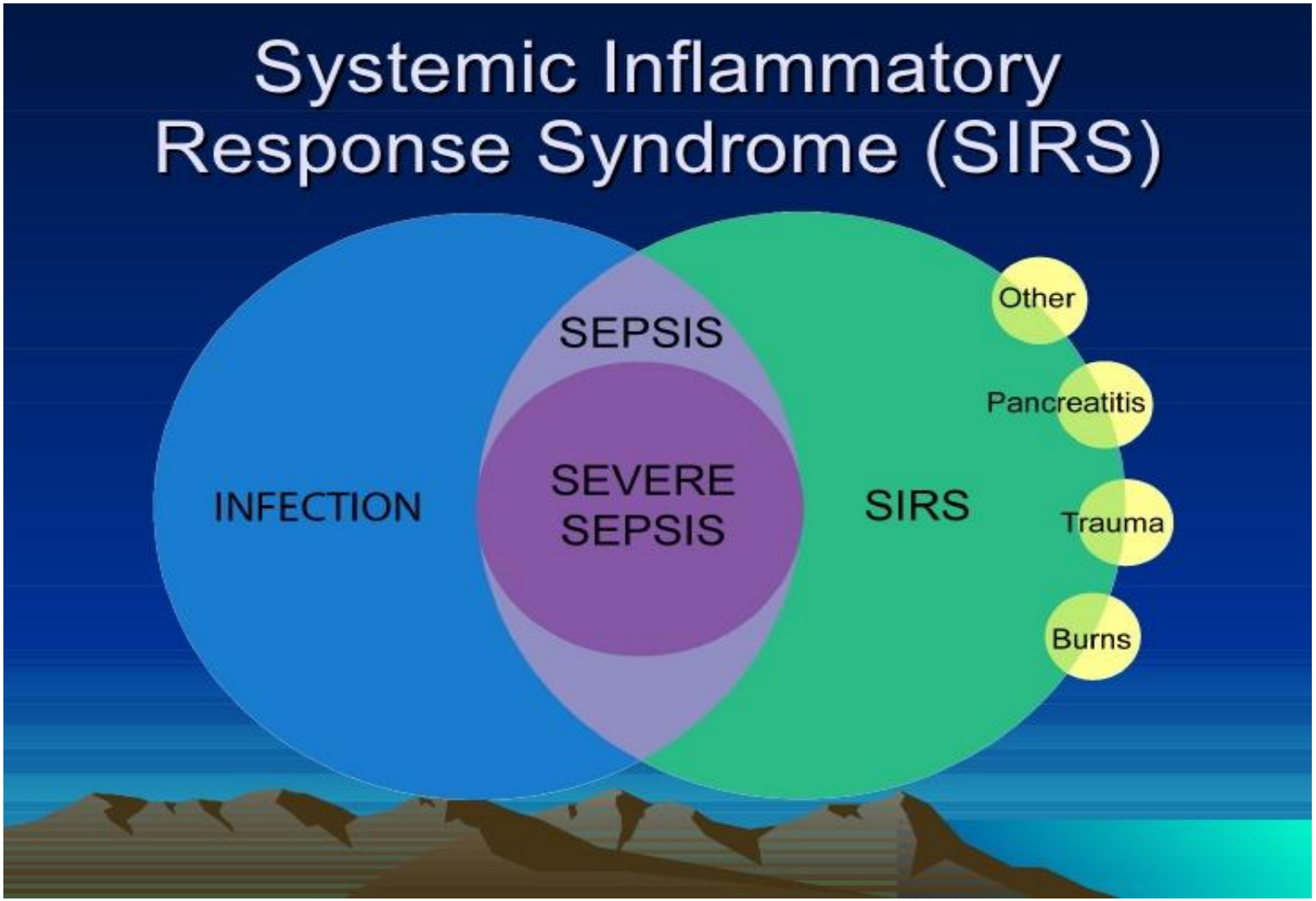
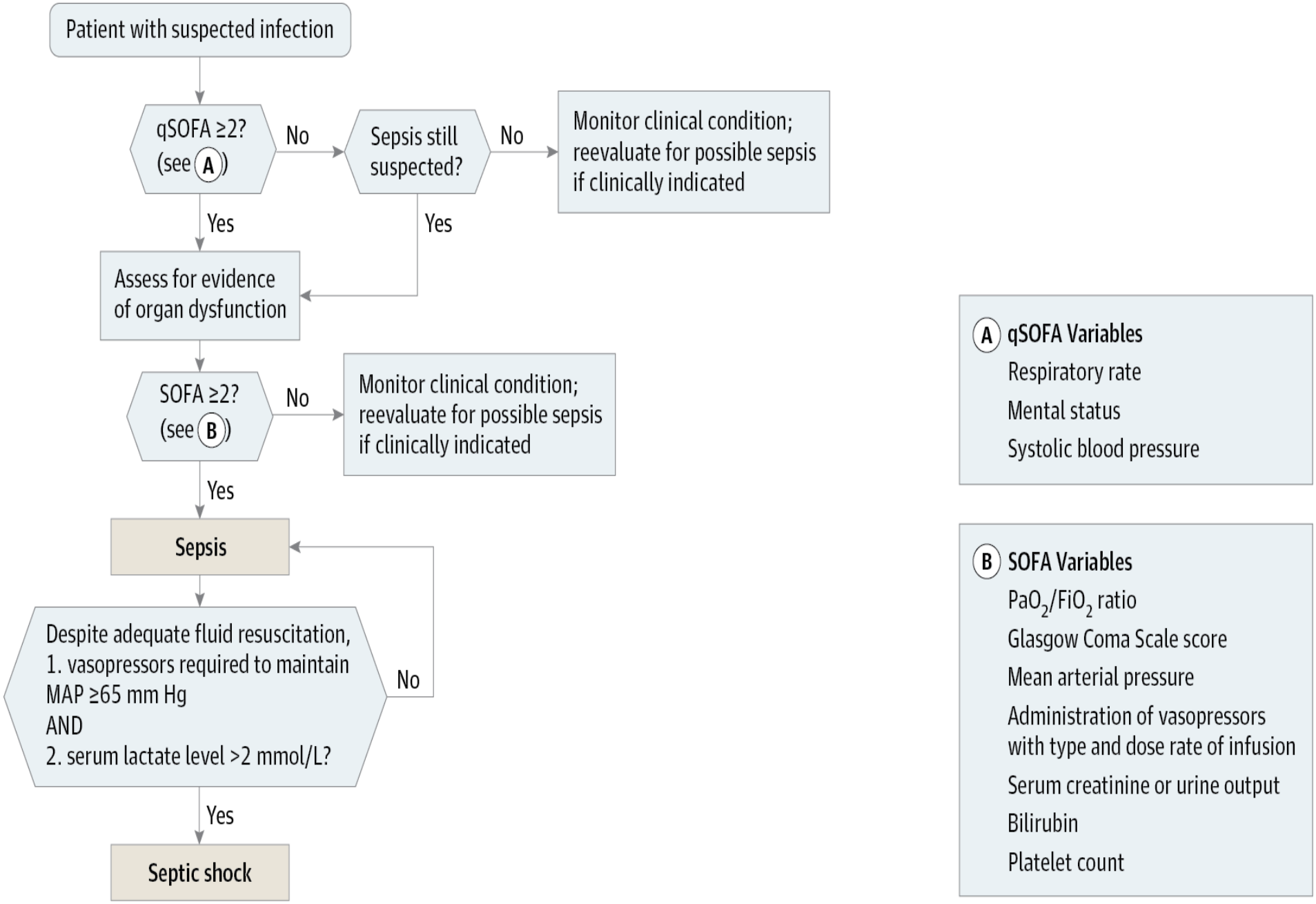


