



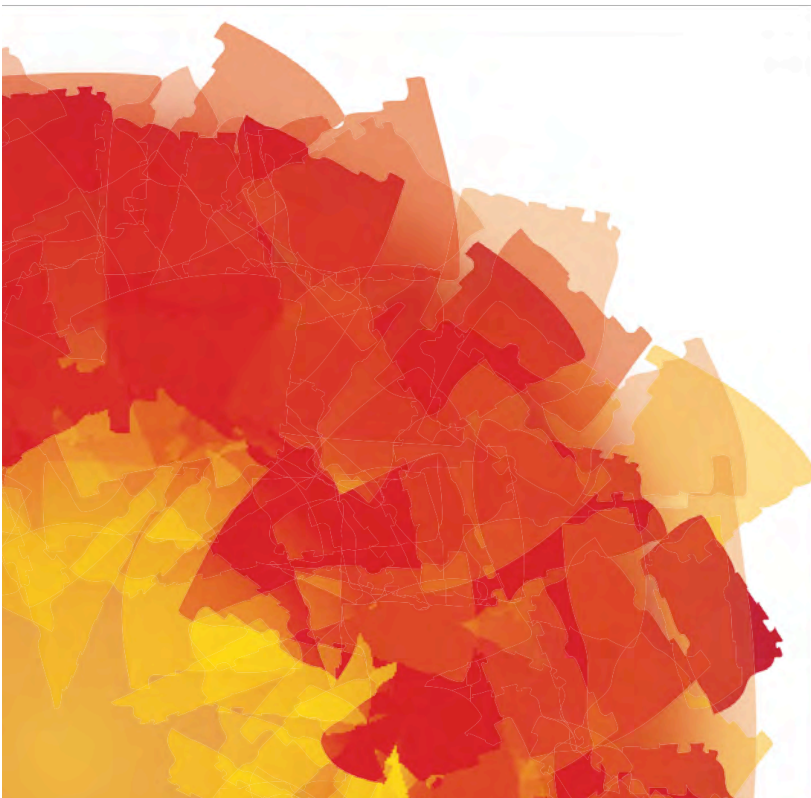
The Royal College of  
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# Toolkit: Emergency Department management of Sepsis in adults and young people over 12 years- 2016

This clinical toolkit has been developed in partnership with the Royal College of Emergency Medicine and in full communication with the National Institute for Health and Care Excellence (NICE). It is designed to provide operational solutions to the complexities challenging the reliable identification and management of sepsis which are compatible with the 2016 NICE Clinical Guideline on Sepsis (NG51), and complements clinical toolkits designed for other clinical areas.



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*Staff working in Emergency Departments (ED) should be familiar with the significant morbidity and mortality associated with sepsis and possess the knowledge and skills to recognize it early and initiate resuscitation and treatment. The ED provides a key role in identifying patients at risk of sepsis, followed by risk stratification for sepsis and septic shock, initiating resuscitation and treatment, and ensuring the correct onward management of patients identified with sepsis.*

*EDs are vital to the success of collaborative care pathways for the seamless management of patients with sepsis from the prehospital environment, through the ED, and to admission in either a ward bed or the Critical Care Unit. Sepsis responds well to early treatment and, if required, rapid escalation of therapy.*

## **I Background**

The UK mortality rate for patients admitted with sepsis is 30%<sup>1</sup> - approximately 5 times higher than for ST elevation myocardial infarction and stroke - and is responsible for approximately 44,000 deaths and 150,000 hospital admissions in the United Kingdom (UK) per year<sup>2</sup>. The majority of these patients will arrive via the ED. In the United States, the number of patients transported by Emergency Medical Services with sepsis now outnumbers those with heart attack or stroke<sup>3</sup>. In 2007 in the UK, sepsis was found to account for 12% of early inpatient deaths after ED admission: this is likely to have been an underestimate due to a further 26% of deaths coded as of respiratory cause<sup>4</sup>. Hospitalizations for sepsis have more than doubled over the last 10 years<sup>5,6</sup>.

Sepsis is a time-critical condition. In the most severe cases, septic shock, for every hour that appropriate antibiotic administration is delayed, there is an 8% increase in mortality<sup>7</sup>. The Sepsis Six is an initial resuscitation bundle designed to offer basic intervention within the first hour. In a prospective observational study, it was independently associated with survival suggesting that, if it alone were responsible for outcome differences, the number needed to treat (NNT) to prevent one death is 4.6<sup>8</sup>. This compares to an NNT of 42 for Aspirin in major heart attack and 45-90 for PCI in ST elevation myocardial infarction.

Sepsis is poorly recognized and treated. A 24-month, large scale prospective improvement programme across 30 countries measuring the delivery of the Severe Sepsis Resuscitation Bundle showed compliance rising from 10 to just 21% in self-selected centres<sup>9</sup>. More recently in 2013 in the UK, the Royal College of Emergency Medicine (RCEM) audited performance against self-imposed standards for the management of severe sepsis and septic shock and identified similarly concerning results, with antibiotics administered in only 32% of patients within the first hour from time of arrival in the ED<sup>10</sup>.

This toolkit, first produced in 2014 and introducing the concept of Red Flag Sepsis as a simplified set of bedside criteria to facilitate rapid initiation of care, has been updated for 2016 to take into account two significant new developments- the revised Consensus International Definitions for Sepsis published in JAMA in February 2016<sup>11</sup>, and the NICE Clinical Guideline on Sepsis released in July of that same year<sup>12</sup>.

## 2 Professional responsibility & accountability

RCEM is committed to continued and sustainable improvement in the management of patients with sepsis, and has produced a 'Sepsis Pack', which is available [here](#).

