What the ED clinician needs to know about SEPSIS - 3

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Barts Health
Aims:

(1) To review the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

(2) Consider their strengths and limitations

(3) Suggest how I think they should be applied to the emergency department
what do I do now?
Old definitions (2003)

- Sepsis
- Severe sepsis
- Septic shock
Sepsis = infection + SIRS
SIRS criteria

• Are any 2 of the following present?
  • Heart rate > 90 /min
  • Respiratory rate > 20 /min or PaCO2 <4.3 kPa
  • WCC > 12 or < 4 x 10⁹/L or >10% immature bands
  • Temperature > 38°C or < 36°C
• Uncomplicated sepsis = infection + SIRS

• Severe sepsis = sepsis + one or more organ dysfunction

• Septic shock = sepsis + hypotension despite adequate fluid resuscitation or lactate >4 mmol/L at any point
Why were new definitions required?

• Last reviewed 2001

• Limitations of SIRS

• Definitions severe sepsis/ septic shock inconsistently used
Problems SIRS

• Not very good at separating infected patients who will do badly from those who will do well.

• SIRS often = appropriate reaction to infection

• Many hospitalised patients meet SIRS criteria

• Recent study showed demonstrated that 1 in 8 patients admitted to critical care units with infection and new organ failure did not have the requisite minimum of 2 SIRS criteria to fulfill the definition of sepsis
Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).
How the Sepsis-3 guidelines were developed

• Working group put together by Society Critical Care Medicine and European Society Intensive Care Medicine

• 19 members (crit care, ID, surgery, pulmonary specialists)
  • Expert opinion
  • Literature searches
  • Big data analysis

• Then sent for peer review and endorsement 31 societies including European Resuscitation Council & Academy of Medical Royal Colleges (UK)
Aims – differentiate sepsis from uncomplicated infection:

• (1) Pathophysiological definition

• (2) Operational definition (clinical criteria)

• (3) Bedside screening tool
Pathophysiological definition

• **Sepsis** is life-threatening organ dysfunction due to dysregulated host responses to infection.

• **Septic shock** is a subset of sepsis where underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
No more severe sepsis. No more ‘simple sepsis’. Just sepsis and septic shock.
How the operational definition & screening tool were derived

• Retrospective cohort study of patients with infection. Looking at what consolidation of clinical features could predict poor outcome.

• Large data sets from electronic health records
• Derivation and verification studies performed.
Inclusion

• >/ 18 years old

• Suspected infection: defined as combination having body fluid sent for culture and antibiotics given
Outcome

• No gold standard

• Proxy outcomes for sepsis = in hospital mortality or need for ICU >/ 3 days
Clinical criteria

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

• So sepsis = infection + increase in SOFA score of 2 or more

• This group have 10% mortality
What is a SOFA score?
Components of SOFA score

- Respiratory (PaO2/FiO2 ratio)
- Coagulation (platelets)
- Liver (bilirubin)
- Cardiovascular (MAP and need for inotropes and vasopressors)
- GCS
- Renal (creatinine and urine output)
## SOFA score

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{PaO}_2/\text{FiO}_2 ), mm Hg (kPa)</td>
<td>≥400 (53.3)</td>
<td>&lt;400 (53.3)</td>
<td>&lt;300 (40)</td>
<td>&lt;200 (26.7) with respiratory support</td>
<td>&lt;100 (13.3) with respiratory support</td>
<td></td>
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<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Platelets, ( \times 10^3 ) /µL</td>
<td>≥150</td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
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<tr>
<td><strong>Liver</strong></td>
<td></td>
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<tr>
<td>Bilirubin, mg/dL (µmol/L)</td>
<td>&lt;1.2 (20)</td>
<td>1.2-1.9 (20-32)</td>
<td>2.0-5.9 (33-101)</td>
<td>6.0-11.9 (102-204)</td>
<td>&gt;12.0 (204)</td>
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<tr>
<td><strong>Cardiovascular</strong></td>
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<tr>
<td>MAP ≥70 mm Hg</td>
<td>MAP &lt;70 mm Hg</td>
<td>Dopamine &lt;5 or dobutamine (any dose)(^b)</td>
<td>Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1(^b)</td>
<td>Dopamine &gt;15 or epinephrine &gt;0.1 or norepinephrine &gt;0.1(^b)</td>
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<tr>
<td><strong>Central nervous system</strong></td>
<td></td>
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<tr>
<td>Glasgow Coma Scale score(^c)</td>
<td>15</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
<td></td>
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<tr>
<td><strong>Renal</strong></td>
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<tr>
<td>Creatinine, mg/dL (µmol/L)</td>
<td>&lt;1.2 (110)</td>
<td>1.2-1.9 (110-170)</td>
<td>2.0-3.4 (171-299)</td>
<td>3.5-4.9 (300-440)</td>
<td>&gt;5.0 (440)</td>
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<tr>
<td>Urine output, mL/d</td>
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Abbreviations: \( \text{FiO}_2 \), fraction of inspired oxygen; MAP, mean arterial pressure; \( \text{PaO}_2 \), partial pressure of oxygen.

