Don't Forget The Bubbles

SIRS, SEPSIS AND SHOCK

Facilitators Guide

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Topic: **SIRS, Sepsis and Shock**
Author: **Michelle Alisio**
Duration: **2 hours**
Facilitator level **Senior trainee and above**
Learner level **Anyone who sees paediatric patients**
Equipment required: **Crunchie bars (x3), tongue depressors (x6), sleek tape, IO drill with needles (IO needles and 18 or 22G LP needles), saline flush, 3-way tap and giving set, gauze, umbilical clamp, micropore.**

OUTLINE

- **Basics (5 mins)**
- **Main session: (4 x 15 minutes) case discussions covering grey areas, diagnostic dilemmas; advanced management and escalation**
- **Quiz (10 mins) covering key points and evidence**
- **Practical Procedure (30min)**
- **Infographic sharing (5 mins): 5 take home learning points**

PRE-READING FOR LEARNERS

Expectation is for the learners to have read the basic pathophysiology links and some (not all) of the rest of the links

Sepsis/Shock Pathophysiology (video 10 minutes)
St Emlyns Blog: Paediatric Sepsis (20 minutes)
Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children (lengthy) OR DFTB summary (10min)
RCEMlearning: Recognising Paediatric Sepsis (15 minutes)
Paediatrics for Primary Care: Sepsis (10 minutes)
DFTB: FEAST trial analysis (10 minutes)

Podcasts

Ideally, the learners should have listened to these podcasts too
PEM Playbook: Approach to Shock (40 minutes)
DFTB: Fluid Assessment in Sepsis (20 minutes)

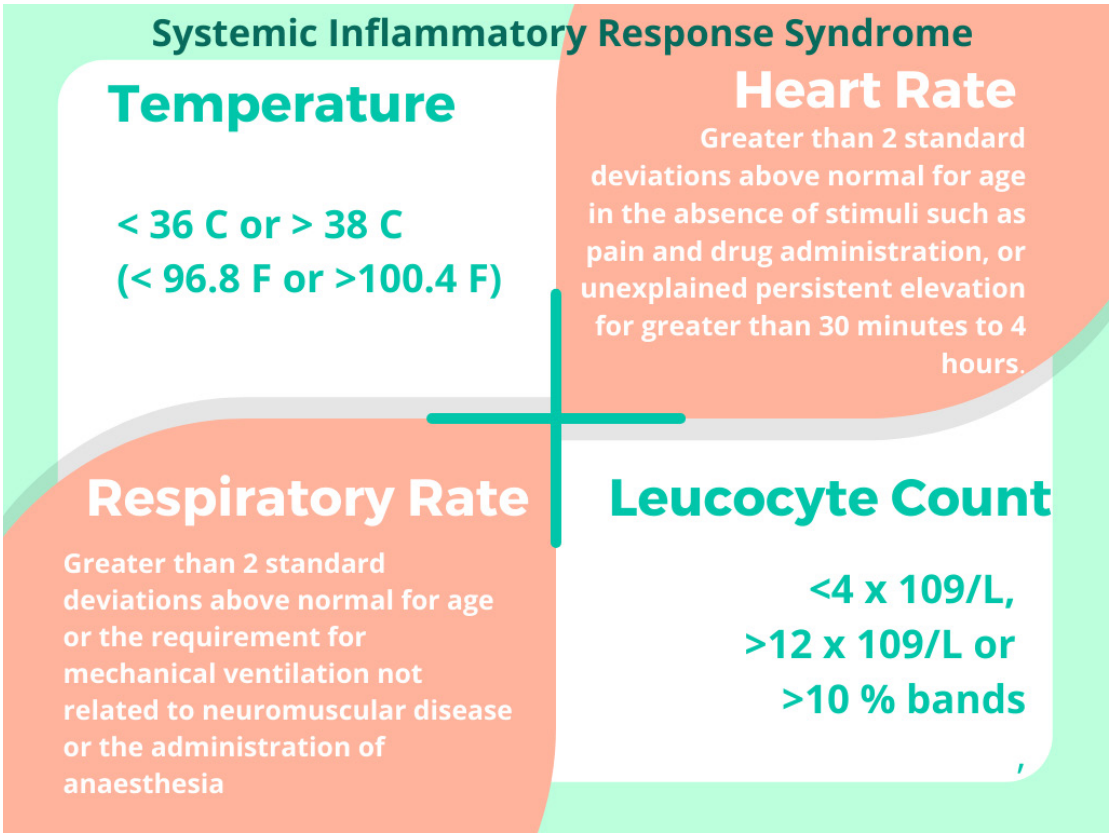
Practical Procedure

OpenPediatrics: Placement of an Intraosseous (IO) Line (video 23 minutes)
PEM Playbook: Paediatric Vascular Access

SIRS, Sepsis and Shock (from Research Gate 2018)

Systemic inflammatory Response Syndrome (SIRS) is an inflammatory state affecting the whole body because of a dysregulated host response between both pro- and anti-inflammatory processes. It can result from infectious and non-infectious causes, the latter which include autoimmune conditions, trauma, burns and anaphylaxis to name a few.

SIRS is the beginning phase of an inflammatory cascade of events, resulting in organ dysfunction, shock and ultimately multi-organ dysfunction syndrome (MODS) if left untreated. It is clinically recognised by 4 parameters. To fulfil SIRS criteria in Paediatrics, two of the following need to be met where one of which must be abnormal temperature or leucocyte count.



SIRS represents a whole organism response to a variety of quite different immune challenges. The cells responsible are mononuclear leukocytes, platelets and polymorphonuclear leucocytes (PMN) which release cytokines. These cytokines are soluble, low molecular weight glycoproteins which act as inflammatory mediators to regulate both innate and specific immune responses.

At low concentration, these cytokines have only paracrine effect but at higher concentration these have endocrine effect and act systemically. Tissue Necrosis Factorα (TNF) and Interleukin 1 (IL-1) are the first cytokines to be released within 1 hour of an insult and cause fever, release stress hormones and cleave the Nuclear Factor Kappa B (NFκB) inhibitor. Below is a diagram of the SIRS cascade

Pathophysiology of SIRS showing homeostatic imbalance in favour of pro- inflammatory state leading to the development of SIRS