NHS England established sepsis as an indicator in both Domains 1 and 5 of the National Outcomes Framework, and issued a stage 2 alert on sepsis in September 2014. This signposted to clinical toolkits such as this, to education programmes, examples of good practice, and other available resources.

In 2015 and 2016, the Secretary of State for Health issued public commitments to action on sepsis. This has resulted in actions including a national CQUIN commissioning lever for EDs in 2015/16, and a further CQUIN applying across the whole hospital for 2016/17. Discussions with NHS England raise the possibility of a more permanent commissioning lever, akin to a best practice tariff, to follow; and it is highly likely that sepsis will in future be included in public-facing mortality data dashboards.

In her report of September 2013 entitled 'A Time to Act', the Parliamentary and Health Service Ombudsman called upon the NHS and the Department of Health to act rapidly to reduce unnecessary deaths from sepsis<sup>13</sup>. As a direct result of this work, NICE has produced a clinical guideline to which this toolkit pertains, and will produce an accompanying Quality Standard against sepsis, the latter carrying statute for implementation.

We have learned valuable lessons from the report arising from the recent survey on sepsis conducted by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), in particular that sepsis is a condition presenting primarily via EDs and Acute Medical Units, and resulting primarily from community- rather than hospital-acquired infections. Delays at every stage of healthcare were identified and felt to be contributory to adverse outcome, in addition to delays in patients' initial contact with healthcare<sup>1</sup>.

It is the responsibility of those commissioning services from, designing clinical systems for, and working within EDs that their efforts focus on early recognition, urgent intervention using existing consensus guidelines from NICE, the UK Sepsis Trust and Surviving Sepsis Campaign, and timely escalation for patients with sepsis.

## 3 Definitions

In February 2016, the International Consensus Definitions for Sepsis Task Force published recommendations for 'Sepsis-3'<sup>11</sup>. Major changes from earlier definitions included that the Systemic Inflammatory Response Syndrome (SIRS) criteria<sup>14</sup> were to no longer form part of the diagnostic criteria for sepsis, and that earlier efforts to define organ dysfunction criteria would be replaced with a validated (in Critical Care) organ dysfunction tool known as SOFA (Sepsis-related Organ Failure Assessment score). Furthermore, the term 'severe sepsis' was abandoned, such that the international consensus group recommended the use only of the terms 'infection', 'sepsis', and septic shock.

Following publication of the Sepsis-3 definitions and the NICE clinical guideline, the Sepsis Trust has agreed with stakeholders a pragmatic interim approach to the recognition of sepsis for the UK. This approach is detailed below.

Sepsis is characterized by a dysregulated host response to infection mediated by the immune system and resulting in organ dysfunction, potentially multi-organ failure, shock and death. International guidelines recommend the application of standards of care including first-hour antibiotics to patients with sepsis and septic shock.

### **Rationale for not recommending qSOFA alone:**

It is unrealistic to expect organizations or individuals to formally calculate a SOFA score at presentation (and particularly outside hospital) prior to initiating time-critical life saving therapy.

To this end, the International Consensus Definitions Task Force used a combination of retrospective analyses of large data sets and prospective validation of smaller data sets to construct an 'optional' tool, using a simplified set of criteria, called 'quick-SOFA' or 'qSOFA'. This tool would require that an aggregate of two parameters breach threshold, the combination of which in the analyses conducted predicted death or a prolonged Critical Care stay.

qSOFA will present operational difficulty to many organizations to implement, as it would demand the introduction of a second aggregate scoring system for patients who are likely to have already been identified as at risk using an aggregate track and trigger system such as the National Early Warning Score (NEWS). qSOFA has yet to be robustly prospectively validated, and particularly has not been shown to be superior to NEWS in identifying patients with infection at risk of deterioration.

Furthermore, Sepsis-3 describes as only having 'infection' or 'sepsis'. There is, unlike in the Red Flag Sepsis pathways and the 2001 definitions set, no 'interim' group in which early scheduled review can be readily recommended. Outside hospitals, on which the validity of data the Task Force have used is not entirely clear, it may well be that qSOFA (predicting death or prolonged Critical Care stay) occurs at a point in the course of illness later than ideal for transfer to hospital.

*For these reasons, we (UKST, RCEM and NICE) do not currently recommend the use of qSOFA as the primary bedside test for sepsis in the U.K. It is likely to be a useful and important redundancy to the proposed screening strategy in organizations benefiting from electronic observations and clinical prompts.*

## 4 Determining who to screen for sepsis (the denominator population)

A high degree of vigilance is required for early identification of the septic patient. Personnel tasked with patient triage, early assessment and the early investigation of undifferentiated patients should be trained in sepsis recognition. All patients presenting with physiological disturbances in the presence of signs and symptoms compatible with an infective illness should be formally screened for sepsis. At each opportunity, a binary decision should be reached for all patients screened: this patient could have sepsis, or this patient does not have sepsis.

Suspicion of an infective cause is all that is required i.e. ED staff do not need positive cultures, swabs or other investigations. The most common causes are respiratory, abdominal and urinary tract but staff must also be aware that there are many other causes. A comprehensive list is beyond the scope of this document but must be included in training.

Since the minimum NEWS compatible with a qSOFA score of 2 (the recommended trigger threshold) is 4, UKST, RCEM and NICE believe it reasonable to propose that the existing NEWS escalation recommendations of an aggregate score of 3 or higher be used as a trigger to screen for sepsis. An aggregate score of 3 has been demonstrated recently to carry almost a 93% sensitivity and 77% specificity for a (Sepsis-2) diagnosis of severe sepsis or septic shock<sup>15</sup>.