\(^a\) Adapted from Vincent et al.\(^{27}\)

\(^b\) Catecholamine doses are given as µg/kg/min for at least 1 hour.

\(^c\) Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.
### Ability to predict mortality outside of the ICU

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<th>Area under the ROC curve</th>
<th>Sensitivity for mortality</th>
<th>Specificity for mortality</th>
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<td>SIRS &gt;/ 2</td>
<td>0.76</td>
<td>64%</td>
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<td>SOFA &gt;/ 2</td>
<td>0.79</td>
<td>68%</td>
<td>67%</td>
</tr>
<tr>
<td>qSOFA &gt;/ 2</td>
<td>0.81</td>
<td>55%</td>
<td>84%</td>
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‘Screening test’ = q SOFA

- qSOFA (Quick SOFA) Criteria
  - **Hypotension** Systolic BP ≤100 mm Hg
  - **Altered mentation**
  - **Tachyphoea** Respiratory rate ≥22/min
## Ability to predict mortality outside of the ICU

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Q SOFA and mortality

- Score 0 = < 1%
- Score 1 = 2-3%
- Score 2 = 8%
- Score 3 = 20%
qSOFA

• Has been validation in one recently published trial.

• Prospective trial of 879 patients in 30 European EDs compared qSOFA, SIRS and severe sepsis in patients presenting with a suspected infection.

• Hospital mortality was < 3% for patients with a qSOFA score lower than 2 vs 24% for those with qSOFA score of 2 or higher

• The qSOFA performed better than both SIRS and severe sepsis in predicting in-hospital mortality,

• Area under the receiver operating curve (AUROC) of 0.80 (95% CI, 0.74-0.85) for qSOFA vs 0.65 (95% CI, 0.59-0.70) for both SIRS and severe sepsis.

• The hazard ratio of qSOFA score for death was 6.2 (95% CI, 3.8-10.3) vs 3.5 (95% CI, 2.2-5.5) for severe sepsis.
Septic Shock

- Septic shock = sepsis with:
  - (1) persisting hypotension requiring vasopressors to maintain MAP $\geq 65$ mm Hg &
  - (2) A serum lactate level $>2$ mmol/L

- Despite adequate volume resuscitation.

- With these criteria, hospital mortality is in excess of 40%.
Some thoughts ..................................
Sepsis is a syndrome. No gold standard.
The new guidelines do not specify what suspected infection means.
SOFA and qSOFA will not tell you who needs treatment
New definitions mean that we can stop calling simple infection sepsis.
Is there still a role for lactate?
qSOFA – potential problems

• What about patients with permanent altered mental state? e.g. dementia
• Rapid assessment of altered mental state can be hard when language barrier
• RR is not well measured

• Not as sensitive as SIRS

• Needs interpretation
qSOFA - strengths

• Simple
• No bloods
• Constructed after interrogation of big data
Managing suspected sepsis in adults and young people aged 18 years and over - in an acute hospital setting

Stratify risk of severe illness and death from sepsis using the risk criteria in the stratification tool for adults, children and young people aged 12 years and over