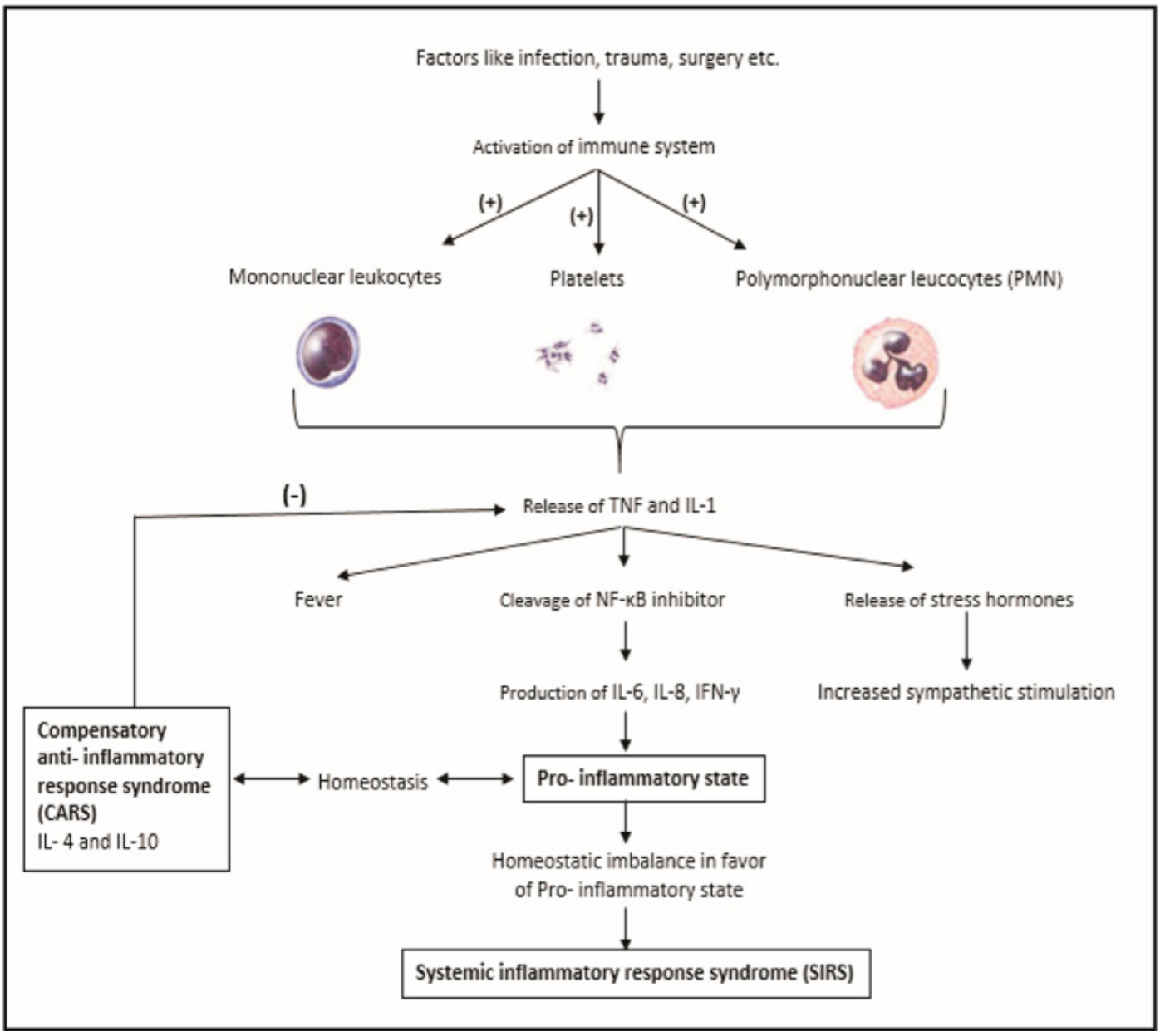


Image courtesy of Research Gate 2018

The changes involved in the process are basically responsible for uncontrolled systemic vasodilatation, decreased peripheral vascular resistance and hypotension, poor tissue perfusion, third space loss, lactic acidosis and hemodynamic instability which may be refractory to volume and inotropic support.

There is rise in energy demands, increased oxygen consumption, increased carbon dioxide production with metabolic acidosis, increased gluconeogenesis, lipolysis and aerobic glycolysis which are responsible for severe catabolic state and refractory to exogenous protein supplementation. Thus, pro- inflammatory state, is responsible for tachycardia, tachypnoea, hyperpyrexia or hypothermia, hypotension, oliguria, leucocytosis / leucopaenia, narrowed pulse and increased minute ventilation which are included in the diagnostic criteria for SIRS.

SIRS benefits:

Easy to use at the bedside, does not require sophisticated equipment or expertise, quick.

SIRS problems:
SIRS criteria have a poor ability to differentiate between self-limiting viral infections and sepsis. We send approximately 85% of children that meet SIRS criteria for sepsis home from the Paediatric Emergency Department (PED) without antibiotics. Meeting SIRS criteria is common in the PED.

Conversely, SIRS criteria lack specificity to identify children with infection at substantially higher risk of mortality. 30% of children admitted to ICU after being diagnosed by a clinician as septic do not meet the SIRS criteria for sepsis.

SIRS was built upon a foundation of basic clinical and laboratory abnormalities that were readily available in almost all clinical settings. SIRS criteria are non-specific and must be interpreted carefully within the clinical context and possibly be used as an early marker of severe or critical illness.

SIRS with a suspected source of infection is termed sepsis. Sepsis with one or more end-organ failure was severe sepsis, and with hemodynamic instability despite intravascular volume repletion is called septic shock. Regardless of the terms used together they represent a physiologic continuum with progressively

worsening balance between pro and anti-inflammatory responses of the body. Damian Roland uses the Sepsis spectrum traffic light analogy to highlight the challenges of recognising sepsis in children. Read more about it here http://rolobotrambles.com/sepsisspectrum/

Sepsis definition

Sepsis is a life-threatening condition that is challenging to diagnose early and accurately in children. Sepsis has complex pathophysiology causing a dysregulated inflammatory response due to infection resulting in organ dysfunction.
Because sepsis has a varied and nonspecific clinical presentation, affecting heterogeneous groups of people; a simple and objective definition is not easy.

Sequential Organ Failure Assessment (SOFA) score proposed for defining sepsis in adults has not been validated for children. Performance of the Pediatric Logistic Organ Dysfunction (PELOD-2), which is the closest to the SOFA score applied in adults, has not been prospectively validated in children with sepsis admitted to the paediatric ICU and is not an instrument used in emergency services and hospitalisation units, where there are many children with sepsis.

The recent Surviving Sepsis Campaign approach essentially divides children into those needing antibiotics within 3 hours (where sepsis is possible and maybe developing but the child isn't shocked and those that need antibiotics within one hour who have objective signs of organ dysfunction and shock.
This approach hasn't been universally adopted and for the purpose of training this guide utilises the one hour approach for all those children felt to have sepsis.

CASE SCENARIO 1

Zach's mum is very worried about her 3-week old son. This is her first child.
The pregnancy and birth were uncomplicated, except her 'water' broke early before she delivered. She said Zach hadn't breastfed well these last 2days and is more sleepy than usual today. He has no diarrhoea or vomiting and he feels hot to touch but she doesn't have a thermometer at home. On general appearance Zach is lethargic, HR 165, and his skin is mottled.
His glucose is 1.9 mmol/L and you notice a subtle twitching of his limbs. The team recognises that Zach could have sepsis and get on with administering high flow nasal cannula oxygen (HFNC), getting a scalp vein, correcting the glucose and giving antibiotics all within the first hour.

1. What is the most likely organism? In this age group, what other organisms would you consider in your differential and what first line antibiotics should you administer?
2. How else could the team have gained vascular access quickly?
3. Using an A,B,C,D approach; how would you have managed Zach?

Discussion points:

1. Things to consider in septic neonates and infants < 2months

These groups are at increased risk of invasive bacterial infections which include Group B Streptococcal disease (GBS), Listeria monocytogenes or Listeriosis and Escherichia Coli. An overgrowth of the yeast candida usually shows as a diaper rash or oral thrush.

Congenital infections are transmitted from mother to infant, either during pregnancy or delivery and are most often caused by viruses and parasites namely HIV; rubella; chickenpox; syphilis; herpes; toxoplasmosis; and cytomegalovirus (CMV). Some early signs of a possible congenital infection include: a large or small head, small body size, seizures, problems with the eyes, skin rashes, jaundice, enlarged abdominal organs, and a heart murmur.

Bacterial infections in the neonate present with one or more non-specific clinical signs such as feeding problems, lethargy, abdominal distension, diarrhoea,

jaundice, apnoea, tachycardia to name a few.
Ensure a neutral thermal environment (and monitor temperature) and ensure adequate nutrition. Enteral feeding where possible, via oro/nasogastric tube after ileus obstruction, apnoea or other contraindications to enteral feeding have been excluded. Give IV fluids if enteral feeding is not possible.
Antibiotics: always refer to your local guideline or consult with the Microbiologist on call if you are unsure. General approach in this age group:
<1 month of age give Cefotaxime and Ampicillin and Aciclovir
>1 month give Ceftriaxone

2. Vascular access

In a resuscitation setting, umbilical vein access continues to be the preferred route in neonates. However, umbilical veins can only be accessed up to 2 weeks and at this stage they are dry and require approximately 1 hour of saline gauze soaking before attempting access.