Table 1. Variables for Candidate Sepsis Criteria Among Encounters With Suspected Infection

Systemic Inflammatory Response Syndrome (SIRS) Criteria (Range, 0-4 Criteria)	Sequential [Sepsis-related] Organ Failure Assessment (SOFA) (Range, 0-24 Points)	Logistic Organ Dysfunction System (LODS) (Range, 0-22 Points)[a]	Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Range, 0-3 Points)
Respiratory rate, breaths per minute	Pao_2/Fio_2 ratio	Pao_2/Fio_2 ratio	Respiratory rate, breaths per minute
White blood cell count, 10^9/L	Glasgow Coma Scale score	Glasgow Coma Scale score	Glasgow Coma Scale score
Bands, %	Mean arterial pressure, mm Hg	Systolic blood pressure, mm Hg	Systolic blood pressure, mm Hg
Heart rate, beats per minute	Administration of vasopressors with type/dose/rate of infusion	Heart rate, beats per minute	
Temperature, °C	Serum creatinine, mg/dL, or urine output, mL/d	Serum creatinine, mg/dL	
Arterial carbon dioxide tension, mm Hg	Bilirubin, mg/dL	Bilirubin, mg/dL	
	Platelet count, 10^9/L	Platelet count, 10^9/L	
		White blood cell count, 10^9/L	
		Urine output, L/d	
		Serum urea, mmol/L	
		Prothrombin time, % of standard	


Patient with suspected infection
qSOFA ≥2? (see A)
No
Sepsis still suspected?
No
Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Yes
Yes
Assess for evidence of organ dysfunction
SOFA ≥2? (see B)
No
Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Yes
Sepsis
Despite adequate fluid resuscitation,
1. vasopressors required to maintain MAP ≥65 mm Hg
AND
2. serum lactate level >2 mmol/L?
No
Yes
Septic shock
A qSOFA Variables
Respiratory rate
Mental status
Systolic blood pressure
B SOFA Variables
PaO_2/FiO_2 ratio
Glasgow Coma Scale score
Mean arterial pressure
Administration of vasopressors with type and dose rate of infusion
Serum creatinine or urine output
Bilirubin
Platelet count

