THE UK SEPSIS TRUST

Clinical Toolkit 6: Emergency Department management of Paediatric Sepsis

This clinical toolkit has been developed by the UK Sepsis Trust. Sepsis in paediatrics is often difficult to diagnose and symptoms may mimic other common neonatal and childhood illnesses. This toolkit is designed to provide operational solutions to the complexities challenging the reliable identification and management of sepsis in children presenting to the non-specialist Emergency Department and complements clinical toolkits designed for other clinical areas. The overall objective is to make sure we recognise sepsis early and treat it aggressively in time critical way and are therefore finally able to decrease the preventable deaths it causes. We acknowledge use of some content from the Emergency Medicine Toolkit and the Acute Medicine Toolkit developed by the UK Sepsis Trust & Royal College of Physicians.

First published: September 2015

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Toolkit: Emergency Department management of Paediatric Sepsis

Introduction

Emergency Departments (EDs) are often the first point of contact for a sick child. The knowledge and skills to recognize a child with sepsis early amongst those children with benign febrile illness, and initiate appropriate resuscitation and treatment, is likely to prove a very important determinant in reducing mortality and morbidity associated with sepsis. Given the time dependent changes in outcomes, EDs play a crucial role in the management of the child with sepsis. The working hypothesis for creating this toolkit is that all health professionals, after appropriate training, are capable of recognising sepsis early and instituting basic treatment in whatever setting the patient is initially seen.

Background

Sepsis is a significant health problem associated with the use of extensive healthcare resources[1]. Globally, sepsis is responsible for 20 to 30 million deaths per year including 6 million neonates and children[2], and it is estimated that almost 60% of deaths in children under 5 years of age are attributable to infection[3]. A large international prevalence study (Sepsis PRevalence, OUtcomes, and Therapies (SPROUT)) of severe sepsis in paediatric intensive care units around the world has recently found that the global prevalence of severe sepsis in paediatric intensive care units was 8.2% (95% confidence interval 7.6% to 8.9%)[4]. This problem is not only limited to developing countries but represents a significant clinical challenge even in developed countries.

Febrile illness in childhood is a common reason for presentation to the ED. In one study from a single ED in the UK 20% of the 30,000 attendances in one year were found to be due to fever[5], it being the second most common cause for attendance after breathing problems. However, not all children with sepsis will present with fever. Signs and symptoms can be subtle and interpretation is dependent on a culture of awareness and suspicion of the condition. Mortality in children with infection once they are admitted to PICU is 15-20%, yet overall cohort mortality for sepsis is under 10%. It's essential we spot sepsis early.

Severe sepsis is a time-critical condition. In the most severe cases in adults, those with septic shock, for every hour that appropriate antibiotic administration is delayed, there is a 7.6% increase in mortality[6]. There are practical reasons leading to delays in sepsis care in the Emergency Department: delays in recognition of sepsis and delays in implementation of resuscitative measures[7]. Detection of septic shock in children can be more difficult, at least in part, because of the greater ability of children to compensate during the early stages[8]. This, together with difficulties in venous access, lack of familiarity with paediatric physiology and operational process issues can lead to delays in recognition and management. Tools for recognition and standardized management approaches have been shown to be effective against some of these barriers which have led to improved treatment times and a reduction in variability of care[9]. Hospital length of stay is known to be reduced by compliance with treatment bundles comprising early recognition of septic shock, obtaining vascular access, administering intravenous (IV) fluids, delivery of vasopressors for fluid refractory shock, and antibiotic administration[10]. It was recognised that lack of knowledge regarding recommendations, lack of early recognition, difficulties in securing vascular access and inability to administer IV fluids quickly were the key barriers. In a follow up study[11] with education/training of all key stakeholders, hospital-wide advertisement of the goals and regular measurement of efficacy of key interventions, adherence to the bundle and admissions to ICU reduced, and mortality improved.

Presently, the diagnosis of severe sepsis (which will in the remainder of this document be used to also include cases that present as or progress to septic shock) is highly dependent on the clinical acumen of the caregiver and thus potentially subject to error. Creating an effective screening tool for children is challenging because vital signs (i.e. heart rate (HR), respiratory rate (RR), and blood pressure (BP) and some laboratory values are age-dependent; what is normal for 1 year old infant will be highly abnormal for a 15 year child.