High risk criteria

- Objective evidence of new altered mental state
- Respiratory rate: 25 breaths per minute or more OR new need for oxygen (more than 40% FiO2) to maintain saturation more than 92% (or more than 88% in known chronic obstructive pulmonary disease)
- Heart rate: 130 beats per minute or above
- Systolic blood pressure 90 mmHg or less or systolic blood pressure more than 40 mmHg below normal
- Not passed urine in previous 18 hours, or for catheterised patients passed less than 0.5 ml/kg of urine per hour
- Mottled or ashen appearance
- Cyanosis of skin, lips or tongue
- Non-blanching rash of skin

1 high risk criterion

Arrange immediate review by senior clinical decision maker (person authorised to prescribe antibiotics, such as CT3/ST3 and above or advanced nurse practitioner).

Moderate to high risk criteria

- History from patient, friend or relative of new onset of altered behaviour or mental state
- History of acute deterioration of functional ability
- Impaired immune system (illness or drugs including oral steroids)
- Trauma, surgery or invasive procedures in the last 6 weeks
- Respiratory rate: 21-24 breaths per minute
- Heart rate: 91-130 beats per minute (for pregnant women 100-130 beats per minute) OR new onset arrhythmia
- Systolic blood pressure 91-100 mmHg
- Not passed urine in the past 12-18 hours, or for catheterised patients passed 0.5-1 ml/kg of urine per hour
- Typanic temperature less than 36°C
- Signs of potential infection, including redness, swelling or discharge at surgical site or breakdown of wound

2 or more moderate to high risk criteria OR SBP: 91-100 mmHg

Clinician to review person’s

Only 1 moderate to high risk criterion

Low risk criteria

Suspected sepsis, but:
- Normal behaviour
- No high risk or moderate to high risk criteria met

Suspected sepsis and no high risk or high to moderate risk criteria met
1 high risk criterion

Arrange immediate review by senior clinical decision maker (person authorised to prescribe antibiotics, such as CT3/ST3 and above or advanced nurse practitioner).

Carry out venous blood test for the following:
- blood gas including glucose and lactate measurement
- blood culture
- full blood count
- C-reactive protein
- urea and electrolytes
- creatinine
- clotting screen.

Give intravenous antibiotics without delay, and at least within one hour of identification of high risk criteria.

Use an intravenous antimicrobial from agreed local formulary and in line with local (where available) or national guidelines.

Discuss with consultant

- Lactate > 4 mmol/L OR SBP < 90 mmHg
  - Give i.v. fluid (500 ml over less than 15 minutes) without delay
  - Refer to critical care
  - Carry out observations, at least every 30 minutes or continuous monitoring in ED. Consultant to attend if not already present if patient does not improve

- Lactate 2 - 4 mmol/L
  - Consider i.v. fluids.

- Lactate ≤ 2 mmol/L
  - If no definitive condition identified, repeat structured assessment at least hourly
  - Ensure review by a senior decision maker within 3 hours for consideration of antibiotics.

2 or more moderate to high risk criteria OR SBP: 91-100 mmHg

Clinician to review person’s condition and venous lactate results within 1 hour

Carry out venous blood test for the following:
- blood gas including lactate measurement
- blood culture
- full blood count
- C-reactive protein
- urea and electrolytes
- creatinine.

Lactate > 2 mmol/L OR assessed as having AKI* = escalate to high risk

Lactate ≤ 2 mmol/L and no AKI*

Clinical assessment and manage according to clinical judgement

Suspected sepsis and no high risk or high to moderate risk criteria met

Manage definitive condition / infection if diagnosed

See Acute kidney injury (NICE guideline CG169)
ED/ AMU Sepsis Screening & Action Tool

To be applied to all non-pregnant adults and young people over 12 years with fever (or recent fever) symptoms, or who are clearly unwell with any abnormal observations.