Ultrasound-guided peripheral intravenous (PIV) access for the external jugular vein; ultrasound-guided central venous access of femoral vein (for temporary use until definitive femoral catheter can be inserted). If two x failed PIV attempts then go straight to the intra-osseous route.

3. Sepsis management

Once suspected or recognised then early goal directed therapy or 'bundles of therapy' can be administered: aggressively manage sepsis and patients get better, it's been proven.
The SEPSIS 6 is a set of interventions which can be delivered by any junior healthcare professional working as part of a team. Sepsis 6 uses objective physiological measures from PEWS, emphasises importance of tachycardia, identifies high risk groups and includes early interventions all within the first hour.

PAEDIATRICS

Paediatric Sepsis 6

Severe sepsis is a CLINICAL EMERGENCY. Early treatment improves outcomes.

STOP

Recognition: A child with suspected or proven infection AND at least 2 of the following:

- Core temperature < 36°C or > 38°C (observed or reported in previous 4 hours)
- Inappropriate tachycardia (Refer to National PEWS)
- Altered mental state (including: sleepiness / irritability / lethargy / floppiness)
- Reduced peripheral perfusion / prolonged capillary refill / cool or mottled peripheries

THINK

Reduce Threshold:

Some children are at higher risk of sepsis. You may consider treatment with fewer signs than above. These include, but are not restricted to;

- Infants < 3/12
- Immunosuppressed / Immunocompromised / chemotherapy / long term steroids
- Recent surgery
- Indwelling devices / lines
- Complex neurodisability / Long term conditions (may not present with high PEWS but observations may vary from their baseline)
- High index of clinical suspicion (tachypnoea, rash, leg pain, biphasic illness, poor feeding)
- Significant parental concern

Think is this SEPSIS? If yes

DO

0 min

15 min ideal

60 min acceptable

Respond with Paediatric Sepsis 6 within 1 hour:

1. **Give high flow oxygen**
2. **Obtain intravenous or intraosseous access and take blood tests:**
   - Blood cultures
   - Blood glucose - treat low blood glucose
   - Blood lactate (or gas)
3. **Give IV or IO antibiotics:** Broad spectrum as per local policy

If shocked:

4. **Consider fluid resuscitation**:
   - Titrate 20 ml/kg isotonic fluid over 5 - 10 min and repeat if necessary
   - Aim to reverse shock – trend to normal heart rate, BP and peripheral perfusion
   - assess for fluid overload after ≥ 40 ml/kg fluids.
   - If no signs of fluid overload and remains shocked titrate further 20mls/kg fluid
5. **Consider inotropic support early:**
   - Adrenaline (reconstitute whilst administering 3rd fluid bolus. 0.3mg/kg in 50mls 5% dextrose. Commence 1ml/hr = 0.1mic/kg/min).
   - Can be given via peripheral IV or IO access
6. **Involve senior clinicians / specialists early**
   - Discuss with PICU if inotropes commenced

Further management discussion points:
Discuss early with (local) or regional intensive care services who offer decision making support and retrieval if necessary.

Airway and breathing:
Indications for immediate endotracheal intubation and mechanical ventilation are hypoxia, with severe respiratory distress indicating a progression of pulmonary oedema; severe persistent shock; fluctuating or decreasing conscious level (Glasgow Coma Score 8 or less, or a decrease of 3 points within 1hr) or signs of raised ICP. When possible the cardiovascular system should be stabilised before intubation, and the potential for acute decompensation should be anticipated. Inotropes, when indicated, should be started before intubation.

It is important that infants are reassessed clinically after commencing on High Flow Nasal Cannula (HFNC) oxygen in order to judiciously intervene in those who do not respond and may require escalation of respiratory support especially in settings where HFNC oxygen is used outside of an intensive care setting.

There was no need for urgent intubation, but because Zach remained lethargic after the first hour or resuscitation and was at increased risk of recurrent seizures and apnoea (hypoxia) he was intubated and ventilated once admitted to PICU.

Circulation:
Rapidly administered 10% dextrose containing fluid was initially required to help correct Zach's hypoglycaemia. Guidance suggests that if a glucose bolus is given it should be followed by a maintenance infusion. Further slower infusions to optimise and sustain an increased intravascular volume can also be administered watching HR, perfusion and liver edge closely or by more sophisticated means (if available) like echocardiography and central venous monitoring. These could be given as 10mL/kg crystalloid boluses over a 20-30minute period. The patient should be catheterised at this stage to monitor urine output as this is a marker of end organ perfusion.
Zach is septic with Group B Streptococcus meningitis complicated by seizures.
He is hypoglycaemic because he has not fed well and is mildly dehydrated.
He has shown clinical improvement after the first hour of resuscitation.
He is less tachycardic, not mottled anymore but he is still lethargic.
He is transferred to PICU for further care and intubated because of recurrent seizure and apnoea risk.

CASE SCENARIO 2

12-year-old Martin known with sickle cell disease comes in febrile with chest pain, a cough, leg, and back pain. The leg and back pain are always typical of his disease. Sats 97%, tachypnoeic with a respiratory rate (RR) of 30. Heart rate (HR) 140 beats per minute, normal Blood Pressure (BP) 110/80 mmHg. He receives Morphine and Fluids. His legs feel better but his chest is still bothering him. RR is still 30 and his HR still 140. You take some bloods. Hb 9.9 g/L, WCC 23.5x109/L, Platelets 143 x109/L. Chest-xray: plump looking cardiac silhouette but no pulmonary infiltrates. His BP drops to 90/60 mmHg and he is given face mask oxygen as his saturations drop to 86%.

1. Could this be septic shock? If so, what could the likely organism/s be?
2. Outline your approach to Martin's management with a focus on his fluid status.
3. Should Martin receive a fluid challenge? If so, which fluid, how much and how fast?

Discussion points:

1. Is this septic shock?

Yes, Martin could have septic shock. He is functionally asplenic and therefore at increased risk of infections with encapsulated organisms (streptococcus pneumoniae, Klebsiella pneumoniae, group B streptococci, Escherichia coli, Neisseria meningitides and Haemophilus influenzae). He should have blood cultures taken and receive early antibiotics (Ceftriaxone).

Shock is multifactorial and we need to identify the primary cause. Remember there are also other causes of shock: Cardiogenic, Obstructive, Hypovolaemic and Distributive. Read more with PEM Playbook for a practical approach on shock.

2. Fluid assessment in septic children (from DFTB: Fluid Assessment in Sepsis)

There is no volume loss in sepsis and shock. There is an imbalance between oxygen demand and oxygen delivery. The main goal is to improve perfusion. Oxygen delivery (D02) is determined by cardiac output (CO), Haemoglobin concentration (Hb), how much oxygen is bound to haemoglobin (Sa02) and the partial pressure of oxygen (Pa02).
Note: BP is not part of the equation.
Note: the main aim is to increase CO
The equation:
DO2 = (cardiac output) x [(haemoglobin concentration) x SaO2 x 1.39] + (PaO2 x 0.003)