Professional responsibility & accountability

The Royal College of Paediatrics and Child Health and Royal College of Emergency Medicine are committed to continued, sustainable improvement in the management of all patients with sepsis.

NHS England has 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. It signposts to clinical toolkits such as this, and to education programmes, examples of good practice, and other available resources. NHS England is working with the UK Sepsis Trust and professional body stakeholders to identify and accredit exemplar centres from which others can learn. 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. As a direct result of this work, NICE will produce a clinical guideline due in July 2016 and subsequent Quality Standard against sepsis, the latter carrying statute for implementation.

We will learn valuable lessons from the report arising from the forthcoming report of the survey on sepsis conducted by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), although this will be focused on the adult population. Until that time, it is the responsibility of those commissioning services from, designing clinical systems for, and working within EDs to focus their efforts on early recognition, urgent intervention using existing consensus guidelines from the UK Sepsis Trust and Surviving Sepsis Campaign, and timely escalation for patients with sepsis. Commissioning for excellence in adults and children has been supported by a national CQuIN (Commissioning for Quality and Innovation) since April 2015.

International definitions for childhood sepsis

(from the International Consensus Conference on Pediatric Sepsis)[12]

Infection:

Suspected or proved infection with any pathogen

Systemic inflammatory response syndrome:

Generalised inflammatory response, defined by the presence of ≥2 of the following criteria (abnormal temperature or white cell count must be one of the criteria):

- Abnormal core temperature (< 36 degrees or > 38.5°C)
- Abnormal heart rate (>2 standard deviations above normal for age, or less than 10th centile for age if child aged < 1 years)
- Raised Respiratory rate (>2 standard deviations above normal for age, or mechanical ventilation for acute lung disease)
- Abnormal white cell count in circulating blood (above or below normal range for age, or >10% immature white cells)

However, the white cell count is not routinely available at initial assessment and therefore is not usefully included in an initial screen. Not all children with fever will go on to have blood tests.

Sepsis:

Systemic inflammatory response syndrome in the presence of infection

Severe sepsis:

Sepsis in the presence of cardiovascular dysfunction, acute respiratory distress syndrome, or dysfunction of ≥2 organ systems

Septic shock:

Sepsis with cardiovascular dysfunction persisting after at least 40 mL/kg of fluid resuscitation in one hour

Refractory septic shock:

Fluid refractory septic shock— shock persisting after ≥60 mL/kg of fluid resuscitation

Catecholamine resistant septic shock:

Shock persists despite treatment with catecholamines (that is, dopamine or adrenaline (epinephrine) infusion, or both, or noradrenaline (norepinephrine) infusion)

Describing the solutions – how can we be good at treating sepsis?

Organizations should be explicit about whether the intent is to initiate standardized care in patients once severe sepsis (including septic shock) has developed, or in all patients including those with uncomplicated sepsis who still represent a high-risk population. International guidelines recommend the application of standards of care including first-hour antibiotics to children with severe sepsis and septic shock, but some organisations have elected not to 'wait' for organ dysfunction to develop. The importance of full and complete evaluation, the use of early warning scores to track trend, and of national guidance such as NICE feverish illness[13] to elicit Red Flag Sepsis signs and an appropriate understanding of higher risk groups (such as very young children, those with chronic conditions and those for whom no focus of fever can be found) should be included in any education package and operational policy. Whichever strategy an organization adopts, it is key that the decision is clear and communicated to all staff.

2) Early Recognition:

a) Screening stage 1: Identify systemic inflammation

Sepsis arises when the body's response to infection causes systemic effects that manifest as two or more of the systemic inflammatory response syndrome (SIRS). The original definitions of SIRS and Sepsis were proposed for adults by the American College of Chest Physicians and Society of Critical Care Medicine[14] containing physiological values and biochemical parameters appropriate for adults.

In children, the normal range for physiological parameters varies according to the child's age and a number of other factors such as temperature and fear. Therefore, some alterations to the definitions were required[12].