Patient details (affix label):

Staff member completing form:
Date (DD/MM/YY):
Name (print):
Designation:
Signature:

Important:
Is an end of life pathway in place? Yes
Is escalation clinically inappropriate? Yes
Initials
Discontinue pathway
1. Does patient look sick?
   OR has NEWS (or similar) triggered?
   - Low risk of sepsis
     Use standard protocols, consider discharge (approved by senior decision maker) with safety netting

2. Could this be due to an infection?
   - Yes, but source unclear at present
   - Pneumonia
   - Urinary Tract Infection
   - Abdominal pain or distension
   - Cellulitis/septic arthritis/infected wound
   - Device-related infection
   - Meningitis
   - Other (specify: ________________________________)

3. Is any ONE Red Flag present?
   - Responds only to voice or pain/ unresponsive
   - Acute confusional state
   - Systolic B.P ≤ 90 mmHg (or drop >40 from normal)
   - Heart rate > 130 per minute
   - Respiratory rate ≥ 25 per minute
   - Needs oxygen to keep SpO₂ ≥92%
   - Non-blanching rash, mottled/ ashen/ cyanotic
   - Not passed urine in last 18 h/ UO <0.5 ml/kg/hr
   - Lactate ≥2 mmol/l
   - Recent chemotherapy

4. Any Amber Flag criteria?
   - Relatives concerned about mental status
   - Acute deterioration in functional ability
   - Immunosuppressed
   - Trauma/ surgery/ procedure in last 6 weeks
   - Respiratory rate 21–24
   - Systolic B.P 91–100 mmHg
   - Heart rate 91–130 OR new dysrhythmia
   - Not passed urine in last 12-18 hours
   - Temperature < 36°C
   - Clinical signs of wound, device or skin infection

   - Send bloods (if 2 criteria present, consider if 1)
     To include FBC, U&Es, CRP, LFTs, clotting
   - Ensure urgent senior review
     Must review with results within 1 hour

   - Is AKI present? (tick)
     - YES
     - NO

   - Clinician to make antimicrobial prescribing decision within 3h
     - Discharged?
     - Initials

Red Flag Sepsis!! Start Sepsis 6 pathway NOW (see overleaf)

This is time critical, immediate action is required.
Make a treatment escalation plan and decide on CPR status
Inform consultant (use SBAR) patient has Red Flag Sepsis

Action (complete ALL within 1 hour) Reason not done/variance

1. Administer oxygen
   Aim to keep saturations > 94%
   (88-92% if at risk of CO2 retention e.g. COPD)
   Time complete
   Initials

2. Take blood cultures
   At least a peripheral set. Consider e.g. CSF, urine, sputum
   Think source control! Call surgeon/radiologist if needed
   CXR and urinalysis for all adults
   Time complete
   Initials

3. Give IV antibiotics
   According to Trust protocol
   Consider allergies prior to administration
   Time complete
   Initials

4. Give IV fluids
   If hypotensive/ lactate >2mmol/l, 500 ml stat.
   May be repeated if clinically indicated
   do not exceed 30ml/kg
   Time complete
   Initials

5. Check serial lactates
   Corroborate high VBG lactate with arterial sample
   If lactate >4mmol/l, call Critical Care and recheck after each 10ml/kg challenge
   Time complete
   Initials

6. Measure urine output
   May require urinary catheter
   Ensure fluid balance chart commenced & completed hourly
   Time complete
   Initials

If after delivering the Sepsis Six, patient still has:
- systolic B.P <90 mmHg
- reduced level of consciousness despite resuscitation
- respiratory rate over 25 breaths per minute
- lactate not reducing
- or if patient is clearly critically ill at any time
  Then call Critical Care Outreach immediately!

Space available for local short antimicrobial guideline/escalation policy
what do I do now?
How to apply in the emergency department

• Can stop calling simple infection sepsis.
• qSOFA useful in identifying subgroup of infected patients likely to do badly therefore role triage, prehospital and as part of clinical assessment.
• Only apply it if you suspect the patient has an infection to start with
• It requires no bloods and is quick
• Being qSOFA negative does not mean you do not need treatment for infection
• SIRS probably still has role in considering infection
• As always none of this replaces clinical judgement
Conclusion

- Goodbye SIRS for diagnosing sepsis (may still be useful as part of screen for infection).

- Term sepsis is restricted to sick group of patients with mortality rate of around 10%

- SOFA score useful in ensuring same language is spoken (research research, epidemiology) not so much so for ED bedside

- qSOFA – specific but not very sensitive at predicting poor outcome
“It’s an unbelievably complex subject, nobody knew that health care could be so complicated.”