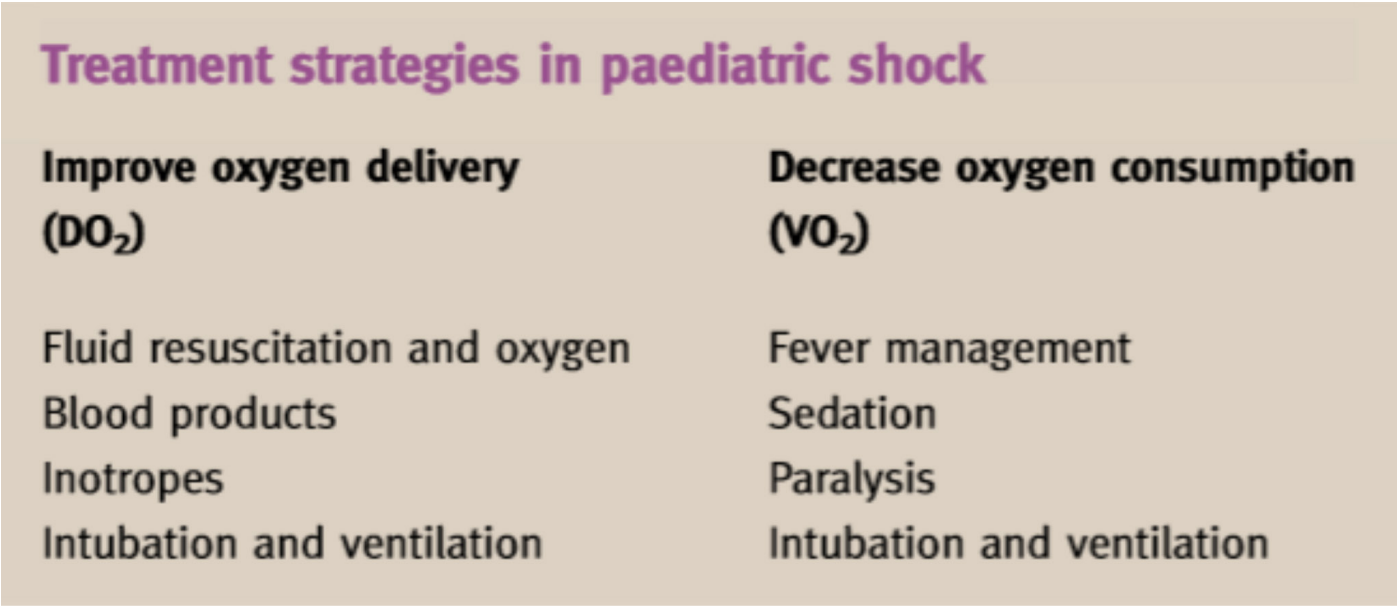


Image courtesy of Fluid Management in Paediatric Shock

Practically, in order to decrease oxygen demand you can bring down the fever, sedate and use mechanical ventilation. Increase oxygen delivery by administering oxygen, transfuse blood or red cells. By giving fluids, you increase CO, but not all patients benefit from fluid therapy particularly if they are already in a compensated state or show signs of fluid overload or have other elements of obstructive or cardiogenic causes of shock. In these instances, there is a dose effect:
more fluid equals more harm (=mortality).

Frank Starlings in Fluid Responsiveness

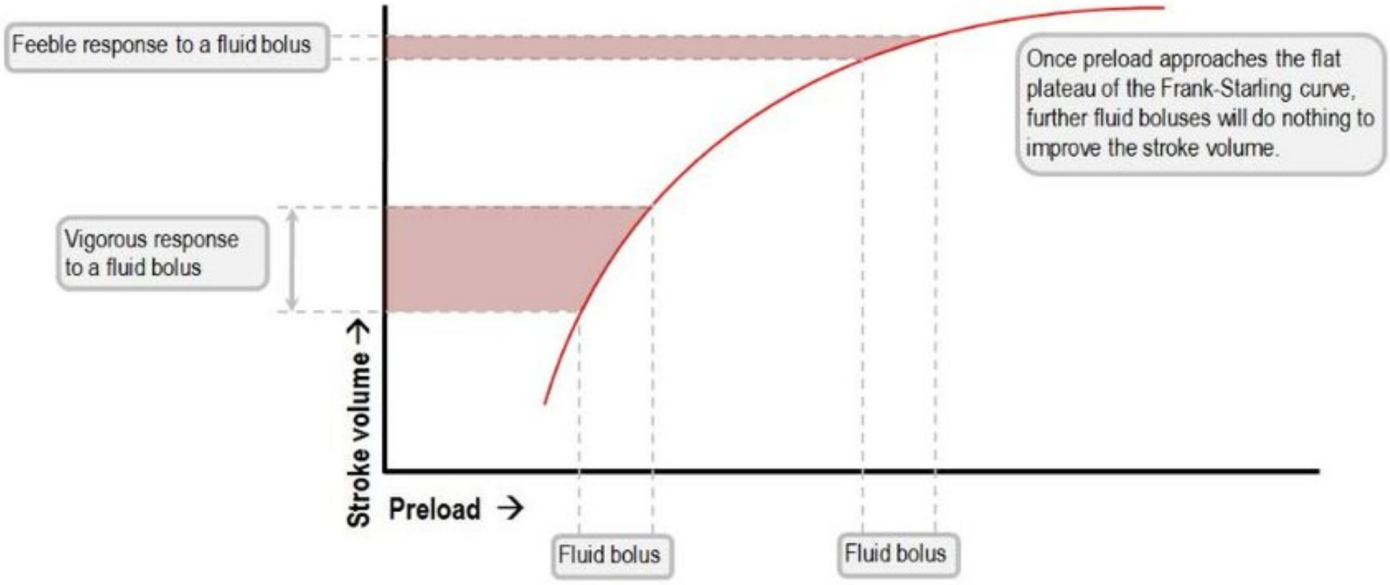


Image courtesy of Research Gate

3 steps to a fluid assessment:

1. Patient history – ask about input and output (feeds, fluids, urine, diarrhoea, vomiting) and do a risk stratification i.e. young, central indwelling device, immunocompromised etc.

2. Examination – look for signs of shock: inadequate perfusion, tachycardia out of proportion to the exam, normal or low BP, tachypnoea, normal or altered level of consciousness, persistently abnormal or multiple abnormal vital signs or individual sign that is extremely abnormal. Assess for signs of fluid overload: i.e. no physiological improvement with fluid, worsening respiratory status, increased FiO2 requirement, large liver, muffled heart sounds or gallop, raised jugular venous pressure (JVP).

3. Extended examination using POCUS – put the patient on the frank starling curve. Is the patient on the steep part of the curve? Fluid will increase CO.

Or on the flat part of the curve? Here the cardiac myocytes are maximally stretched. Giving fluid here will increase right atrial pressures (RAP) which do not lead to increases in CO. The patient is no longer 'fluid responsive'.

3 US views:

Lung US: presence of B-lines = pulmonary oedema = will not benefit from fluid

IVC: collapsing and small diameter = give fluid

Dilated and fixed IVC = no fluid

Heart: hyperdynamic = give fluid

Poor function, poorly contracting heart = no fluid

How much fluid? (DFTB: FEAST trial analysis)

We hesitate to administer fluid because of randomised evidence that fluid in sepsis is harmful in some settings i.e. FEAST study 2011. FEAST taught us that fluid can kill. Important points to note about the FEAST trial include:

- Poor resource setting where children are more likely to present late therefore negating the positive effects early fluid resuscitation.
- Many children presented with severe anaemia, a situation where haemodilution with intravenous fluids would further worsen oxygen carriage and tissue hypoxia.
- Approximately half the children in the study presented obtunded with cerebral malaria, a situation which may be exacerbated by excess fluid administration.

So, if you're going to give fluid, ensure the patient needs it first and always reassess before giving more.

Surviving Sepsis suggests giving 10mL/kg boluses up to 40-60mL/kg in total if an ICU facility is available over the first hour. Discontinue if signs of fluid overload develop.
In healthcare systems with no availability of intensive care, if hypotension is present, it is suggested to administer up to a total of 40 mL/kg.

Which fluid?

Balanced/buffered crystalloids are preferred (i.e. Plasmalyte-148 and compound sodium lactate (CSL)) over isotonic saline as their tonicity and electrolyte content matches closely to that of blood plasma.