Suspicion of an infective cause is all that is required to initiate screening, and staff undertaking triage and early assessment should be trained in paediatric sepsis recognition. The most common sources are respiratory, urinary or gastrointestinal but staff must also be aware that there are many other causes and sufferers may not show any signs of localisation. All patients presenting with physiological disturbances that could meet the SIRS criteria should also be formally screened for sepsis, as should any child with purpuric rash. We would suggest using 'Modified paediatric SIRS criteria suggestive of infection' as defined below:

Box 1: Modified paediatric SIRS criteria suggestive of infection

- Core temp <36°C or > 38.5°C.
- Inappropriate tachycardia (or bradycardia) for age.
- Altered mental status (including sleeping/ irritability/ lethargy/ floppiness.
- Reduced peripheral perfusion/ prolonged capillary refill /reduced urine output or wet nappies.

If a child with suspected or proven infection has at least two of the above criteria then it should be assumed sepsis is present and screening should proceed for Red Flag Sepsis (defined below).

Box 2: Age-specific vital signs and laboratory variables[12]

(Lower values for heart rate, leukocyte count, and systolic blood pressure are for the 5th and upper values for heart rate, respiration rate, or leukocyte count for the 95th percentile).

	Heart Rate, Beats/Min	Heart Rate, Beats/Min	Respiratory Rate	Leukocyte Count	Systolic Blood Pressure
	Tachycardia	Bradycardia	Breaths/Min	Leukocytes $10^3/mm^3$,	mmHg
Birth to 1 week	>180	<100	>50	>34	<65
1 week to 1 month	>180	<100	>40	>19.5 or <5	<75
1 month to 1 year	>180	<90	>34	>17.5 or <5	<100
2 to 5 years	>140	NA	>22	>15.5 or <6	<94
6 to 12 years	>130	NA	>18	>13.5 or <4.5	<105
13 to 18 years	>110	NA	>14	>11 or <4.5	<117

One example of age specific vital signs is displayed in Box 2. It is important that staff are aware of the age related ranges which can be normal for a given age. The exact values for ranges of physiological parameters for each age group are constantly debated and will vary slightly according to different sources. A value outside of the range used must be interpreted in the context of the full clinical examination of the child. The importance of recording a full set of observations, tracking trends and the utilisation of age specific early warning scores must be highlighted in any education package.

b) Screening stage 2: Screening for Red Flag Sepsis

International definitions for severe sepsis and septic shock rely upon screening for a complex battery of physiological and laboratory tests, as described in Box 4. Whilst suitable for defining study populations, these criteria are not practical in aiding urgent decision-making in the ED. Many of the organ dysfunction criteria described in Box 4 are based on laboratory values which might not be available in the ED in the first hour following the patient's presentation. We recommend the adoption of a modified set of criteria, termed Red Flag Sepsis and detailed in Box 3, which are measurable at the bedside as an operational solution to the complexities in recognition according to established consensus definitions. Red Flag Sepsis criteria in children are based upon the organ dysfunction criteria described above coupled with the NICE traffic light system from the Feverish Illness guideline (parameters highlighted in red below) (CG160)[13] and provide a pragmatic framework on which timely intervention decisions can be made.

Box 3: Red Flag Sepsis criteria for children

- Hypotension, defined as Systolic Blood Pressure <2 SD for age, Mean Blood Pressure <2 SD for age (age times 2 + 70) (see Box 2)
- Blood gas lactate >twice upper limit of normal
- Prolonged capillary refill >5 seconds
- Pale/ mottled/ ashen/ blue or non-blanching (purpuric) rash
- Oxygen needed to maintain saturations >92 %
- Respiratory rate >60 min^{-1} or >5 below the normal, or grunting
- AVPU = V, P or U
- Parents report excessively dry nappies, lack of response to social cues, significantly decreased activity or weak, high-pitched or continuous cry

There is no systems substitute for clinical experience and acumen in dealing with sick children, but Red Flag Sepsis will help early identification of those children with systemic response to infection.

A full set of observations should be performed, including blood, ideally with continuous monitoring of heart rate, respiratory rate, blood pressure and oxygen saturations. Serum lactate should be measured from a venous or capillary sample, or as part of an arterial blood gas sample and in addition to a full set of screening blood tests. IV access should be obtained but must not delay blood sampling if difficult. A chest x-ray, urinalysis and culture of urine and any other relevant specimens should be requested and reported as appropriate to rule in or rule out possible sources of infection.