Unlike the Critical Care-focused definition in Sepsis-3, health professionals working at the interface between community and hospital care need to identify those patients who are not yet critically ill, but are likely to become so. The qSOFA and SOFA criteria will *all* be captured in either the 'moderate to high risk' or 'high risk' criteria within the NICE guideline (which forms the basis for this toolkit), and we believe that this presents a safer and more operationally deliverable strategy within the UK.

*We recommend that patients be screened for sepsis if they present with unexplained illness, if they clearly look unwell and have a likely infective cause, or if they present with (or subsequently deteriorate to) an individual parameter score of 3 or aggregate score of 4 or higher on the National Early Warning Score (NEWS) (or locally derived equivalent).*

## 5 Screening strategies determined by route of entry

Opportunities for sepsis screening will vary according to the route by which a patient has presented, and this toolkit will complement other toolkits for prehospital services, prehospital services, NHS Pathways/111, primary and community care and Acute Medicine.

### *a) Patients arriving by ambulance using pre-alert*

The clinical toolkit for prehospital services recommends that Paramedics and Community First Responders be trained to screen for sepsis using the NEWS track-and-trigger scoring system. Supported by guidance from the Joint Royal Colleges Ambulance Liaison Committee (JRCALC) and by prehospital screening tools, practitioners may pre-alert receiving EDs. Pathways should be developed through collaborative workshops involving ED staff, ambulance service staff, patient representatives, managers and commissioners.

Patients pre-alerted as suspected sepsis should be routed directly to the Resuscitation area and assessed immediately for likelihood of infection, consideration of other causes of acute illness, and if sepsis is suspected the presence of Red Flag or moderate risk criteria (see below). A Sepsis Team should ideally be available to see these patients. An example of a Sepsis Team and their roles within the ED is given in the UK Sepsis Trust Toolkits Appendix 'Change management and the Sepsis Team'.

### *b) Patients arriving to the ED having been sent via NHS Pathways/111, primary and community care*

These patients will already be suspected of having sepsis. It is therefore the duty of the ED staff to ensure that the patient is seen immediately, ideally in the Resuscitation area, where they can undergo sepsis screening similar to 5a) above.

### *c) Patients arriving by ambulance without pre-alert, 'walk-ins' and patients referred directly to an inpatient specialty team*

Sepsis is a time-critical condition and EDs must have a system in place to escalate patients with suspected sepsis emergently. During Triage in the ED, all patients who present with unexplained illness, who clearly look unwell and have a likely infective cause, or who present with an individual parameter score of 3 or aggregate score of 4 or higher on the National Early Warning Score (NEWS) (or locally derived equivalent) should be prioritised for initial assessment, triaged to Majors or the Resuscitation area, and reviewed within 30 minutes by a competent clinician.

At initial assessment of self-presenting and patients arriving by ambulance who have not been pre-alerted, sepsis screening should be initiated immediately as outlined in 5a) above and detailed below.

## 6 Confirming that Sepsis Risk Stratification is required

Sepsis screening should be done as a two-part process; confirming that sepsis risk stratification is required and, in the population thus identified, screening for the level of severity of sepsis, or Sepsis Risk Stratification. During Sepsis Risk Stratification, as soon as Red Flag Sepsis, Amber Flag Sepsis or septic shock is confirmed, treatment and/or investigations should be initiated without waiting for the results of any further tests.

NICE NG51, in using an improved set of Red Flag Sepsis criteria and introducing a second group of Amber Flag Sepsis criteria to identify patients at lower risk but who still warrant close assessment, has reduced the reliance on laboratory tests seen in earlier pathways. For some patients, however, the early exclusion or diagnosis of sepsis and its risk stratification will only be possible after measuring lactate and creatinine levels. The time taken to receive results can be significantly reduced by the use of point-of-care-tests (POCTs). It should therefore be the aim of every ED to assess capacity and need for each of the POCTs required to exclude, diagnose and/or risk stratify sepsis as quickly as possible, and to institute urine output monitoring for all patients with suspected but as yet unconfirmed sepsis.

Every ED should decide on the maximum time that they are prepared to withhold treatment, in full or in part, whilst waiting for blood test results. When particular tests routinely exceed this time, POCT alternatives should be explored. Standards are recommended in the UKST Clinical Toolkit for microbiology services and for other laboratory services.

Patients flagged at triage or initial assessment as requiring sepsis screening should be assessed urgently by a competent clinician.

The clinician should ask 3 questions:

- Does sufficient clinical concern exist about this patient that sepsis is a possibility?
- Am I satisfied that this illness is likely to be of infective cause?
- Is full escalation of care appropriate for this patient?

Clinical concern might be manifest by an unexplained illness, if a patient clearly looks unwell and has a possible infective cause, or if a patient presents with (or subsequently deteriorates to) an individual parameter score of 3 or aggregate score of 4 or higher on the NEWS (or locally derived equivalent). Experienced clinicians may continue screening based upon clinical gestalt.

In the ED, it is not always possible to define a source of infection in a patient presumed to have sepsis. Common sources of infection are detailed in Schematic 1, but it is important to reinforce that patients with signs and symptoms of infection in the absence of a clear source should continue to be presumed to have sepsis.

The clinician should question whether this acute illness might be explained by a non-infective illness such as pancreatitis, acute coronary syndrome, poisoning or pulmonary embolism and request diagnostic tests as appropriate.

Should a patient have a relevant advance directive precluding active intervention, or a competent and informed patient refuse treatment, clearly treatment would be inappropriate. For some patients, severe co-morbidity and pre-existing limitations to functional status may make escalation to Critical Care inappropriate although basic interventions are likely to remain appropriate- such cases should be discussed with a senior clinician urgently.

