

Sepsis: Updates

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ABSTRACT

Sepsis is a life-threatening organ dysfunction that results from the body's response to infection. To protect against sepsis prompt recognition, careful hemodynamic support, appropriate antibiotics, and control of the source of infection are required. With the trend in management, one should understand sepsis physiology and follow the best practice guidelines. Sepsis and particularly septic shock should be recognized as medical emergency as in stroke and acute myocardial infarction. Early recognition and rapid institution of resuscitative measures are critical. Although recognition of sepsis can be a challenge and the best management practices continue to evolve.

This article reviews guidance on the diagnosis and management of sepsis and septic shock with attention to maximizing adherence to best practice and controversies in definition, diagnostic criteria, and management.

Key words: *Sepsis, Septic shock, Organ dysfunction*

INTRODUCTION

Sepsis is triggered by a systemic infection and is a life-threatening, dysregulated response to infection. Immune abnormalities induced by invading pathogens or tissue damage produce both the inflammatory and immunosuppressive features of the disease, which causes organ dysfunction and can lead to death. Sepsis may lead to cellular abnormalities and perfusion deficits, causing septic shock.

Optimal management strategies for sepsis have been an issue of intense research since a landmark study by Rivers and colleagues¹ published in 2001 identified a 16% mortality reduction with randomization to an early aggressive care bundle termed early goal-directed therapy (EGDT). EGDT involves the administration of fluids, inotropes, and blood, and the achievement of hemodynamic goals to improve tissue oxygenation, as indicated by a central venous oxygen saturation (SpO_2) > 70%.

After 3 recent multicenter trials (in UK, USA & Australia) failed to validate the results of that study, however, EGDT is no longer recommended. Nonetheless, in general, early,

aggressive management of sepsis is recommended and has been shown to improve outcomes².

ESICM (European Society of Intensive Care Medicine) & SCCM (Society of Critical Care Medicine) published a guideline for management of sepsis³, "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016". Our topic is to overview the guideline with recent update.

Definition & Diagnosis of SEPSIS & SEPTIC SHOCK

The diagnosis of sepsis has undergone a metamorphosis since the inception of standardized definitions in 1991. Shifting away from the systemic inflammatory response syndrome (SIRS) criteria previously utilized, in 2014 the Society of Critical Care Medicine and the European Society of Intensive Care Medicine convened a task force and, by an expert consensus process, agreed in 2016 on updated definitions and criteria to be tested clinically. The Third International Consensus Definitions for Sepsis and Septic Shock ("Sepsis-3") redefined sepsis as below.

Table. 1: Sequential Organ Failure Assessment Score (SOFA Score)

Variables	SOFA Score				
	0	1	2	3	4
Respiratory	PaO ₂ /FiO ₂ >400 SpO ₂ / FiO ₂ > 302	PaO ₂ /FiO ₂ <400 SpO ₂ / FiO ₂ <302	PaO ₂ /FiO ₂ <300 SpO ₂ / FiO ₂ <221	PaO ₂ /FiO ₂ <200 SpO ₂ / FiO ₂ <142	PaO ₂ /FiO ₂ <100 SpO ₂ / FiO ₂ <67
Cardiovascular (doses in mcg/kg/min)	MAP ≥ 70mm hg	MAP ≥ 70 mm Hg	Dopamine ≤ 5	Dopamine > 5 Norepinephrine ≤ 0.1	Dopamine >15 Norepinephrine > 0.1
Liver (bilirubin, mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12
Renal (creatinine mg/dL)	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9	> 5.0
Coagulation (platelets x 10 ³ /mm ³)	≥150	<150	<100	<50	<20
GCS Score	15	13-14	10-12	6-9	<6

According to sepsis -3, a new (or presumed new) increase in SOFA score above baseline in the presence of infection makes the diagnosis of sepsis. Increasing SOFA scores are associated with incremental increases in mortality. MAP=Mean arterial pressure, PaO₂:Arterial Oxygen Pressure, FiO₂:Fraction of inspired Oxygen.

SEPSIS:

Sepsis is a life-threatening organ dysfunction due to a dysregulated host response to infection.

Sepsis clinical criteria: Organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score.

Sepsis-3 also derived a bedside assessment tool for sepsis screening in patients with infection who are not in intensive care units (ICUs). Called the *quick SOFA* (qSOFA) score, it includes 1 point for each of 3 criteria.

qSOFA

Patients with suspected infection who have 2 or more of: (Mnemonic **HAT**)

- Hypotension – systolic blood pressure < 100 mmHg
- Altered mental status - GCS <15
- Tachypnoea - respiratory rate ≥22 breaths /min

This scoring system does not act as the sole criteria for ruling sepsis in or out, rather it is an adjunct to aid early recognition of patient at high risk for sepsis.

In MICU of Apollo Hospital Dhaka, we recorded SOFA score for last three months. We studied over 30 patients randomly.

Overall result of mortality is as follows:

SOFA score > 11, mortality rate is > 85%.