Box 4: Organ dysfunction criteria according to international definitions[12]

Cardiovascular dysfunction
Despite administration of isotonic intravenous fluid bolus 40 mL/kg in 1 hour ● Systolic BP remains below normal for age OR ● Need for vasoactive drug to maintain BP in normal range OR ● Two of the following: Unexplained metabolic acidosis: base deficit >5.0 mEq/L Increased arterial lactate >2 times upper limit of normal Oliguria: urine output <0.5 mL/kg/hr Prolonged capillary refill: >5 secs Core to peripheral temperature gap >3°C
Respiratory
● PaO_2/FiO_2 <300 in absence of cyanotic heart disease or preexisting lung disease OR ● $PaCO_2$ 65 torr or 20 mmHg over baseline $PaCO_2$ OR ● Proven need for 50% FiO_2 to maintain saturation 92% OR ● Need for non-elective invasive or noninvasive mechanical ventilation
Neurologic
● Glasgow Coma Score <11 OR ● Acute change in mental status with a decrease in Glasgow Coma Score 3 points from abnormal baseline
Hematologic
● Platelet count 80,000/mm^3 or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic hematology/oncology patients) OR ● International normalized ratio >2
Renal
● Serum creatinine 2 times upper limit of normal for age or 2-fold increase in baseline creatinine
Hepatic
● Total bilirubin 4 mg/dL (not applicable for newborn) OR ● ALT 2 times upper limit of normal for age

2) Recognition strategies determined by route of entry

Opportunities for sepsis identification will vary according to the route by which a patient has presented, and this toolkit will complement other toolkits produced by the UK Sepsis Trust. The assessment and screening process for sepsis in children should be the same regardless of the location in which it is first done. Individuals who may be involved in the assessment of the sick child must ensure they maintain appropriate skills and have a low threshold for referring on to a paediatric specialist should there be uncertainties.

a) Children arriving by ambulance using pre-alert.

The clinical toolkit for adult prehospital services recommends that Paramedics and Community First Responders be trained to screen for sepsis using the NEWS track and trigger scoring system in adults. UK Sepsis Trust will work through 2016 to produce an equivalent for children based upon this toolkit and its recommendations. Supported by guidance from the Joint Royal Colleges Ambulance Liaison Committee (JRCALC) and by prehospital screening tools, practitioners will in time pre-alert receiving EDs when presented with a child with potential Red Flag Sepsis. Pathways should be developed through collaborative workshops involving ED staff, ambulance service staff, patient representatives, managers and commissioners. Emergency Departments may be pre-alerted to the arrival of a child with sepsis on the basis of abnormal physiology for age, reduced GCS, seizures, purpuric rash or other clinical signs suggestive of serious underlying disease.

b) Children arriving to the ED having been sent via NHS Pathways/111, or via primary and community pediatric care.

These patients may already be suspected of having sepsis. It is the duty of the ED staff to ensure that the patient is seen and assessed immediately, and ideally moved to an area of appropriate care such as the Resuscitation area, where they can undergo sepsis screening.

c) Children 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 and/ or initial assessment in the ED, all patients who may have sepsis should undergo screening for the presence of sepsis and, if present, the patient should be risk stratified accordingly.

As well as the general impression at the time of triage/ initial assessment, the presence of abnormal observations should be enough to initiate sepsis screening using a Red Flag Sepsis tool. Some EDs use Early Warning Scores (such as PEWS) and the ED must decide the lowest score that will trigger escalation and a sepsis screen.

3) Urgent intervention

Commence Paediatric Sepsis 6 immediately if ANY ONE of the Red Flag Sepsis criteria is present, and a clinical diagnosis of sepsis has been made by a clinician.

Sepsis is a medical emergency, and therefore all measures should be in place to tackle it like an emergency – prioritizing prompt diagnosis and treatment. It has been demonstrated that the administration of antibiotics is time critical[(15)(16)] and the Surviving Sepsis Campaign improvement programme showed an Odds Ratio for death of 0.86 in adult patients receiving antibiotics within the first three hours following presentation[(17)].