**Schematic I: Confirming that Sepsis Risk Stratification is required**

1. Is NEWS 3 or above?  Tick

And/or does patient look sick?

↓ Y

2. Could this be due to an infection?  Tick

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: .....)



## 7 Sepsis Risk Stratification

NICE NG51 built upon the UK Sepsis Trust's Red Flag Sepsis approach, launched in 2014, which aimed to identify which patients should immediately be commenced on life saving therapy. The first step in Sepsis Risk Stratification should be to confirm or exclude the presence of any ONE high risk, Red Flag Sepsis criterion as detailed in Schematic 2:

Schematic 2: Sepsis Risk Stratification: Red Flag Sepsis criteria

**3. Is any ONE red flag present?**

Responds only to voice or pain/ unresponsive	<input type="checkbox"/>
Systolic B.P $\leq$ 90 mmHg (or drop $>40$ from normal)	<input type="checkbox"/>
Heart rate $>$ 130 per minute	<input type="checkbox"/>
Respiratory rate $\geq$ 25 per minute	<input type="checkbox"/>
Needs oxygen to keep SpO <sub>2</sub> $\geq$ 92%	<input type="checkbox"/>
Non-blanching rash, mottled/ ashen/ cyanotic	<input type="checkbox"/>
Not passed urine in last 18 hours	<input type="checkbox"/>
Urine output less than 0.5 ml/kg/hr	<input type="checkbox"/>
Lactate $\geq$ 2 mmol/l	<input type="checkbox"/>
Recent chemotherapy	<input type="checkbox"/>

Any patient with presumed sepsis who has one or more Red Flag Sepsis criteria should be assumed to have sepsis or septic shock, and immediately commenced on the Sepsis Six Care Pathway (section 10).

*A patient who looks unwell with presumed infection who displays at least ONE Red Flag Sepsis criterion has Red Flag Sepsis and should immediately be placed on the Sepsis Six pathway*

The Red Flag Sepsis criteria detailed above are modified by NICE from an original set developed by the UK Sepsis Trust in September 2014. It includes parameters individually allocated a score of 3 in NEWS, together with parameters known to be associated with increased risk in sepsis, and is intended to help identify patients with 'formal' sepsis according to a change in SOFA score who are awaiting confirmatory laboratory or radiographic tests. Their inclusion in Sepsis Risk Stratification is recommended in order to avoid unnecessary delay in initiating life-saving therapy in patients with sepsis with threatened cardiovascular or respiratory compromise.

Organizations should choose whether they wish to formally confirm the presence of sepsis using a change in SOFA score of two points or more. For patients presenting to the ED, the baseline SOFA score will normally be assumed to be zero. If formal sepsis screening is undertaken, if subsequent results are not confirmatory for sepsis then a senior competent decision maker should consider alternative diagnoses and review the need for ongoing antimicrobial therapy and other aspects of the Sepsis Six pathway.

#### Case Study 1

A 32 year old woman presents to the ED with dysuria and loin pain for three days. She has a temperature of 38.8 degrees, a respiratory rate of 22 and a tachycardia of 105 beats per minutes. Other observations are normal. Alerted by her NEWS score of 4, the triage nurse is concerned by these observations and ensures that she is seen immediately by the ED registrar for sepsis screening.

The ED registrar confirms the presence of abnormal physiology and suspects that she has pyelonephritis. She arranges for the patient to be closely monitored, gains IV access and sends off blood tests including blood cultures, 'U&Es', coagulation screen and LFTs. She also sends a venous blood gas sample as the ED blood gas machine measures serum lactate.

The nurse looking after the patient informs the registrar that the lactate has been reported as 3.6 mmol/l. The ED registrar diagnoses Red Flag Sepsis and instigates treatment immediately, following the 'Sepsis Six'.

Under the original Red Flag Sepsis Pathway, patients without Red Flag criteria were scheduled for regular re-assessment and review with results of blood tests. Mindful of Sepsis-3, NICE have provided more specific guidance to identify patients at moderate risk, which we term 'Amber Flag' criteria. Patients who have no Red Flag Sepsis Criteria should immediately be screened for Amber Flag Sepsis (Schematic 3).

#### Schematic 3: Sepsis Risk Stratification: Amber Flag Sepsis criteria

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

The presence of one or more Amber Flag criteria should, as a minimum, prompt clinician review and consideration of laboratory blood tests and blood gases for serum lactate within 1 hour (NICE NG51).

Whilst the NICE Guideline recommends that blood tests be taken (rather than considered) with clinician review *with results* within one hour only if 2 or more Amber Flag criteria are met, in the ED environment RCEM and UK Sepsis Trust believe it reasonable to recommend this action in the presence of any one (or more) Amber Flag criterion.

*A patient with presumed infection who displays at least ONE Amber Flag Sepsis criterion (in the absence of Red Flag Sepsis) should have bloods sent immediately to include full blood count, urea and electrolytes, C-reactive protein and liver function tests and be reviewed with results within one hour by a doctor at training level ST3+ (or health professional of equivalent training such as an Emergency Care Practitioner)*

At clinician review with blood tests, should the patient be identified as having an acute kidney injury, their risk level should be escalated to Red Flag Sepsis and they should immediately be commenced on the Sepsis Six Care Pathway (Section 10).

Patients with Amber Flag Sepsis in the absence of acute kidney injury should have an antimicrobial prescribing decision documented and, if appropriate, antimicrobial therapy administered within 3 hours. As with the Sepsis Six Care Pathway, consideration should be given to source of infection (including the sampling of appropriate cultures) and whether source may be amenable to control whenever antimicrobial therapy is prescribed.