SURVIVING SEPSIS GUIDELINES

Surviving Sepsis Campaign

COMPARISON OF RECOMMENDATIONS FROM 2012 TO 2016

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

SURVIVING SEPSIS CAMPAIGN RECOMMENDATION HIGHLIGHTS

	2012	2016
SEPSIS DEFINITION	Systemic manifestation of infection + suspected infection Severe sepsis: sepsis + organ dysfunction	Life threatening organ dysfunction caused by dysregulated response to infection No severe sepsis category
INITIAL RESUSCITATION	at least 30 cc/kg in first 3 hours Crystalloid fluid (no recommendations on 0.9% NaCl vs balanced solution) Albumin if patients require "substantial" fluids (weak)	
	Protocolized care including CVP ScVO2 Normalize lactate	Use dynamic resuscitation markers (passive leg raise) Target MAP of 65mmHg Reassess hemodynamic status to guide resuscitation Normalize lactate
VASOPRESSORS	target MAP of 65 mmHg 1. Norepinephrine 2. Epinephrine if not at target MAP OR vasopressin to reduce norepinephrine requirement 3. Avoid dopamine in most patinets	
STEROIDS	Only indicated for patients with septic shock refractory to adequate fluids and vasopressors	
ANTIBIOTICS	One or more antibiotics active against presumed pathogen Combination therapy (double coverage) for neutropenic patients and pseudomonas	Initial broad spectrum antibiotics (ex: vancomycin + piperacillin-tazobactam) Against combined therapy (i.e. do not double cover pseudomonas) May use procalcitonin to guide de-escalation
SOURCE CONTROL	Achieve within 12 hours, if feasible	Achieve as soon as medically and logically feasible
VENTILATOR	6 cc/kg tidal volume prone patients with severe ARDS (P/F <150 in 2017 guideliens)	
	no recommendation	Against high frequency oscillatory ventilation (HFOV)
	weak recommendation for noninvasive ventilation in select patients with sepsis induced ARDS	Unable to make recommendation on noninvasive ventilation

Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med [Internet] 2017;1.

Initial resuscitation

Infusion venous fluid recommendation:

- Initial fluid challenge ≥ 1000ml or minimum of 30ml/kg of crystalloids in the 1st 4-6hours
  (strong recommendation, grade 1C)

- Crystalloids is the initial fluid for resuscitation
  (strong recommendation, grade 1A)

- Add albumin to the initial fluid resuscitation
  (weak recommendation, grade 2B)

Follow

- Dynamic over static variables be used to predict fluid responsiveness, where available
  (weak recommendation, low quality of evidence).

- Initial target mean arterial pressure (MAP) of 65 mm Hg in patients with septic shock requiring vasopressors
  (strong recommendation, moderate quality of evidence).

- Resuscitation to normalize lactate in patients with elevated lactate levels
  (weak recommendation, low quality of evidence).

Reassessment of volume status and tissue perfusion

- Either: Vital signs, cardiopulmonary, capillary refill, pulse, and skin findings
- Or two of the following:

✓CVP

✓ScvO2

✓Bedside cardiovascular ultrasound

✓Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

Antibiotics

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

- Abx within 1 hr hypotension: *79.9% survival*
- **Survival decreased *7.6%* with each hour of delay**
- Mortality increased by 2nd hour post hypotension
- Time to initiation of Antibiotics was the single **strongest predictor of outcome**

Antibiotics

1. Administration of IV antimicrobials be initiated as soon as possible after recognition and within one hour for both sepsis and septic shock

(strong recommendation, moderate quality of evidence)

2new. Empiric broad-spectrum therapy for patients presenting with sepsis or septic shock.

(strong recommendation, moderate quality of evidence).

3. Empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted (BPS).

Antibiotics

4. Against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury) (BPS).

5. Dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock (BPS).

6. Empiric combination therapy aimed at the most likely bacterial pathogen(s) for the initial management of septic shock

(weak recommendation, low quality of evidence)

Antibiotics

7. Combination therapy not be routinely used for ongoing treatment of most other serious infections, including bacteremia and sepsis without shock

(weak recommendation, low quality of evidence)

8^{new}. Against combination therapy for the routine treatment of neutropenic sepsis/bacteremia

(strong recommendation, moderate quality of evidence)

9. De-escalation with discontinuation of combination therapy in response to clinical improvement and/or evidence of infection resolution (BPS).

10. Antimicrobial treatment duration: 7 to 10 days
(weak recommendation, low quality of evidence).
11. Longer courses are appropriate in specific patients *(*)*
(weak recommendation, low quality of evidence).
12. Shorter courses are appropriate in some patients *(**)*
(weak recommendation, low quality of evidence).
13. Daily assessment for de-escalation (BPS).

(*) slow clinical response, undrainable foci of infection, bacteremia with S aureus, some fungal and viral infections, or immunologic deficiencies, including neutropenia
(**) rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with anatomically uncomplicated pyelonephritis

14new. Measurement of procalcitonin levels can be used to support *shortening the duration of antimicrobial therapy* in sepsis patients

(weak recommendation, low quality of evidence).

15new.Procalcitonin levels can be used to *support the discontinuation of empiric antibiotics*

(weak recommendation, low quality of evidence).

Source control

1. Specific anatomic diagnosis of infection requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock (BPS).

2. Prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established (BPS).

Thank you !!