There is inconclusive evidence in paediatric practice for the use of colloids vs crystalloids as resuscitation fluids. Surviving sepsis campaign guidelines suggest the use of crystalloids over albumin and there is little pooled meta-analysis to suggest a benefit to using colloids vs crystalloids except in one specific situation: the use of albumin for resuscitation in septic shock associated with dengue fever.

Blood products are highly effective volume expanders due to their high oncotic load. They are commonly used to replace losses such as in acute trauma, disseminated intravascular coagulation and consumptive thrombocytopaenia.

Keep an eye out for the PRoMPT BOLUS study results – a large multi-centre randomised control trial comparing outcomes in septic children resuscitated with balanced crystalloids vs 0.9% saline fluid.

How fast?

Surviving sepsis suggests fluid therapy administration over the first hour, titrated to clinical markers of cardiac output and dis-continued if signs of fluid overload develop for the initial resuscitation of sepsis or septic shock.

Before giving fluid, a member of the team brings the ultrasound (US) machine and performs a Point-of-Care-Ultrasound (POCUS) and notices that Martin in fact has a large pericardial effusion impeding his heart contractility. The team decides not to give fluids or blood products intravenously as this would further reduce his cardiac output. The team have prepared to intubate in case there is further deterioration but luckily the PICU team arrived to take over management. They are organising an urgent CT Chest for Martin. He remains on high-flow nasal cannula oxygen and is commenced on peripheral adrenalin to optimise him for intubation. and pericardiocentesis.

ADVANCED CASE SCENARIO 1

Johnny, an 8-month-old with chicken pox was brought to the emergency unit for persistent fever and vomiting for 3 days. The chicken pox rash had started a week prior to presentation. He had no diarrhoea, was awake, alert and able to drink from a bottle. His work of breathing was mild and he was not hypoxic.

The attending team concerned with his tachycardia and prolonged capillary refill time (CRT) of 4 seconds initiated fluid therapy and the relevant antibiotics. He received 3x 10mL/kg fluid boluses, Ceftriaxone and Aciclovir after bloods and cultures were taken.

After 2hours Johnny was still febrile but looking better, comfortable on handling, vitals unchanged, chest-xray had no infiltrates but there was a new concern regarding Johnny's abdominal rash which resembled cellulitis.

Blood Tests	
Hb	12
WCC	15.6
Platelet	299
Na	131
K	4.9
Urea	2.4
Creat	15
CRP	278

Blood Gas	
pH	7.39
pCO2	5.1
pO2	4.7
HCO3	23
BE	-2
Lactate	3
Glucose	4.6

Observations	
HR	180
RR	30
Sats	100%
BP	93/72
AVPU	A

1. How would you manage the persistent fever?
2. Is Johnny in septic shock? How reliable is a capillary refill time (CRT) in a shocked child?
3. What additional antimicrobial therapy should Johnny receive?
4. Should Johnny be intubated?
5. Can children with a proven viral illness also have a concomitant severe bacterial infection (SBI)?

Discussion points:

1. Non-steroidal anti-inflammatory drugs (NSAIDS) and varicella

(https://dontforgetthebubbles.com/podcast/dftb-podcast-ibuprofen-chickenpox/)
Chickenpox is an acute disease caused by varicella-zoster virus and is characterised by a vesicular rash, and often fever or malaise. Secondary bacterial complications are rare but most frequently involve bacterial infections of the skin and soft tissues caused by GAS and Staphylococcus aureus.

It has been suggested that NSAIDs (i.e Ibuprofen) may be a risk factor for severe skin and soft tissue infections with varicella infection in small low-quality evidence papers, but the actual occurrence of necrotizing fasciitis is extremely rare. Even if Ibuprofen does increase the risk, it increases the risk by a very small absolute amount.

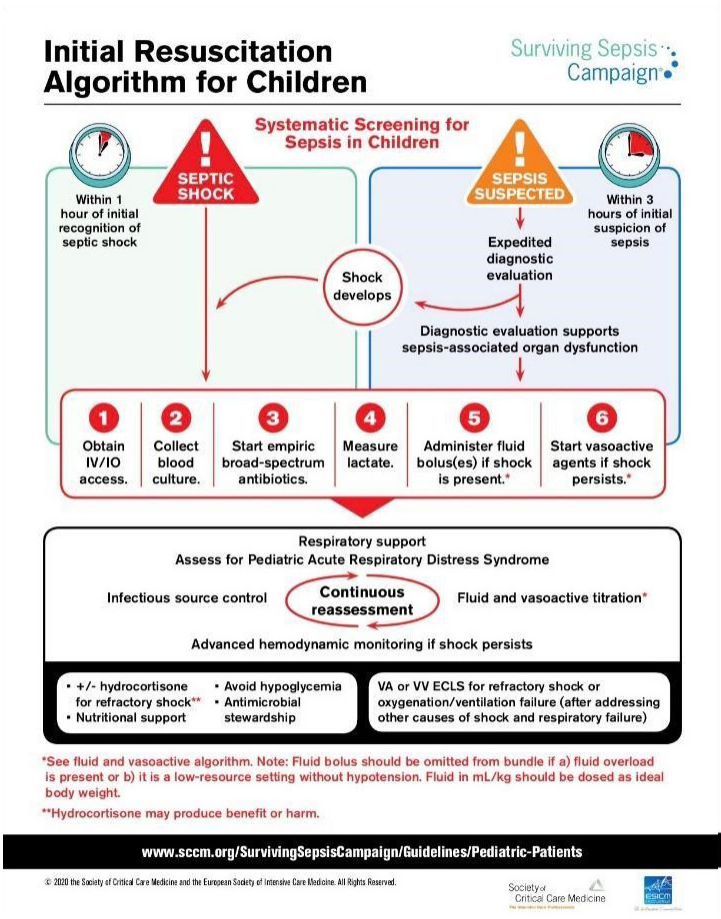
There is a consistent bias in multiple case control studies called confounding by indication. Meaning, if you give ibuprofen then you will get invasive disease but actually it might be the reverse; if you are very unwell with severe disease you may be more likely to have been given ibuprofen. This bias is difficult to tease out.

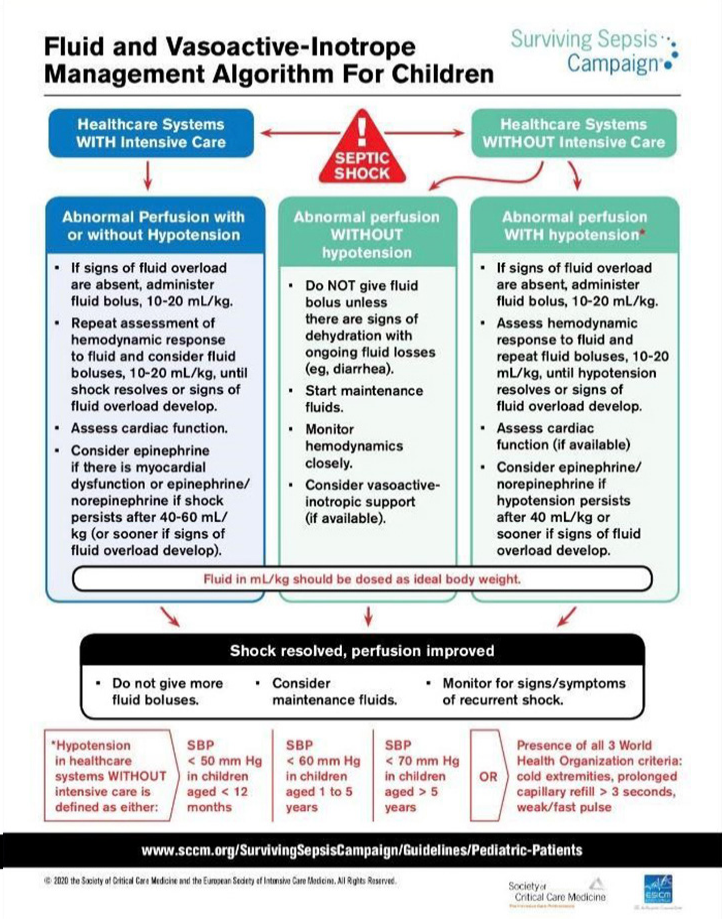
There is no certainty whether there is a real cause or association between NSAID use in chicken pox and severe skin and soft tissue infections. General advice is for the public to avoid using NSAID's for fever management in children with chicken pox (but can be given at health care professional discretion) and continue regular safe dosing of paracetamol.