The key immediate interventions that increase survival are described in a bundle termed the Paediatric Sepsis Six (PS6). Various studies have shown that adherence to ACCM-PALS guideline for management of paediatric sepsis is associated with improved outcomes, however adherence to these guidelines is poor[(18)(9)].

The Paediatric Sepsis 6 is designed to help deliver the initial steps of the ACCM-PALS guidelines (rather than replace them) in a simple and timely fashion. Developed by the UK Sepsis Trust Paediatric Group, the Paediatric Sepsis Six is modelled on the adult Sepsis Six programme. The adult programme has been shown to improve adherence to resuscitation bundles and early goal directed therapy guidelines, and is associated with reduced mortality[(15)]. It is designed to empower medical and nursing staff to recognise sepsis early and initiate treatment rapidly. The aim, through education, is to engender a culture where sepsis is an emergency requiring urgent intervention.

Where doubt exists, a clinician experienced in the recognition of sepsis in children should be consulted immediately and the basic components of the Paediatric Sepsis 6 initiated as appropriate. Care pathways should permit variance in complex or unclear cases. Examples would be:

- Difficult capillary sampling casts doubt over the validity of a lactate measurement
- Clinicians are not convinced that a bacterial infection exists in an individual child- for example, viral gastroenteritis with dehydration might mimic sepsis
- Co-existing conditions- for example a child with congenital heart disease may inappropriately trigger based on tachycardia

The Paediatric Sepsis 6 should be completed within one hour of initial identification, without waiting for the results of further investigations. Following delivery of the Paediatric Sepsis 6, children should be placed on a standardized pathway of care to ensure optimal sepsis management as recommended by the Surviving Sepsis Campaign regardless of the time of day or experience of the staff.

Venous access is of prime importance and has been emphasized in all paediatric life support courses. Since these children can have extremely poor perfusion and can challenging to cannulate, the most senior and experienced clinician should attempt to gain IV access, if after 2 attempts IV access is still not possible, intraosseous access should be obtained (details as APLS/PALS guidelines).

For respiratory distress and hypoxemia give oxygen by facemask; if signs and symptoms are severe (and if available) give high flow nasal cannula oxygen or nasopharyngeal CPAP. If mechanical ventilation is required then cardiovascular instability during intubation is less likely after appropriate cardiovascular resuscitation.

Box 5: Paediatric Sepsis 6

Paediatric Sepsis 6

Name:

Date of Birth:

Hospital No.:

Affix Hospital Label if available

Recognition of a child at risk:

If a child with suspected or proven infection AND has at least 2 of the following:

- Core temperature < 36°C or > 38.5°C
- Inappropriate tachycardia (Refer to local criteria / APLS Guidance)
- Altered mental state (including: sleepiness / irritability / lethargy / floppiness)
- Reduced peripheral perfusion / prolonged capillary refill

Lower threshold of suspicion for: age < 3 months, chronic disease, recent surgery, or immunocompromised

THINK: Could this child have SEVERE SEPSIS, SEPTIC SHOCK or RED FLAG SEPSIS* - Ask for review by an experienced clinician.

Date/Time of escalation	
Sign	

High certainty of Sepsis
Respond with Paediatric Sepsis 6:

Date/Time of review	Sign

Complete all elements within 1 hour

	Date/Time	Sign
1. Give high flow oxygen:		
2. Obtain IV / IO access & take blood tests:		

a. Blood cultures
b. Blood glucose - treat low blood glucose
c. Blood gas (+ FBC, lactate / CRP as able)

	Date/Time	Sign
3. Give IV or IO antibiotics:		

- Broad spectrum cover as per local policy

	Date/Time	Sign
4. Consider fluid resuscitation:		

- Aim to restore normal circulating volume and physiological parameters
- Titrate 20 ml/kg Isotonic Fluid over 5 - 10 min and repeat if necessary
- Caution with fluid overload:
  Examine for crepitations & hepatomegaly

	Date/Time	Sign
5. Involve senior clinicians / specialists early:		
6. Consider inotropic support early:		

- If normal physiological parameters are not restored after ≥ 40 ml/kg fluids
- NB adrenaline or dopamine may be given via peripheral IV or IO access