SOFA score < 11, mortality rate is < 15%.

It is just predicted mortality rate by using SOFA score. It shouldn't interfere with management plan. It has prognostic value during admission.

Septic Shock:

Sepsis-3 also redefined septic shock as “hypotension not responsive to fluid resuscitation,” with the added requirement for vasopressors to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg and a lactate > 2 mmol/L

Table. 2: Differentiate other types of shock:

Traits	Septic	Hypovolemic	Cardiogenic
Character of pulse	Full Bounding pulse	Weak thready pulse	Weak thready pulse
Periphery/Skin condition.	Warm, pink, flushed skin.	Cool, Pale skin	Cool, pale. Sweaty/moist skin due to sympathetic over activity.
Fever	Usually present	Usually not present	Usually not present
Shortness of breath	May be present (if source of infective foci is lungs)	Absent	Present, due to lung congestion
Lungs	Usually clear	Clear	Basal creps (due to LVF)
Precordium	Clear	Clear	Muffling of heart sound in case of temponade
CVP	Variable	Low (<8 cmH ₂ O)	High (>12 cmH ₂ O)
Low BP, Tachycardia, Decrease urine output.	Common feature in septic, hypovolemic & cardiogenic shock.		

Table. 3: Comparison with previous definition:

Sepsis category	Sepsis-3 (2016)	sepsis-2 (2001)
Sepsis	SOFA score >2 + Suspected Infection	2 of 4 SIRS criteria + Suspected Infection
Severe sepsis	Not included in 2016 guideline	Sepsis + two or more organ dysfunction or lactate > 4
Septic Shock	Vasopressor requirement to maintain MAP > 65 mmHg + Serum lactate > 2 mmol/L.	Sepsis induced hypotension persisting after adequate fluid resuscitation + presence of organ dysfunction.

Systemic Inflammatory Response Syndrome (SIRS): Any two of the four signs of inflammation: (1). T >100.9⁰ For < 96.8⁰F (2). HR>90/minute (3). Resp> 20/minute of PaCO₂<32 (4). WBC> 12000 or < 4000

Timeline of the SSC (Surviving Sepsis Campaign) Guidelines:

- 1992- First working definition of sepsis & SIRS by Bone et al.
- 2001-Early goal-directed therapy (EGDT)
- 2002- SSC was launched by SCCM & ESICM
- 2004- First sepsis management guidelines which they update in every 4th year.
- 2012- Sepsis 3 Hour & 6 Hour Bundle was launched.
- 2014- The sepsis-3 task force convened SCCM, ESICM.
- 2016- Most recent sepsis Guidelines.
- 2018- Update and “Hour-1 Bundle”

Investigation to support sepsis:

1. Total Leukocyte count
2. Lactate- Marker of tissue hypoperfusion
3. Biomarker:
 - CRP
 - Procalcitonin
 - Cytokines
 - Newer Marker.
4. Source of infection identification according to suspicion.
5. Blood culture (Both aerobic & anerobic)
6. Urine culture
7. Sputum/Tracheal Aspirate/Catheter tip/wound swab/Pus culture.

Management of Sepsis & Septic Shock:

We mentioned in the timeline SSC guideline suggest “3 hour & 6-hour bundle” care for management of sepsis in 2012⁴. In 2018 they compiled this “3 hour & 6 hour” to Hour-1 Bundle⁵.

#Surviving Sepsis Campaign Care Bundles: 3 hours & 6-hour bundle in 2012:

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 ≥ 4 mmol/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 (ScvO₂)*
- 7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥ 8 mm Hg, ScvO₂ of $\geq 70\%$, and normalization of lactate.

#Surviving Sepsis Campaign Hour-1 Bundle of Care Elements: in 2018

- Measure lactate level*
- Obtain blood cultures before administering antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30mL/kg crystalloid for hypotension or lactate level ≥ 4 mmol/L.
- Apply vasopressors if hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg.

* Remeasure lactate if initial lactate is elevated (> 2 mmol/L).

*This is also not recommended now.

#The UK Sepsis Trust was founded in 2012 by world-leading sepsis expert, NHS consultant Dr Ron Daniels BEM. They recommend “SEPSIS SIX” to be implemented within first hour⁶

1. Give high flow oxygen via non rebreathing mask.
2. Take blood cultures & consider source control
3. Give IV antibiotics according to local protocol.
4. Start IV fluid resuscitation by Hartmann’s or equivalent
5. Check lactate
6. Monitor hourly urine output. Consider catheterization.