2. Septic shock and hyperlactataemia

Surviving sepsis campaign defines septic shock as a severe infection leading to cardiovascular dysfunction (including hypotension, need for treatment with vasoactive medication or impaired perfusion).

Yes, Johnny is in septic shock. He also fulfils all four SIRS criteria as well as cardiovascular organ dysfunction because of impaired perfusion, a borderline BP despite fluid therapy, extreme tachycardia and a high lactate (3mmol/L). Blood lactate levels provide a valuable indirect marker of tissue hypoperfusion and although not specific (and occasionally affected by the conditions of the blood draw such as in use of a tourniquet), they can be rapidly obtained by point-of-care tests and are quantifiable surrogates for tissue hypoxia.
There is no optimal threshold to define 'hyperlactataemia' in paediatrics.
In a PICU study, the mortality rate for children with hypotension requiring vasopressors with lactate greater than 2mmol/L was 32% compared with 16.1% if lactate was less than 2mmol/L.





Value of CRT in septic shock?

A central or peripheral CRT poorly differentiates a febrile child and a shocked child. Tachycardia is an important objective measure which can be caused by fever. Tachycardia without palpable peripheral pulses equals sepsis/shock. CRT and peripheral coolness or warmth are good to follow but not the most reliable indicators of septic shock. A prolonged CRT of more than 2 seconds can be used as a 'red flag' but a normal CRT should not reassure a clinician.

3. Antimicrobial therapy in suspected invasive GAS

Hours later, once Johnny was already admitted to the Paediatric ward, microbiology updated the team with a positive blood culture showing Streptococcus species which was later confirmed as Group A streptococcus (GAS) bacteraemia.

Surviving sepsis campaign guidelines recommend the administration ofbroad-spectrum antibiotics within 1 hour of recognition of septic shock. Those assessed as septic but without clinical signs of shock can allow 3 hours for appropriate blood cultures and investigations to be obtained before starting antimicrobial therapy.

Empiric broad-spectrum antibiotic therapy refers to the use of single or multi-drug antimicrobial therapy. The initial choice should take into account the specific clinical history (e.g. age, site of infection, concomitant disease states, indwelling devices, recent hospital exposure). Ceftriaxone, a third-generation cephalosporin, is the recommended antimicrobial for community-acquired sepsis by the National Institute for Health and Care Excellence (NICE). Vancomycin should be added in settings where MRSA or ceftriaxone-resistant pneumococci are prevalent. Additionally, an aminoglycoside or substitution of a carbapenem is appropriate in settings where ceftriaxone resistance is common in gram-negative bacteria. Recommendations for immunocompromised patients, neonates and intra-abdominal sources of infection to name a few can be found in the latest Surviving Sepsis Campaign guidelines 2020.

Johnny had an invasive GAS infection: necrotizing fasciitis. Clindamycin is needed to limit toxin production and enhance bacterial clearance.

Streptococcal exotoxins act as superantigens to stimulate T-cell responses and induce cytokine synthesis which leads to capillary leak, shock and organ failure.

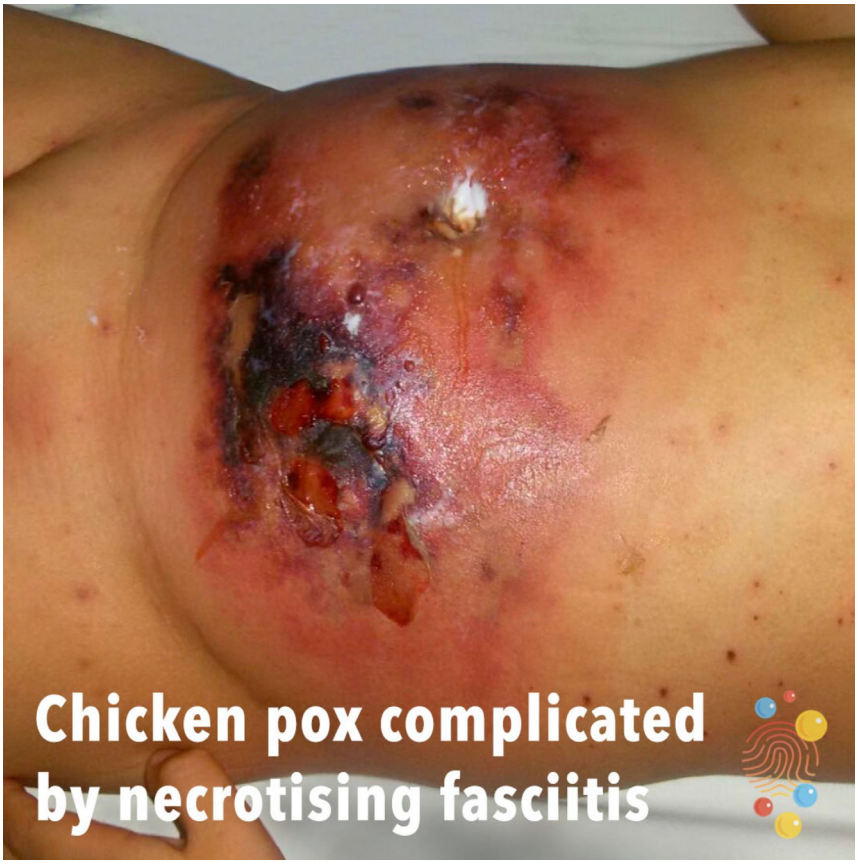
Clindamycin is a protein synthesis inhibitor acting as a superantigen inhibitor, suppressing pro-inflammatory cytokine production and is bacteriostatic. Clindamycin should therefore be administered as soon as invasive GAS infection is suspected.

The understanding that invasive GAS infections induce an inflammatory cascade does introduce the concept of immunomodulation with the use of intravenous immunoglobulin (IVIG). While IVIG is advocated for use in several sepsis syndromes, there are few randomised control trials and conflicting evidence about its effect in lowering mortality in sepsis. The use of IVIG needs to be weighed against its cost, potential adverse effects including immune-mediated haemolysis and anaphylaxis.

4. When to intubate?

Early, if you can do it safely and you have the best people around to do it.
Even a gentle induction is not tolerated well in the later stages of sepsis and shock.
Preferably oral cuffed endotracheal tubes (ETT) during resuscitation
(which can then be changed to a nasal ETT in PICU).

Johnny was intubated in the Paediatric ward together with help of the anaesthetist and PICU team. An urgent plastic surgical referral was made and Johnny was booked for urgent exploratory surgery.



5. Viral illness with a concomitant severe bacterial infection (SBI)
Yes. Necrotizing fasciitis and toxic shock syndrome (TSS) are two of the most severe clinical manifestations of invasive GAS. Varicella zoster infection is an important predisposing factor, particularly for soft tissue infection, and there is some evidence that up to 30% of children admitted with varicella have secondary bacterial skin infections.