If a patient with presumed new infection has no Red Flag or Amber Flag criteria, they should be assumed to be at low risk and decisions to admit or discharge, with or without scheduled review, made according to clinical judgment. We recommend the provision of verbal and written safety netting instructions to guide patients and carers in the event of their deterioration if discharge is planned.

*A patient with presumed infection who displays at least ONE Amber Flag Sepsis criterion but at clinician review is judged not to have acute kidney injury should have an antimicrobial prescribing decision made, documented and (if appropriate) effected by a doctor at training level ST3+ (or health professional of equivalent training such as an Emergency Care Practitioner) within 3 hours*

The ED team should process-map patient pathways for patients arriving with possible sepsis. Points of repetition, unnecessary steps and functional bottlenecks where progress is delayed by competition for available resources should be identified and addressed.

In addition to blood cultures, other samples should be sent as appropriate to identify pathogens and source of infection. Investigations such as a chest x-ray, urinalysis and culture of urine and any other relevant specimens and/ or bedside ultrasound examinations should be requested and reported as appropriate to rule in or rule out possible sources of infection.

#### Case Study 2

A normally fit and active 72 year old man who takes medication for hypertension only is brought to the ED by his wife. She is concerned that he has recently had a productive cough and this morning appears to be confused. His oxygen saturations are low at 92%, his heart rate 99 and his temperature 38.1°C but all other observations are normal. Alerted by a NEWS of 4, the triage nurse is concerned and asks the ED consultant to see the patient next.

The ED blood gas machine is being serviced and so the ABG sample is sent to the laboratory.

The ED consultant suspects a chest infection but there are no immediately identifiable Red Flag Sepsis criteria. He also notes that there are no physiological Amber Flag criteria so continues to question the patient and his wife. He notes the acute confusion, and the patient informs him that he is unable to remember when he last passed urine.

The patient is monitored and placed on supplemental oxygen which improves his oxygen saturations to 95%. A portable chest x-ray is taken which shows bilateral infiltrates.

The ED consultant decides that the patient has Amber Flag sepsis and, in the context of pneumonia instigates treatment with blood cultures and antibiotics immediately, pending the laboratory results. He asks that the urine output be monitored and makes a note to check the blood results in 45 minutes.

## 8 Lactate

The lactate level in sepsis is highly predictive of death<sup>16</sup> (see Box 1) and poor outcomes and, when initially elevated, the degree of reduction following resuscitation ('lactate clearance') predicts survival<sup>17</sup>. A significant proportion of patients with sepsis who have normal blood pressure have elevated serum lactate and outcomes for these patients with 'cryptic shock' are as poor as for those with overt septic shock<sup>18</sup>.

In the analysis of criteria predictive of death in Sepsis-3, at each level of qSOFA score, lactate provided additional prediction of death<sup>19</sup>.

EDs have in recent years become increasingly familiar with the routine use of serum lactate in assessing risk in patients presenting with presumed sepsis. Therefore, whilst NICE NG51 recommends that lactate be sampled following confirmation of the presence of High Risk (or two or more moderate risk) criteria, operationally we recommend that lactate be included in the Red Flag Sepsis criteria sought at the first stage of Sepsis Risk Stratification. Here, the NICE NG51 pathway and the pathway recommended converge, since NICE recommends that if a lactate of greater than 2 mmol/l is identified in the

presence of any high risk or moderate risk criteria, a pathway of care equivalent to the Sepsis Six be commenced.

When cryptic shock has been identified from a venous or capillary lactate sample, this should be corroborated with an arterial sample to exclude error arising from regional perfusion abnormalities. A capillary or venous lactate from a correctly calibrated device which is normal is reassuring as a stand-alone.

Consideration should be given to the routine use of serum lactate at triage or initial assessment of all patients admitted to the Majors or Resuscitation areas (or equivalent).

### Box 1: The relationship of lactate level in sepsis to mortality

Lactate	Mortality
<2	15%
2-4	25%
>4	38%

From: Trzeciak S, Dellinger RP, Chansky ME, Arnold RC, Schorr C, Milcarek B, *et al. Intensive Care Med* 2007, 33(6):970-7

#### Case Study 3

A normally well 28 year-old man self-presented to the ED with shortness of breath and a productive cough. He had a temperature of 38.5 degrees. Despite all other observations being normal, the triage nurse was concerned based upon clinical experience, moved him to the Majors area and arranged for the ED technician to gain IV access and send bloods.

The ED technician cannulated him and performed routine bloods including blood cultures because of his high temperature. A venous blood gas, which includes serum lactate, was performed routinely as is the protocol for all patients in Majors. The lactate was 4.3mmol/L.

From his training on a multi-disciplinary sepsis course, the ED technician recognized the seriousness of this result and informed the ED doctor, requesting that the patient be seen immediately. The ED technician went to fetch the 'Sepsis Trolley' and the patient's named nurse stopped what she was doing to assist the doctor and get ready to draw up antibiotics and give fluids as necessary.

Septic shock, for the purposes of operational implementation in the ED, can be considered as a population of patients who will benefit from immediate fluid resuscitation- we agree with NICE NG51 that this be defined as hypotension (systolic blood pressure less than 90 mmHg) or hyperlactataemia (serum lactate greater than 4 mmol/l).

Following initial assessment, and once any necessary investigations have been completed, an initial assessment diagnosis should be recorded using ONLY the following terms:

Septic shock  
Red Flag Sepsis  
Amber Flag Sepsis  
No current evidence of sepsis

'Sepsis' as a stand-alone term at initial assessment (as opposed to the formal diagnosis which organizations may apply later) is not acceptable: documentation must record acuity as described.

