A Quick Review on SSC 2021

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Oct 2021

Intensive Care Med
https://doi.org/10.1007/s00134-021-06506-y

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Check for updates

- ✓**Definition**
- ✓**Screening**
- ✓**Initial resuscitation**
- ✓**Infection management**
- ✓**Hemodynamic management**
- ✓**Additional therapy**

Definition

Sepsis is a life-threatening organ dysfunction caused by a deregulated host response to infection.

Septic shock is a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.

Initial Resuscitation

Initial Resuscitation

Resuscitation

SSC 2021 recommendation

Recommendations
4. Sepsis and septic shock are medical emergencies, and we **recommend** that treatment and resuscitation begin immediately *Best Practice Statement*

- **Timely, effective fluid resuscitation is crucial for the stabilization of sepsis-induced tissue hypoperfusion in sepsis and septic shock.**

Initial Resuscitation

Resuscitation

SSC 2021 recommendation

5. For patients with sepsis induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 h of resuscitation

Weak recommendation, low-quality evidence

- **To avoid over- and under-resuscitation, fluid administration beyond the initial resuscitation should be guided by careful assessment of intravascular volume status and organ perfusion.**

Resuscitation Assessment

Resuscitation

SSC 2021 recommendation

6. For adults with sepsis or septic shock, we **suggest** using dynamic measures to guide fluid resuscitation, over physical examination or static parameters alone

Weak recommendation, very low-quality evidence

Remarks

Dynamic parameters include response to a passive leg raise or a fluid bolus, using stroke volume (SV), stroke volume variation (SVV), pulse pressure variation (PPV), or echocardiography, where available

7. For adults with sepsis or septic shock, we **suggest** guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate

Weak recommendation, low-quality evidence

Remarks

During acute resuscitation, serum lactate level should be interpreted considering the clinical context and other causes of elevated lactate

8. For adults with septic shock, we **suggest** using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion

Weak recommendation, low-quality evidence

Dynamic parameters contain:

- PLR;
- Fluid bolus;

to assess SVV and/or PPV and/or CO.

Static parameters contain:

- MAP;
- CVP;
- HR.

Serum lactate is an important biomarker of tissue hypoxia and dysfunction, but is not a direct measure of tissue perfusion.

Temperature of the extremities, skin mottling and capillary refill time (CRT) have been validated and shown to be reproducible signs of tissue perfusion.

MAP cut-off

Resuscitation

SSC 2021 recommendation

Recommendation
9. For adults with septic shock on vasopressors, we **recommend** an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets *Strong recommendation, moderate-quality evidence*

- **Previous SSC guidelines recommended targeting a MAP of greater than 65 mm Hg for initial resuscitation.**

Infection

Diagnosis of infection

infection

SSC 2021 recommendation

Recommendation
11. For adults with suspected sepsis or septic shock but unconfirmed infection, we **recommend** continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected
Best Practice statement