Necrotizing fasciitis is a rare complication of varicella zoster infection but is a serious condition with devastating sequelae requiring prompt diagnosis and plastic surgical management. Necrotising fasciitis is clinically unimpressive, often difficult to recognise and often confused with cellulitis. Symptoms and signs that may suggest necrotizing fasciitis are severe pain out of keeping with the skin lesion, rapid progression, poor therapeutic response and blistering necrosis. Delay in treatment can be fatal or cause extensive skin and soft tissue loss. Explorative surgery must be carried out promptly if there is any clinical suspicion. Staying with co-infections, one study showed that febrile infants less than or equal to 60days of age with viral infections are at low (1%), but a non-negligible risk of severe bacterial co-infection (bacteraemia and bacterial meningitis).

ADVANCED CASE SCENARIO 2

14-month Ellie, with no past medical history presented with a 2-day history of fever, nasal congestion and a dry cough. Her father called the ambulance when Ellie became drowsy and somewhat unresponsive for a brief period.
On arrival at ED, she was clinging onto mum, tears in her eyes, her cheeks were bright red and she was very aware of everyone at her side. Her heart rate (HR) 145bpm, respiratory rate (RR) 20 breaths per minute, Temperature 38.3°C, Saturations (sats) fluctuated between 91-95% and if you looked carefully she had subtle intercostal recessions only. Her chest was otherwise clear, no organomegaly, no skin rash but her hands and feet were cool. Ellie's mum tells you that she gave her Calpol approximately 6hours ago.
Ellie's Paediatric Early warning score (PEWS) is 5 and is taken into majors.

Is Ellie at risk of sepsis? If so, why?
The nurse is concerned about Ellie and asks you to please see her next.
What do you think is wrong with Ellie?

You do a thorough joint and ENT exam. Her ears and tonsils look normal and her throat is a little red but you decide to give her a good nasal suction.
She hates it but you (and mum) are rather chuffed with the large amount of mucous you have managed to remove. You subsequently see her sats increase to 98% and her intercostal recessions have subsided. She's keen to drink and does very well without vomiting. You think she's more likely to have a viral infection.

Would any investigations assist you with her management?
What investigations and why?
Discuss how you would manage Ellie? Would you admit her?

Discussion points:

Cause for fever is more important than treating it
Fever is a physiological response to infections; pyrogens stimulate the hypothalamus to increase the body temperature which inhibits pathogen replication thereby protecting the body. The fever itself is of less importance than the cause for the fever and the main issue is to exclude an underlying dangerous infection rather than treating the fever with antipyretic interventions.

Approximately 15-20% of children present to the emergency department with a fever and only 0.5-1% will be due to sepsis. When managing a child with fever, focus on the clinical assessment to determine the risk of a serious illness such as pallor or cyanosis, depressed level of consciousness, grunting, tachypnoea, reduced skin turgor and bulging fontanelle. Treat fever in febrile convulsions and in situations such as shock with reduced output.

Use PEWS as a guideline
The term PEWS covers a multitude of scores and systems which were initially designed to detect deterioration in inpatient settings.
The use of PEWS in Emergency Departments have always been shown to be poorly specific and no studies have shown adequate ability to determine need for hospitalisation. High scores are associated with need for Intensive care so should never be ignored but a low PEWS score is poor at ruling out a serious underlying condition.

Management discussion points:
Diagnosing sepsis in children is not easy. There is no right or wrong answer here. You will see many of these kinds of patients in your career, many even in one shift. Realistically, you cannot do septic screens and admit every single child who comes in with a fever. So, be an advocate for this patient and use your greatest skill: the clinical examination. Be like Sherlock Holmes, look for the abnormal and
try find the source of the fever.

Management outcome discussion:
Your registrar is available, so you discuss Ellie's case, you re-examine Ellie together with your registrar and conclude that this is probably a viral upper respiratory infection (URTI). You explain the course of the illness and support the parents
on how to look after Ellie at home, safety net and discharge Ellie home.

OR

Despite this, you still do a septic screen and give a stat dose of ceftriaxone.
Ellie really despises you now, you forgot to use emla before taking bloods.
Mum is also upset because blood spilled all over the bed and her clothes.
You've explained your management plan clearly to Ellie's mum, she understands and continues to be a team player. Ellie's urine dipstick is clear, you prescribe paracetamol and put her in the Clinical Decision Unit (CDU) for repeat observations, clinical review and checking of results. Her C-reactive protein (CRP) is 20 mg/L, WCC (12x109/L), she is no longer febrile, drinking like a champion and back to baseline. Her PEWS is now 1.

Over-investigating and chasing numbers (gppaedstips)

NICE guidelines are safe however if followed closely, staff are more likely to over-investigate. This is because sepsis is difficult to diagnose.
There is no mathematical equation to define sepsis. All the features of sepsis are non-se[cific and you cannot rely on any one feature to be present all of the time"Sepsis doesn't appear, it develops". There is a misconception that the point where sepsis began can always be identified. This is simply not the case. A viral illness bringing you to hospital one day, may well still have been a viral illness regardless of whether you present to the hospital the next day with sepsis.

Clinical suspicion is better used to identify sepsis than a blood test. In practice, decisions often rely on the experience of the clinicians involved so if sepsis is a possibility it is wise to involve a clinician who has had significant exposure to seriously ill children in an ED setting. Ask for senior advice.

CRP and Procalcitonin (PCT) (10.1136/archdischild-2011-300178

No marker of infection can rule in or rule out sepsis in all children and inflammatory markers should not be relied on to decide whether a child has an acute bacterial infection or sepsis.

PCT is better able to discriminate against severe bacterial infection than CRP and PCT is particularly useful in the early stages of infection. PCT is able to differentiate between SIRS and sepsis while CRP is not.
CRP is not a good predictor of sepsis.

QUIZ QUESTIONS (10 MINUTES)

Question 1.

Match the following columns:

Staphylococcus Aureus (c)	a. Toxic Shock Syndrome, Scarlet fever
Pneumococcus (f)	b. Meningitis, Sepsis in < 3months
Haemophilus (e)	c. Endocarditis, Osteomyelitis, Septic Arthritis
Group A Streptococcus (a)	d. UTI, Appendicitis, Hospital-Acquired
Neisseria Meningitidis (g)	e. Sinusitis, Orbital Cellulitis, Epiglottitis (less common due to vaccine)
Group B Streptococcus (b)	f. Bacterial Meningitis (invasive disease decreased with vaccine)
Gram negative sepsis (d)	g. Sepsis, Meningitis

Staphylococcus aureus is a gram positive, bacterium (looks like clusters of grapes under a microscope). Approximately 30% of the population are asymptomatic carriers; and can be found as part of normal flora of the upper respiratory tract and skin. Complications are included above as well as abscesses and pneumonias. Cloxacillin is the recommended antibiotic choice for sensitive staph (MSSA) and Vancomycin for resistant staph (MRSA).

Invasive disease of Haemophilus influenzae and Streptococcus pneumoniae are less commonly seen due to vaccinations.

Group A Streptococcus (GAS) is a gram positive, beta-haemolytic coccus in chains. It is responsible for diseases such as strep throat, impetigo and cellulitis. Complications include post strep glomerulonephritis, paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), rheumatic fever, scarlet fever and toxic shock syndrome (TSS). Treatment should include penicillin, and clindamycin added for TSS.

Meningococcaemia caused by the virulent gram-negative Neisseria meningitidis is relatively rare. Fever and petechial rash/purpura and poor perfusion can equate to meningococcaemia but not always. Leg pain and refusal to walk, cold hands and feet and abnormal skin colour are also important, subtle signs to be vigilant about when assessing a child with suspected meningococcaemia.

Group B streptococcus (GBS), Listeria monocytogenes and Escherichia Coli (E.Coli) are 3 important bacteria to remember in sick neonates. Early-onset GBS (<7days) presents commonly as acute respiratory distress or septicaemia. Late-onset GBS (7- 89days) present with meningitis, seizures. Intrapartum screening and antibiotic programs have not reduced incidence in late-onset GBS.