Document reason(s) for variation overleaf

High certainty NOT Sepsis or Unsure

	Date/Time	Sign
Not Sepsis Document reasons		
Unsure		

Review within 1 hour

Not Sepsis Document reasons		
Sepsis Start Sepsis 6		
Unsure		

Review within 1 hour

Not Sepsis Document reasons		
Sepsis Start Sepsis 6		
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Sepsis Start Sepsis 6		

Paediatric Sepsis 6 version 11.1 August 2015 in collaboration with the UK Sepsis Trust Paediatric Group. For further information please contact jtong@nhs.net

Empiric antibiotics (for an example of a suitable guideline see Box 6) should be administered within 1 hour of identification of severe sepsis. Blood cultures should be obtained before administration of antibiotics when possible and this should not delay administration of antibiotics. In adults there is evidence that with every 1 hour delay in starting antibiotics in patients with septic shock there is 7.6% increase in mortality[6]. In paediatrics, though the research is not that robust, studies have shown that children with severe sepsis, when given antibiotics within 1 hour, had their shock reversed in shorter time and their lactate and C reactive protein levels were lower within 24 hours of admission[19]. Evidence is mounting that early intervention with appropriate antibiotics saves lives[20].

In any patient where antibiotics are commenced, need for ongoing therapy and their appropriateness should be reviewed regularly. Prescriptions should include a review date (typically within 48-72 hours when microbiology results should be available) and expected duration. For patients in whom the source of infection or diagnosis is unclear, review should also occur at first Consultant assessment. Where microbiology results provide opportunity for de-escalation and this does not occur, the reason should be documented in the medical notes.

Box 6: Choice of antibiotics: example of good practice

Meningitis	Age under 7 days	Amoxicillin 50mg/kg every 12 hours PLUS Cefotaxime 50mg/kg every 12 hours
	Age over 7 days and under 3 months	Amoxicillin 50mg/kg every 4-6 hours PLUS Cefotaxime 50mg/kg every 6-8 hours
	Age over 3 months	Cefotaxime 50 mg/kg every 8 hours (max single dose 4g) Immunocompromised/on immunosuppressants Meropenem 40 mg/kg every 8 hours (max single dose 2g)
Community acquired sepsis without meningitis	Age under 7 days	Amoxicillin 30 mg/kg every 12 hours plus Cefotaxime 50 mg/kg every 12 hours NB: if baby <48h old you may give: Benzyl penicillin or amoxicillin + gentamicin
	Age over 7 days and under 3 months	Amoxicillin 30 mg/kg every 8 hours, Plus Cefotaxime 50 mg/kg every 8 hours
	Age over 3 months	Cefotaxime 50 mg/kg every 8 hours

Additional considerations:

Difficult IV access:

- Same regimen to be used for IO access if and when obtained.
- Intramuscular Ceftriaxone 50mg/kg od plus Gentamicin 7mg/kg od is an alternative if no IV/IM/IO access is obtained

Microbiology Consultation is advised in case of the following:

- If allergic to first line antibiotic
- If patient has recently been discharged from Hospital
- If the patient is immunocompromised due to any aetiology or is on an immunosuppressant.

Initial resuscitation of hypovolemic shock begins with the infusion of isotonic crystalloids or 4.5% albumin with boluses of up to 20 ml/kg over 5–10 minutes, titrated to reversing hypotension, increasing urine output, and attaining normal capillary refill, peripheral pulses, and level of consciousness without inducing fluid overload. Hepatomegaly or rales (crepitations on auscultation of the chest) are examples of clinical signs of fluid overload, and if present, should prompt support with inotropic therapy.

Begin peripheral inotropic support until central venous access can be obtained in children who are not responsive to fluid resuscitation. Peripheral dopamine or adrenaline can be started pending IO/central access. (Refer to paediatric formulation for how to constitute adrenaline/dopamine for peripheral use). Timely hydrocortisone therapy in children with fluid refractory, catecholamine-resistant shock and suspected or proven absolute adrenal insufficiency may be of benefit.

Attention should be focused on urgent ongoing resuscitation and wider management including control of any source amenable to drainage or removal within 12 hours.