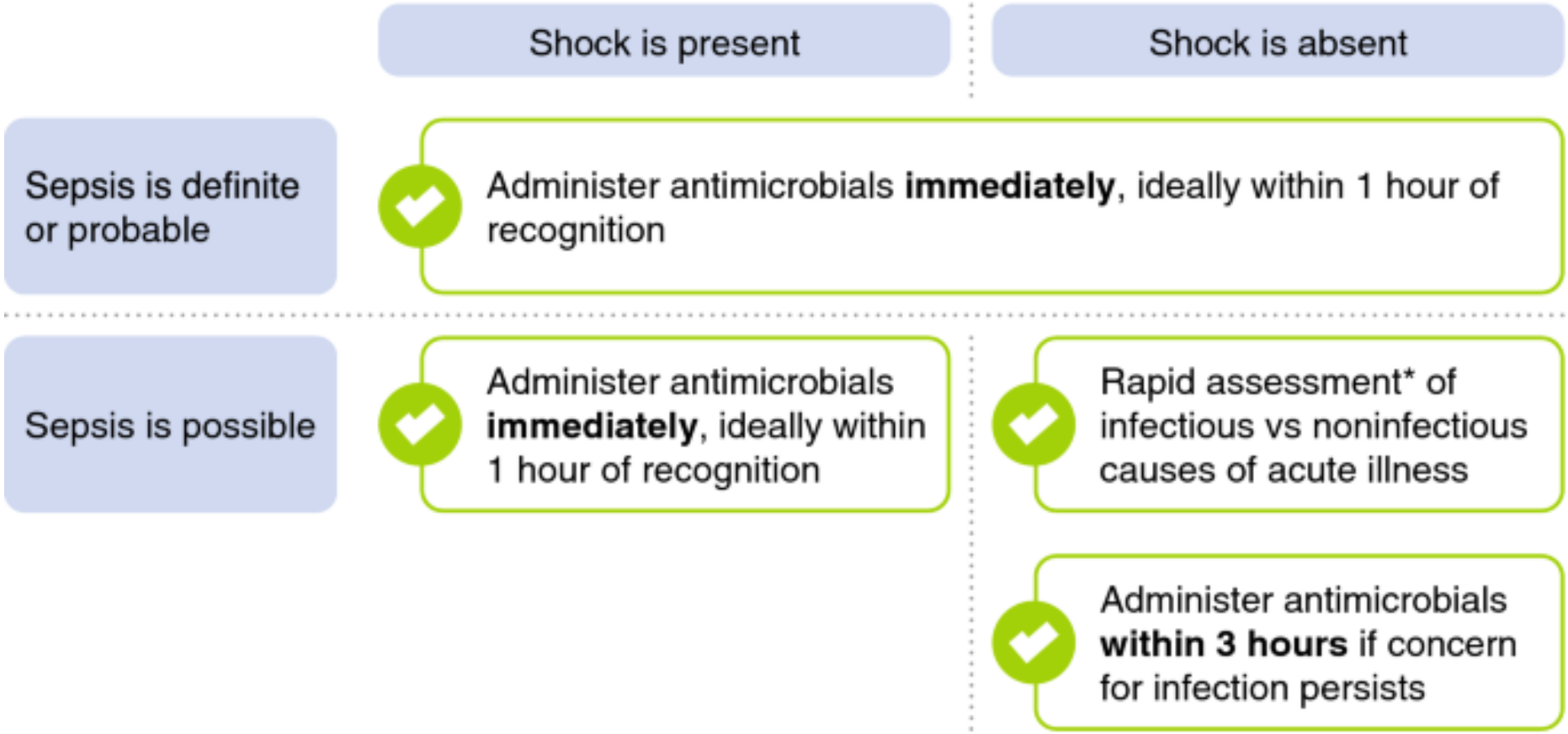
- **As a best practice statement, we recommended that appropriate routine microbiologic cultures (including blood) should be obtained before starting antimicrobial therapy in patients with suspected sepsis and septic shock if it results in no substantial delay in the start of antimicrobials (i.e. < 45 min).**

- **Thus, clinicians are strongly encouraged to discontinue antimicrobials if a non-infectious syndrome is demonstrated or strongly suspected.**

Antibiotic Timing

infection

SSC 2021 recommendation



*Rapid assessment includes history and clinical examination, tests for both infectious and non-infectious causes of acute illness and immediate treatment for acute conditions that can mimic sepsis. Whenever possible this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.

Biomarkers to start antibiotics

infection

SSC 2021 recommendation

Recommendation
16. For adults with suspected sepsis or septic shock, we **suggest against** using procalcitonin plus clinical evaluation to decide when to start antimicrobials, as compared to clinical evaluation alone *Weak recommendation, very low quality of evidence*

- **In a meta-analysis of 30 studies (3244 patients), procalcitonin had a pooled sensitivity of 77% and specificity of 79% for sepsis in critically ill patients.**

Source Control

infection

SSC 2021 recommendation

Recommendation
27. For adults with sepsis or septic shock, we **recommend** rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent source control and implementing any required source control intervention as soon as medically and logistically practical *Best Practice Statement*

Recommendation
28. For adults with sepsis or septic shock, 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 *Best Practice Statement*

Antimicrobial Choice: MRSA coverage

infection

SSC 2021 recommendation

Recommendations

17. For adults with sepsis or septic shock at high risk of methicillin resistant staph aureus (MRSA), we **recommend** using empiric antimicrobials with MRSA coverage over using antimicrobials without MRSA coverage

Best Practice statement

18. For adults with sepsis or septic shock at low risk of methicillin resistant staph aureus (MRSA), we **suggest against** using empiric antimicrobials with MRSA coverage, as compared with using antimicrobials without MRSA coverage

Weak recommendation, low quality of evidence

Vancomycin, Teicoplanin, Daptomycin, Linezolid

Antimicrobial Choice: MRSA coverage

infection

SSC 2021 recommendation

Failure to cover for MRSA in a patient with MRSA may be harmful,
But unnecessary MRSA coverage in a patient without MRSA may also be harmful.