Question 2

Which of the following statements are true?

A. The meningococcal serum PCR result is affected by antibiotics therefore it is important to do this test prior to the administration of antibiotics in suspected meningococcal sepsis.

B. Balanced/buffered crystalloids are preferred (i.e. Plasma Lyte-148, Hartmanns's solution and Ringer's Lactate) over isotonic saline for resuscitation in septic shock.

C. Blood lactate levels provide a valuable indirect marker of tissue hypoperfusion and are not spuriously increased by squeezing of a limb, use of a tourniquet or stored for a prolonged period of time.

D. A Haemoglobin level (Hb), CRP and Blood Culture are investigations you can reliably interpret from bone marrow blood following intraosseous access (IO).

The pre-hospitalisation administration of parenteral benzylpenicillin normally renders blood cultures sterile, and lumbar puncture is undertaken less frequently, especially in young children. Sensitivity to meningococcal serum PCR is unaffected by prior antibiotic treatment. PCR is a rapid, sensitive test that may be used to confirm a diagnosis of meningococcal disease by using peripheral blood samples. Introduction of this test into clinical laboratories may in some cases obviate the need for lumbar puncture to be performed on patients with suspected meningococcal disease.

Squeezing of a limb when acquiring a blood sample can spuriously increase lactate by venous stasis, impaired local perfusion and distress/exertion of the child. Haemolysis does not affect lactate. Prolonged sample storage will spuriously increase lactate unless sent in an oxalate tube or on ice.
ILCOR guidelines and Surviving Sepsis suggest the use of balanced or buffered crystalloids over isotonic saline as a resuscitation fluid in sepsis as their tonicity and electrolyte content matches closely to that of blood plasma. Saline may be associated with decreased renal blood flow and promote inflammation.

Most laboratory tests cannot be performed on aspirated bone marrow blood as the particulate matter may block and damage laboratory equipment. Aspirated IO blood is suitable for blood culture bottles, bedside glucometers, handheld I-STAT instruments (pH, glucose, and lactate) and haematological and biochemistry testing. Sodium, potassium, CO(2), and calcium levels from IO blood should be interpreted cautiously as well as white cell counts (WCC appear elevated) and platelets (which tend to be lower).

Question 3

Which groups of patients are at increased risk of sepsis?

A. Children under 1 year of age
B. Patients with (functional) asplenia (sickle cell, SLE, splenectomy)
C. Patients with a breach to skin barrier function (burns)
D. Patients with congenital/acquired immunodeficiency (CVID, HIV,diabetes)
E. All of the above

Always be aware of certain groups who may be predisposed to sepsis, for example neonates or oncology patients (undergoing chemotherapy), who display less profound features. These individuals may maintain normothermia and also have diminished physiological responses e.g. less tachycardia.

PRACTICAL PROCEDURE (30-45MIN)

Intraosseous (IO) Access

Aims:

- To get a feel for the IO drill, how to assemble it and practice using it on substitute bone (Crunchie bars)
- Practice securing the needle and attaching a fluid giving set.

When to insert an IO?

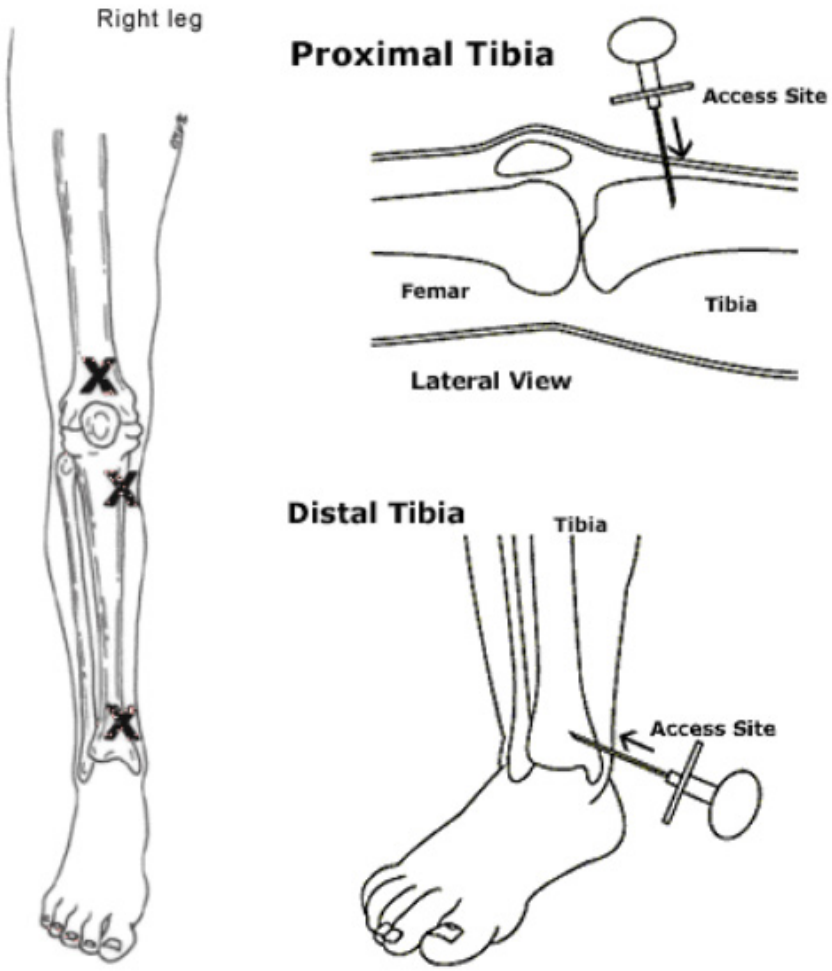
As soon as possible in septic shock and for circulatory access in cardiac arrest. Someone in the team should start getting the IO equipment in septic shock once the first IV vascular access attempt has been made. It should be ready to use when awaiting an out of hospital cardiac arrest case coming to the ED. Umbilical vein remains the preferred access in a neonate.

When not to insert an IO?

- Proximal ipsilateral fracture
- Ipsilateral vascular injury
- Osteogenesis imperfecta
- Cellulitis at the site of insertion

Where to insert an IO?

- Proximal tibia: Anteromedial surface, 2-3 cm below the tibial tuberosity
- Distal tibia: Proximal to the medial malleolus
- Distal femur: Midline, 2-3 cm above the external condyle



How to insert an IO? www.youtube.com/watch?v=RTxbWkHKH-M

How to secure an IO when using an 18/22G LP needle?
www.youtube.com/watch?v=Rer4pH3HgOc
You need gauze, umbilical cord clamp and micropore or opsite.

Complications:
- Failure to enter the bone marrow, with extravasation or subperiosteal infusion
- Through and through penetration of the bone
- Osteomyelitis (rare in short term use)
- Physeal plate injury
- Local infection, skin necrosis, pain, compartment syndrome, fat and bone micro-emboli have all been reported but are rare

Tips:
The 'cannulator' should give the antibiotics.
Take a crossmatch with the second cannulation.

Take-home messages

1. Diagnosing early sepsis is difficult. Its vague, non-specific and often distracts the clinician by another diagnosis. So thinking about sepsis is the first crucial step.

2. Once sepsis is recognised, call for help, deliver treatment and constantly reassess in the first hour. This will save lives.

3. Meeting SIRS criteria is common in the Paediatric Emergency Department (PED) but we send approximately 85% of children that meet SIRS criteria for sepsis home from the PED without antibiotics.

4. Clinical suspicion is better used to identify sepsis than a blood test. So, if you suspect sepsis, involve another (preferably senior) team member to assess.

5. Be particularly mindful when administering fluid boluses to septic children. Constantly reassess their need for fluid, their response to fluid and stop if there are signs of fluid overload.

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