## 10 Urgent Intervention

The key immediate interventions that increase survival are described in a bundle termed the Sepsis Six (Box 2). This bundle has been shown to be associated with significant mortality reductions when applied within the first hour<sup>8</sup>.

**Box 2: The Sepsis Six** (Source: <http://sepsistrust.org>)

1. Administer oxygen to maintain SpO<sub>2</sub> > 94%
2. Take blood cultures and consider infective source
3. Administer intravenous antibiotics
4. Consider intravenous fluid resuscitation
5. Check serial lactates
6. Commence hourly urine output measurement

This bundle should be initiated immediately on diagnosis or suspicion of Red Flag Sepsis, or Amber Flag Sepsis with Acute Kidney Injury. The Sepsis Six should be completed within one hour of initial identification, without waiting for the results of further investigations, and should complement, not detract from, the criteria and standards for the management of sepsis and septic shock set by RCEM.

Following delivery of the Sepsis Six, patients should be placed on a standardized pathway of care to ensure optimal sepsis management regardless of the time of day or experience of the staff.

The Sepsis Six recommends that up to 30mL/kg of crystalloid fluid be rapidly delivered in divided aliquots using crystalloid solutions to patients with sepsis who are hypotensive, who have a serum lactate > 2 mmol/l, or who have Amber Flag Sepsis with an acute kidney injury. Schematic 4 outlines a recommended Sepsis Six pathway.

Some patients with initial hypoperfusion may respond rapidly to smaller volumes. There is strong evidence that expedient delivery of 'basic' aspects of care limits the maximum acuity of intervention required - early resuscitation can prevent the requirement for invasive

monitoring and vasoactive support<sup>20</sup>. Patients who have Red Flag Sepsis who are not hypotensive, have a lactate <2 mmol/l *and* have no evidence of acute kidney injury should have a decision regarding fluid resuscitation made and documented based upon clinical findings.

Should blood pressure, heart rate, urine output and lactate return to normal levels following fluid resuscitation, a management plan should be documented that includes timings of planned clinical review and escalation criteria. Attention should be focused on urgent ongoing resuscitation and wider management including control of any source amenable to drainage or removal within 12 hours.

#### Schematic 4: Sepsis Six Pathway

Action (complete ALL within 1 hour)	Time complete	Initials	Reason not done/variance
<b>1. Administer oxygen</b> Aim to keep saturations > 94% (88-92% if at risk of CO <sub>2</sub> retention e.g. COPD)			
<b>2. Take blood cultures</b> At least a peripheral set. Consider e.g. CSF, urine, sputum <i>Think source control!</i> Call surgeon/ radiologist if needed <i>CXR and urinalysis for all adults</i>			
<b>3. Give IV antibiotics</b> According to Trust protocol Consider allergies prior to administration			
<b>4. Give IV fluids</b> If hypotensive/ lactate >2mmol/l or AKI, up to 30ml/kg Give 500ml stat if no AKI, not hypotensive and lactate normal			
<b>5. Check serial lactates</b> Corroborate high VBG lactate with arterial sample <i>If lactate &gt;4mmol/l, recheck after each 10ml/kg challenge and call Critical Care. Recheck in any patient causing concern</i>			
<b>6. Measure urine output</b> May require urinary catheter Ensure fluid balance chart commenced & completed hourly			

Those with persistent haemodynamic deficit following fluid resuscitation of 30mL/kg, including patients with persistently high lactate or low urine output, require more invasive strategies for ongoing resuscitation. The physiological targets and parameters for Early Goal Directed Therapy according to the original protocol<sup>21</sup> studied by Rivers has been brought into question recently<sup>22</sup>, but few would argue the need to consider invasive

monitoring and haemodynamic support for patients who do not respond to initial fluid resuscitation. The central tenets of advanced haemodynamic support in this group are to adequately restore circulating volume, use vasopressors to correct hypotension, and to assess cardiac output and oxygen delivery.

EDs should ensure that equipment and resources are immediately available to provide advanced haemodynamic support. Where skills are available within the ED to site central venous catheters, or to undertake dynamic ultrasound assessment of the vena cava, then ED staff may initiate targeted volume resuscitation and, where necessary, initiate vasopressor support where skills permit. The RCEM noradrenaline infusion reference guide is available [here](#).

Where skills are not available, or where Critical Care personnel are immediately available and more directly skilled in the provision of invasive monitoring and vasoactive infusions, Critical Care must be involved promptly to ensure that there is no delay in instituting advanced resuscitation. All patients in whom advanced resuscitation has been commenced will require ongoing care, according to response, in a Level I facility as a minimum.

## 11 Timely Escalation

The All Party Parliamentary Group (APPG) on sepsis has recently made a recommendation that organizations should give 'consideration to the development of Sepsis Teams'<sup>23</sup>. Comparisons with heart attack and stroke, where teams are available to be mobilized when prehospital services pre-alert a suspected case, would make this seem obvious. At the very least, there should be nominated medical and nursing leads for sepsis within each ED, and care pathways should identify a tier of resident staff who should assume direct responsibility for coordinating care when a patient with sepsis is identified.

A pragmatic solution to the pressing need to identify specific teams to manage patients with sepsis may lie in existing resources - for example, Critical Care Outreach, Patient at Risk and Medical Emergency Teams. It can be argued that sepsis is a core component of their existing workload. However, these already pressured teams should not be assumed to have capacity to undertake the necessary monitoring and improvement programmes - the fact that resources need allocating to improve outcomes from sepsis is inescapable.

Care pathways should include an observation and review schedule and guidance as to which parameters imply treatment success or failure with an easy-to-follow directive informing when senior and/or intensive care review is required.