Risk factors for MRSA infections

infection

SSC 2021 recommendation

- ✓ Prior history of MRSA infection or colonization,
- ✓ Recent IV antibiotics,
- ✓ History of recurrent skin infections or chronic wounds,
- ✓ Presence of invasive devices,
- ✓ Hemodialysis,
- ✓ Recent hospital admissions and severity of illness

Antimicrobial Choice: Double coverage for G-

infection

SSC 2021 recommendation

Recommendations
19. For adults with sepsis or septic shock and high risk for multidrug resistant (MDR) organisms, we **suggest** using two antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent *Weak recommendation, very low quality of evidence*
20. For adults with sepsis or septic shock and low risk for MDR organisms, we **suggest against** using two Gram-negative agents for empiric treatment, as compared to one Gram-negative agent *Weak recommendation, very low quality of evidence*
21. For adults with sepsis or septic shock, we **suggest against** using double gram-negative coverage once the causative pathogen and the susceptibilities are known *Weak recommendation, very low quality of evidence*

Antimicrobial Choice: Double coverage for G-

infection

SSC 2021 recommendation

Risk of antimicrobial-associated undesirable effects:

- ✓ **Direct toxicity,**
- ✓ ***Clostridioides difficile* infection**
- ✓ **Development of antibiotic resistance**

Risk factors for MDR pathogens

infection

SSC 2021 recommendation

- ✓ **Proven infection or colonization with antibiotic-resistant organisms within the preceding year,**
- ✓ **Local prevalence of antibiotic-resistant organisms,**
- ✓ **Hospital-acquired/healthcare associated (versus community acquired)**
- ✓ **Broad-spectrum antibiotic use within the preceding 90 days,**
- ✓ **Hospitalization abroad within the preceding 90 days.**

Antibiotics choice for double coverage for G- infection

SSC 2021 recommendation

Piperacillin-Tazobactam, Ceftazidime, Cefepime, Meropenem, Imipenem

+

Ciprofloxacin, Levofloxacin,

or

Aminoglycoside (Amikacin, Gentamicin)

or

Colistin

Antifungal Therapy

infection

SSC 2021 recommendation

Recommendations
22. For adults with sepsis or septic shock at high risk of fungal infection, we **suggest** using empiric antifungal therapy over no antifungal therapy *Weak recommendation, low quality of evidence*
23. For adults with sepsis or septic shock at low risk of fungal infection, we **suggest against** empiric use of antifungal therapy *Weak recommendation, low quality of evidence*

Risk factors for fungal infections

infection

SSC 2021 recommendation

- ✓ **Patients with febrile neutropenia who fail to defervesce after 4–7 days of broad spectrum antibacterial**

Risk factors for Candida

infection

SSC 2021 recommendation

Candida colonisation at multiple sites [177–179]
Surrogate markers such as Serum Beta-D-Glucan assay [177]
Neutropenia [180, 181]
Immunosuppression [173, 180, 181]
Severity of illness (High APACHE score) [182, 183]
Longer ICU length of stay [183]
Central venous catheters and other intravascular devices [168, 180, 181, 184]
Persons who inject drugs [185]
Total parenteral nutrition [186]
Broad spectrum antibiotics [178, 187]
Gastrointestinal tract perforations and anastomotic leaks [186, 188–190]
Emergency gastrointestinal or hepatobiliary surgery [190]
Acute renal failure and haemodialysis [186, 188]
Severe thermal injury [191–193]
Prior surgery [186]

Risk factors for endemic yeast

infection

SSC 2021 recommendation

Antigen markers such as cryptococcal, histoplasma or blastomyces assays [194–196]
HIV infection [197–200]
Solid organ transplantation [199, 201–203]
High dose corticosteroid therapy [199]
Haematopoietic stem cell transplantation [204]
Certain biologic response modifiers [205, 206]
Diabetes mellitus [207]

Risk factors for mold infection

infection

SSC 2021 recommendation

Neutropenia [204, 208]
Surrogate markers such as Serum or Bronchoalveolar Lavage Galactomannan Assay [209–211]
Haematopoietic stem cell transplantation [204, 208, 212]
Solid organ transplantation [202, 212–214]
High dose corticosteroid therapy [215, 216]
Certain biologic response modifiers [206, 217, 218]

Choice of Antifungal

infection

SSC 2021 recommendation

The choice of antifungal agent for empiric therapy depends on multiple issues including:

- ✓ **Host factors,**
- ✓ **Prior colonization and infection,**
- ✓ **Prior exposure to prophylactic or therapeutic antifungal therapy,**
- ✓ **Comorbidities,**
- ✓ **The toxicities and drug interactions of the therapeutic options.**

Antiviral therapy

infection

SSC 2021 recommendation

Recommendation
24. We make **no recommendation** on the use of antiviral agents

Risk factors for viral infection

infection

SSC 2021 recommendation

In these patients HSV, EBV, CMV, and respiratory viruses such as adenoviruses, can cause severe disease:

- ✓ **Patients with neutropenia**
- ✓ **HIV infection**
- ✓ **Hematological malignancies**
- ✓ **Hematopoietic stem cell transplantation**
- ✓ **Solid organ transplants**

Delivery of antibiotics

infection

SSC 2021 recommendation

Recommendation
25. For adults with sepsis or septic shock, we **suggest** using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion *Weak recommendation, moderate quality of evidence*

Delivery of antibiotics

infection

SSC 2021 recommendation

- **Beta-lactam antibiotics may be subject to changes in important pharmacokinetic parameters in the setting of sepsis and septic shock resulting in sub-therapeutic concentrations.**

- **As opposed to conventional intermittent infusion (infusion ≤ 30 min), administration by prolonged IV infusion results in sustained beta-lactam concentrations which align with the pharmacodynamics of these drugs.**
  - ✓ **Extended infusion (over at least half of the dosing interval)**
  - ✓ **Continuous infusion (over 24 hours)**

Delivery of antibiotics

infection

SSC 2021 recommendation

Cefepime, Ceftazidime, Piperacillin-Tazobactum, Meropenem are stable in a 3 to 4-hours infusion.

Loading dose

infection

SSC 2021 recommendation

Administration of a loading dose of antibiotic before prolonged infusion is essential to avoid delays to achieving effective beta-lactam concentrations.

Pharmacokinetic & Pharmacodynamic

infection

SSC 2021 recommendation

Recommendation
26. For adults with sepsis or septic shock, we **recommend** optimising dosing strategies of antimicrobials based on accepted pharmacokinetic/pharmacodynamic (PK/PD) principles and specific drug properties *Best Practice Statement*

Pharmacokinetic & Pharmacodynamic

infection

SSC 2021 recommendation

- **Antibiotics are subject to changes in PK/PD parameters in sepsis and septic shock where resultant concentrations may be too low risking clinical failure, or too high leading to toxicity.**

  - ✓ **Augmented renal clearance**
  - ✓ **AKI,**
  - ✓ **Hypoalbuminemia,**
  - ✓ **RRT,**
  - ✓ **Extracorporeal membrane oxygenation**

Pharmacokinetic & Pharmacodynamic

infection

SSC 2021 recommendation

Drug or drug class	PK/PD index associated with bacterial killing or efficacy	Drug concentration target	Considerations for optimised dosing[a]
Antibacterials			
Aminoglycosides	AUC_{0-24}/MIC; C_{max}/MIC	AUC 70–100 C_{max}/MIC 8–10	Use extended interval dosing with patient weight and kidney function
Beta-lactams	$fT_{>MIC}$	C_{min} > MIC	Use prolonged infusions, consider patient weight and kidney function
Colistin	AUC_{0-24}/MIC	Unspecified	Use patient weight and kidney function
Daptomycin	AUC_{0-24}/MIC; C_{max}/MIC	AUC_{0-24}/MIC > 200	Use patient weight and kidney function
Fluoroquinolones	AUC_{0-24}/MIC; C_{max}/MIC	AUC_{0-24}/MIC 80–125	Use kidney function
Vancomycin	AUC_{0-24}/MIC	AUC_{0-24}/MIC 400	Use patient weight and kidney function
Antifungals			
Fluconazole	AUC_{0-24}/MIC	AUC_{0-24}/MIC 100	Use patient weight and kidney function
Posaconazole	AUC_{0-24}/MIC	C_{min} 1–4 mg/L	Use formulation-specific dose
Voriconazole	AUC_{0-24}/MIC	C_{min} 2–6 mg/L	Use patient weight

De-scalation of antibiotics

infection

SSC 2021 recommendation

Recommendation
29. For adults with sepsis or septic shock, we **suggest** daily assessment for de-escalation of antimicrobials over using fixed durations of therapy without daily reassessment for de-escalation *Weak recommendation, very low quality of evidence*

Duration of antibiotics

infection

SSC 2021 recommendation

Recommendation
30. For adults with an initial diagnosis of sepsis or septic shock and adequate source control, we **suggest** using shorter over longer duration of antimicrobial therapy *Weak recommendation, very low quality of evidence*

Biomarkers for discontinue antibiotics

diagnosis

SSC 2021 recommendation

Recommendation
31. For adults with an initial diagnosis of sepsis or septic shock and adequate source control where optimal duration of therapy is unclear, we **suggest** using procalcitonin AND clinical evaluation to decide when to discontinue antimicrobials over clinical evaluation alone *Weak recommendation, low quality of evidence*

Thanks for attention