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, then ED staff may initiate centrally administered inotropic or vasopressor support where skills permit. All patients in whom advanced resuscitation has been commenced will require ongoing care, according to response, in a Level 1 facility[21] as a minimum.

In adults with severe sepsis and septic shock, the lactate level is an important and well-studied prognostic marker of mortality. The lactate level in adults with sepsis is highly predictive of death[22] and poor outcomes and, when initially elevated, the degree of reduction following resuscitation ('lactate clearance') predicts survival[23]. There are not many studies on lactate levels in the pediatric age group with sepsis or septic shock. In neonates, studies have shown a poor correlation between pH or base excess and blood lactate concentration, and independent measurements of the latter are needed[24]. In preterm newborns, hyperlactatemia has been described as an indicator of the presence of sepsis, but the predictive value for the outcome is uncertain[25]. In paediatric severe sepsis and septic shock, results of lactate assays are conflicting with some studies suggesting lactate as a good predictor of mortality[26][27] and others not finding it an independent predictor.

When shock has been identified via a lactate measurement from a venous or capillary lactate sample, an arterial lactate should be drawn where possible once fluid resuscitation has been commenced to corroborate results. A capillary or venous lactate from a correctly calibrated device which is normal is reassuring as a stand-alone.

For Red Flag Sepsis patients- i.e. those who qualify as severe sepsis only via one of the additional criteria described above and highlighted in red- if subsequent blood results are not confirmatory for severe sepsis (where this confirmation is deemed necessary) then a Consultant should consider alternative diagnoses and review the need for ongoing antimicrobial therapy and other aspects of the Paediatric Sepsis 6 pathway.

It should be remembered that Red Flag Sepsis is an operational solution only to prompt earlier intervention, and that to confirm or exclude the presence of severe sepsis or septic shock according to international definitions will in some cases only be possible with blood test results from the laboratory. The time taken to receive results can be significantly reduced by use of a set 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 for all patients with suspected but as yet unconfirmed sepsis to have urine output monitoring.

4) Confirmation according to international definitions *(if required)*

We recommend that organisations evaluate the need to identify sepsis according to the more complex set of organ dysfunction criteria according to international consensus definitions described in Box 4. Where this is deemed necessary, the child should be reviewed by a Consultant within a maximum of one hour with results of the following:

- Blood gases including lactate, PaO_2, $PaCO_2$ and base deficit
- Platelet count
- INR (international normalised ratio)
- Creatinine
- Bilirubin
- ALT

All patients identified with Red Flag Sepsis should have a full set of bloods taken and a monitoring and response plan detailed, irrespective of whether a formal screen for severe sepsis is to be undertaken.

Case Studies

A 3 year old boy presents to the ED with fever and vomiting after 8 hours of progressive listlessness. He has a temperature of 38.8 degrees and a tachycardia of 172 beats per minute, brisk capillary refill, mild tachypnoea, and petechiae over the neck, face and extremities. The triage nurse is concerned by these observations and ensures that he's seen immediately by the Registrar for sepsis screening.

The ED registrar confirms the presence of modified SIRS and suspects that the child has meningococcal disease. 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 measures serum lactate and throat swab.

The ED registrar diagnoses Red Flag Sepsis based upon significant tachycardia and instigates treatment immediately, following the Paediatric Sepsis Six (PS6). Laboratory bloods subsequently demonstrate a raised CRP and white cell count. Treatment was started nearly an hour before it otherwise might have been, possibly significantly more if the child had not been reviewed promptly with results.

A 15 day old baby, born at full term with no perinatal complications and discharged home on day 1, was brought with history of not feeding well for 2 days and decreased activity. Her nappy changes have been less frequent. Her temperature was 36.5°C. She was lethargic, peripherally cold and appeared mottled.

The SHO recognized that the baby is sick and immediately informed the registrar. She was not able to perform any investigations as she had difficulty in blood sampling. The registrar then recognized that the baby had Red Flag Sepsis (based upon dry nappies and mottled skin) and started treatment immediately.

This age group represent a high risk group in which the sepsis may be harder to diagnose using traditional parameters, therefore the threshold for suspicion of sepsis should be high and clinical experience and acumen trusted.