It is vital that patients with sepsis should be reviewed at the earliest opportunity by the most senior available doctor. The RCEM standard is that all patients with severe sepsis and septic shock have senior (ST4 or above) medical review within 60 minutes of arrival.

Many patients with sepsis will have multiple co-morbidities, and may be elderly or frail. For such patients, decisions should be taken at senior level (in consultation with the patient and their family as appropriate) regarding the appropriateness of escalation of care to level 2 ('High Dependency', where a single organ system requires support excluding a need for



invasive ventilation) or level 3 ('Intensive Care', where invasive respiratory support or more than one organ system support is required). Where possible, these decisions should be made and documented prior to the point at which the acuity of the patient's condition has deteriorated - this will not always be feasible.

## **Suggested clinical guidelines for the management of patients attending with or developing sepsis in an ED:**

### ***Amber Flag Sepsis (no AKI):***

- A documented decision to initiate the Sepsis Six or not within 3 hours following presentation
- If antimicrobials are to be administered, this to be complete within 3 hours
- Review by a senior doctor (ST4 or above) within 60 minutes of diagnosis
- Hourly observations whilst in the ED
- Repeat lactate measurement within 2 hours from baseline in order to identify development of cryptic shock (hypoperfusion with normotension)
- Escalate immediately if Red Flag Sepsis or septic shock develop (including patients with normal blood pressure but elevated lactate, known as 'cryptic shock')
- If admitted, arrangements to be made for review by consultant from admitting team within 14 hours
- If discharged home, written and verbal safety-netting advice and advice regarding how to re-access healthcare if patient subjectively deteriorates documented

### ***Red Flag Sepsis or Amber Flag Sepsis with AKI:***

- Sepsis Six to be completed as soon as possible, but always within 60 minutes
- Review by a senior doctor (ST4 or above) within 60 minutes of arrival
- Continuous monitoring or observations every 30 minutes whilst in ED in accordance with NEWS frequency of monitoring and escalation policy
- Repeat lactate measurement within 2 hours
- Escalate immediately if septic shock (including cryptic shock) develops or if organ dysfunction requires need for Critical Care (e.g. acute kidney injury with anuria or acidosis)
- Arrangements made to ensure repeat laboratory blood tests within 14 hours, unless observations indicate earlier need (e.g. reducing urine output, jaundice, bleeding)
- Review by admitting consultant within 14 hours

### ***Septic Shock:***

- Initiation of the Sepsis Six to be completed as soon as possible, but always within 60 minutes
- Review by a senior doctor (ST4 or above) immediately
- Emergency Medicine Consultant to be informed when on duty

- Immediate referral by ED staff to Critical Care Outreach (or equivalent) team
- Personnel assembled with skills to initiate invasive monitoring and/or vasoactive infusions where necessary within 60 minutes of recognition
- Where ventilatory support is required, attendance of appropriately skilled personnel within 30 minutes of recognition

Organizations should also describe within pathways or policies where patients with sepsis should be nursed, and for individual patients escalation status and any ceilings of care should be clearly documented. It should be stressed that although patients may not be determined suitable for full resuscitation or invasive ventilation, treatment limits of non-invasive ventilation, inotropes, vasopressors, or intensive fluid management may be set.

Whenever there has been physician review of patients with sepsis, there should be a documented schedule for when repeat lactate measurement and medical review are planned and what the escalation/ de-escalation parameters are.

## Exemplar Standards for the emergency management of Sepsis

The ED has a key role to play in early sepsis management. It is where rapid identification of the septic patient must occur and it is where important decisions must be made about the appropriate destination for ongoing care and for referral to other specialties and services e.g. to Critical Care, or to Radiology or Surgery for drainage of collections. The delivery of excellent sepsis care demands that clinical pathways describe how patients arrive and are managed in the ED, for example prehospital services or walk-in patients; what support services are available in the ED; and to where the patient will be discharged such as the Critical Care unit or the ward. In designing a clinical pathway, construction of both high level and low level process maps is a helpful starting point.

The standards below are those which have been identified by the UK Sepsis Trust and the APPG for Sepsis as important in the management of sepsis with specific relevance to the ED. They are the 'Exemplar Standards' which organizations should deliver. Achieving these standards will place an ED well on the road to the provision of excellent sepsis care.

1. Clear guidance, policies and clinical pathways to be in place for the management of sepsis and septic shock. Standards for recognition, intervention and escalation must be included.
2. All patients with physiological derangement, an elevated NEWS score (aggregate 4 or higher or individual parameter score of 3), who look clearly unwell or who have clinical suspicion of infection to be screened for the possibility of sepsis, risk stratified seeking the presence of Red Flag Sepsis, Amber Flag Sepsis or septic shock, including a serum lactate measured within 30 minutes of arrival.
3. Clinical pathways to include initiation of all investigations necessary to identify source of infection, to seek laboratory evidence of organ dysfunction, and to include criteria for escalation/ de-escalation of care.
4. The Sepsis Six to be used as a delivery method for early sepsis care and to be delivered within 1 hour post diagnosis in  $\geq 95\%$  of cases.
5. On diagnosis of sepsis (Red Flag or Amber Flag with AKI), the patient should not be transported to a different clinical area prior to completion of Sepsis Six, unless emergency surgery/ specialist intervention or escalation of treatment is required.
6. 24 hour availability of microbiology advice on initiation or escalation of antimicrobial therapy in complex cases or where the source of infection is unclear.
7. Definitive, documented decision made about the presence/ absence of sepsis and the level of severity at time of admission to hospital from the ED.