Summary of the above-mentioned management: as shown in table. 4

Table. 4: Sepsis Six Bundle

To be Completed within first hour of admission
 Actions should be carried out simultaneously

1	<p>Administer Supplementary oxygen (if required)</p> <ul style="list-style-type: none"> Aim to keep Saturation > 94 % COPD: Adjust Target Saturations to 88-92%
2	<p>Blood Culture & Source Management</p> <ul style="list-style-type: none"> Take Blood cultures (before IV antibiotic) Think source confirmation and control Consider also sputum, urine, CSF, line culture/removal Involve appropriate surgical team / radiologist as indicated For Community Acquired Pneumonia start 4-hour CAP bundle
3	<p>Give IV antibiotics</p> <ul style="list-style-type: none"> Administer broad spectrum antibiotic according to local antimicrobial policy
4	<p>Give a fluid challenge (Check and monitor response) IF SBP < 90 mmHg or Lactate > 2</p> <ul style="list-style-type: none"> Give 500ml-1000 ml Hartmann’s or 0.9% NaCl over 15-30 mins. repeat once if necessary The use of Balanced crystalloid (Lactated ringer’s solution/Hartmann’s solution) resulted in a lower rate of adverse kidney effect than Normal Saline⁷. Colloid have no extra benefit over Crystalloid. Don’t use HES Albumin may be used when substantial amount of crystalloid is needed. Exclude other causes of shock before giving up to 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L Target: MAP ≥ 65 mmHg. Start inotropes if MAP ≤ 65 after or during fluid resuscitation. Choice of inotropes: 1st choice: Noradrenaline. 2nd Choice: Noradrenaline + vasopressin. If 2nd choice failed, give IV steroid (Hydrocortisone). If target MAP ≥ 65 mmHg is not achieved Add epinephrine with Noradrenaline & vasopressin. If still (MAP ≥ 65) target is not achieved Add Dopamine (for patient with bradycardia) or Phenylephrine (for patient with tachycardia). <p>If SBP > 90 mmHg and Lactate < 2 consider IV fluids according to urine output, CVP, Vital Sign.</p>
5	<p>Measure lactate</p> <ul style="list-style-type: none"> Obtain blood gas- venous or arterial If lactate > 4 mmol/L refer to critical care Ensure samples are sent for CBC, CRP, U+E, LFT, RFT, coag. screen Repeat lactate after fluid challenge to see lactate clearance. Use Capillary Refilling Time (CRT) if lactate measurement unavailable⁸. Normal CRT < 2 sec Target to normalize lactate within 24 hours.
6	<p>Measure Urine Output</p> <ul style="list-style-type: none"> Ensure hourly fluid balance chart commenced Catheterize if AKI /SBP < 90 / Lactate > 2 Monitor Vital Signs at 15-30 mins intervals until stable. Target urine output at least 0.5 ml/kg/hour

Goal of Resuscitation: (During the first 6 hour of resuscitation)

- MAP ≥ 65 mmHg.
- Urine Output ≥ 0.5 ml/kg/hr. ScvO₂ $\geq 70\%$.
- Hemoglobin 7-9 gm/dL

- Blood Glucose ≤ 10 mmol/L.
- CVP 8-12cmH₂O & 12-15 cmH₂O (For Ventilated patient). CVP is not recommended now. Guideline suggest using dynamic parameters to guide fluid balance such as IVC

collapsibility index, PPV (pulse pressure variation), PLR (Passive leg rising test), SVV (stroke volume variation) whenever possible.

Other recommendations of the SSC guidelines:

- Transfuse PRBC when HB < 7 gm/dL. Target HB 7-9 gm/dL Exceptions are MI, IHD, polytrauma.
- Monitor Vitals, Bi-Basal Creeps, U/O, PLR(Passive leg rising test)PPV(pulse pressure variation),CRT(Capillary refilling time),IVC collapsibility index through USG,SVV(stroke volume variation) by ECHO, CVP to correct fluid balance.
- Ensure DVT prophylaxis & Stress Ulcer prophylaxis.
- Consider low dose steroid (Hydrocortisone 50 mg q6hr*7d or until ICU discharge followed by taper over 3d) if hypotension persists despite adequate fluid resuscitation & vasopressor therapy. IV vitamin C 1.5g q6hr*4d or until ICU discharge, IV thiamine 200mg q12hr*4d or until ICU discharge⁹.
- Maintain sedation & Analgesia according to protocol.
- Start early Enteral feeding within 24 to 48 hours in low calorie & gradually increase toward the calorie & protein goal over the next few days. If patient is hemodynamically unstable & on high inotropes support consider TPN. Additional TPN may be considered where Enteral Nutrition can't be reached within the first 7 days. Use prokinetics (metoclopramide ± erythromycin) for feeding intolerance¹⁰.
- SSC guideline recommends against the use of NaHCO₃ if pH ≥7.15
Early identification of organ dysfunction by using SOFA score & start support of the failing organ.

CONCLUSION

Sepsis is a Medical Emergency. Sepsis and septic shock are leading cause of mortality worldwide. Early detection of sepsis without organ dysfunction can be treated at home with hospital supervision with appropriate antibiotics. Most

people who have sepsis detected at early stage make a full recovery.

Almost all patients with sepsis and septic shock require admission in hospital. In addition, patient with septic shock require admission to an Intensive Care Unit (ICU) & also require multiple organ support. However, sepsis is treatable if it is identified early & treated appropriately & most cases leads to full recovery with no lasting problems.

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