A normally well 14 year old boy with his father 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 due to his respiratory distress and moved him to the 'Majors' area and asked the SHO to review and to gain IV access and send bloods.

The SHO 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.

The SHO recognized the seriousness of this result and informed the Registrar, requesting that the patient be seen immediately due to the presence of Red Flag Sepsis. The Registrar immediately started treatment and arranged for close monitoring.

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 (may add 'refractory' or 'catecholamine-resistant'
Severe Sepsis
Red Flag Sepsis
Uncomplicated sepsis
No current evidence of sepsis

'Sepsis' as a stand-alone term is not acceptable: documentation must record acuity as described. Until test results are back, it may not be possible to definitively record the severity of a patient's sepsis.

5) 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'. 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 child with sepsis is identified.

A pragmatic solution to the pressing need to identify specific teams to manage children with sepsis may lie in existing resources- for example the paediatric cardiac arrest team or the clinical team who assemble on an ambulance pre-alert. These already pressured teams should not be assumed to have capacity to undertake the necessary monitoring and improvement programmes but the fact that resources need allocating to improve outcomes from sepsis is inescapable. The new national CQuIN on sepsis should be considered as an opportunity to initiate investment in improving outcomes from sepsis. 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 children with Red Flag Sepsis, severe sepsis and septic shock should be reviewed at the earliest opportunity by the most senior available doctor, as a minimum with ST4 medical review within 30 minutes of arrival and by a Consultant within 60 minutes.

Some children with sepsis may have co-morbidities or chronic disease. For such children, decisions should be taken at senior level (in consultation with the patient, their family and regular clinical team 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, documented and available to staff in the Emergency Department.

Suggested clinical guidelines for the management of children attending with or developing sepsis in an Emergency Department:

Sepsis (uncomplicated):

- A documented decision to initiate the Paediatric Sepsis 6 or not
- Review by a senior doctor (ST4 or above) within 60 minutes of diagnosis
- Hourly observations whilst in the ED
- Consideration of a baseline lactate measurement and a documented decision if a repeat measurement is required and when.
- Escalate immediately if severe 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, safety-netting advice and advice regarding how to re-access healthcare if patient subjectively deteriorates documented

Severe Sepsis or 'Red Flag' sepsis pending confirmatory tests:

- Paediatric Sepsis 6 to be completed as soon as possible, but always within 60 minutes
- Review by a senior doctor (ST4 or above) within 30 minutes of arrival
- Review by a Consultant within 60 minutes following arrival
- Continuous monitoring or observations in accordance with recommendations for Early Warning Scores used locally, and escalation according to local guidance and resources.
- Repeat lactate measurement within 2 hours if baseline abnormal.
- 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 (responsible) Consultant within 14 hours

Septic Shock:

- Initiation of the Paediatric Sepsis 6 to be completed as soon as possible, but always within 60 minutes
- Review by a senior doctor (ST4 or above) as soon as possible but always within 30 minutes.
- Review by a Consultant as soon as possible but always within 60 minutes.
- Immediate referral by ED staff to Paediatric 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
- Review by admitting (responsible) Consultant within 14 hours

Pathways should also describe where children with sepsis should be nursed and clearly state the escalation status and any ceilings of care for each patient. 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.

Exemplar Standards for the emergency management of sepsis in children

The standards below are those which have been identified by the UK Sepsis Trust and the All Party Parliamentary Group 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 Red Flag Sepsis, severe sepsis and septic shock. Standards for recognition, intervention and escalation must be included.
2. All patients with physiological derangement, an elevated PEWS score above trigger threshold, or with clinical suspicion of infection to be screened for the presence of sepsis, severe sepsis or septic shock and to have a serum lactate within 30 minutes of arrival.
3. Clinical pathways to include initiation of all investigations necessary to confirm or exclude organ dysfunction (see Box 4) and to include criteria for escalation/ de-escalation of care.
4. The Paediatric Sepsis 6 to be used as a delivery method for early sepsis care and to be delivered within 1 hour post diagnosis in ≥95% of cases.
5. On diagnosis of sepsis, the child should not be moved prior to completion of the Paediatric Sepsis 6, 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, including on sepsis in childhood, 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.

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