8. Mandatory annual sepsis training for all clinical members of ED staff.
9. A minimum of 80% of permanent staff to have received appropriate sepsis training at any one time point, audited at least biannually.
10. A nominated Medical and Nursing Lead within the ED who are part of and contribute to the organization's Sepsis Group.
11. Interdisciplinary meetings to be undertaken between the ED and prehospital service staff together with managers and commissioners as appropriate, with remit to refine care pathways for sepsis and ensure compatibility between clinical areas. This work should be undertaken within the remit of, or fed back to, the organization's Sepsis Group.
12. Regular case reviews to be undertaken with Critical Care staff to identify elements of the clinical pathway which work well and opportunities for improvement. This work should be undertaken within the remit of, or fed back to, the organization's Sepsis Group.
13. Sepsis should be on the organization's Risk Register, with an identified Board level person with responsibility for sepsis. The mortality rate from sepsis and pneumonia should be on the monthly quality dashboard.
14. Mandatory prospective data collection and continuous audit on patients with sepsis, measuring the delay to intervention, treatment and outcomes
15. Voluntary reporting of performance data into the public domain.

## References

1. National Confidential Enquiry into Patient Outcome and Death, 2015, London. Just Say Sepsis! Available online at [http://www.ombudsman.org.uk/\\_data/assets/pdf\\_file/0004/22666/FINAL\\_Sepsis\\_Report\\_web.pdf](http://www.ombudsman.org.uk/_data/assets/pdf_file/0004/22666/FINAL_Sepsis_Report_web.pdf), last accessed 20<sup>th</sup> June 2016
2. UK Sepsis Trust, 2016. Derived from data provided by the Health and Social Care Information Centre (HSCIC). Available at <http://sepsistrust.org/our-statistics-and-why-it-matters-march-2016/>, last accessed 20<sup>th</sup> June 2016
3. Seymour CW, Rea TD, Kahn JM, et al. Severe Sepsis in Pre-Hospital Emergency Care: Analysis of Incidence, Care, and Outcome. *American Journal of Respiratory and Critical Care Medicine* 2012; 186(12): 1264–1271
4. Nafsi T, Russell R, Reid CM, et al. Audit of deaths less than a week after admission through an emergency department: how accurate was the ED diagnosis and were any deaths preventable? *Emergency Medicine Journal* 2007; 24: 691-695
5. Vincent JL, Sakr Y, Sprung CL et al. Sepsis in European intensive care units: results of the SOAP study. *Critical Care Medicine* 2006; 34: 344–53
6. Hall MJ, Williams SN, DeFrances CJ, et al.: Inpatient care for septicemia or sepsis: A challenge for patients and hospitals. NCHS data brief Hyattsville, MD: National Center for Health Statistics 2011; 62
7. Kumar A, Roberts D, Wood KE et al. Duration of hypotension prior to initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Critical Care Medicine* 2006; 34: 1589–96
8. Daniels R, Nutbeam I, McNamara G et al. The sepsis six and the severe sepsis resuscitation bundle: a prospective observational cohort study. *Emergency Medicine Journal* 2011; 28(6): 459-460
9. Levy MM, Dellinger RP, Townsend SR et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Critical Care Medicine* 2010; 38(2): 367-74
10. Available via the College of Emergency Medicine website at <http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Audit/Previous%20Audits>, last accessed 16<sup>th</sup> June 2014
11. Singer M, Deutschmann CS, Seymour CW, et al for the Sepsis Definitions Task Force. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016; 23;315( 8): 801-10
12. NICE NG51 (publication pending)

13. Parliamentary and Health Service Ombudsman, 2014, London. Sepsis- a Time to Act. Available online at [http://www.ombudsman.org.uk/\\_data/assets/pdf\\_file/0004/22666/FINAL\\_Sepsis\\_Report\\_web.pdf](http://www.ombudsman.org.uk/_data/assets/pdf_file/0004/22666/FINAL_Sepsis_Report_web.pdf), last accessed 20<sup>th</sup> June 2016
  
14. Levy MM, Fink MP, Marshall JC et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Intensive Care Medicine* 2003; 29: 530–8
  
15. Keep JW, Messner AS, Sladden R et al. National early warning score at Emergency Department triage may allow earlier identification of patients with severe sepsis and septic shock: a retrospective observational study. *Emergency Medicine Journal* 2016; 2016; 33: 37–41.
  
16. Trzeciak S, Chansky ME, Dellinger PR et al. Operationalizing the use of serum lactate measurement for identifying high risk of death in a clinical practice algorithm for suspected severe sepsis. *Academic Emergency Medicine* 2006; 13: 150–1
  
17. Marty P, Roquilly A, Vallee F, et al. Lactate clearance for death prediction in severe sepsis or septic shock patients during the first 24 hours in Intensive Care Unit: an observational study. *Annals of Intensive Care* 2013; 3(1): 3
  
18. Mikkelsen ME, Miltiades AN, Gaieski DF, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Critical Care Medicine* 2009; 37 (5): 1670-7
  
19. Seymour CW *et al.* JAMA. doi:10.1001/jama.2016.0288 Supplementary online content, eFigure 12
  
20. Miller RR, Dong L, Nelson NC, et al. Multicenter implementation of a severe sepsis and septic shock treatment bundle. *American Journal of Respiratory and Critical Care Medicine* 2013; 188(1): 77-82
  
21. Rivers E, Nguyen B, Havstad S et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *New England Journal of Medicine* 2001; 345: 1368–77
  
22. The ProCESS Investigators. A Randomized Trial of Protocol-Based Care for Early Septic Shock. *New England Journal of Medicine* 2014; 370:1683-1693
  
23. Sepsis- the state of the NHS. Annual report of the All Party Parliamentary Group on Sepsis. Available online at <http://sepsisappg.com>, last accessed August 2014