Initial management of the septic child

Dr Yvette Vella
Paediatric Fellow
Wagga Wagga Base Hospital
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The Severe Infection & Sepsis Project

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Sepsis Kills

- International recognition that sepsis is a problem, with 25% mortality in severe sepsis and septic shock in Australia and NZ (ARISE 2007)
- Mortality increases by 7.6% with every hour’s delay in commencing antibiotic therapy after the onset of hypotension (Kumar et al 2006)
- CEC Clinical Focus Report (2009) detected delays in diagnosis or inadequate treatment, variable practice
- Identification can be difficult
- Standardised treatment bundles improve mortality
- Paediatric sepsis pathway and empirical intravenous antibiotic guideline Under development
Paediatric mortality

- 2005 WHO announced that 80% of global child deaths related to 4 severe infections (pneumonia, malaria, neonatal sepsis, and diarrhoea).
- The overall mortality from severe sepsis in children is estimated at about 10%, much lower than that in adults (Watson et al., 2003).
Does this child have early sepsis or septic shock?
Sepsis – Definitions: Adult

• **SIRS criteria** - 2 of the following
  • Temp < 36C or >38C
  • HR > 90
  • RR >24
  • WCC >12 or <4

• **Sepsis** = SIRS + suspected or confirmed infection

• **Severe Sepsis** = Sepsis plus organ dysfunction

• **Septic shock** = Severe Sepsis with sBP < 90mmHg despite adequate fluid resuscitation or the need for inotropes to maintain sBP > 90mmHg

- One of the SIRS (systemic inflammatory response syndrome) criteria had to be either a T change or a WCC alteration
- ↑HR, ↑RR and ↓BP based on age-based normal values in 6 specific age groups
- In paeds “Septic shock” did not require ↓BP but instead either
  - ↓BP or
  - need for vasoactive drug or
  - two of
    - Unexplained BE > -5
    - ↑lactate > 2 X ULN
    - UO < 0.5ml/kg/hr
    - CRT > 5 secs
    - Core toe gradient >3C
RCH Clinical Practice Guideline

Septic Shock

• Features of circulatory and respiratory insufficiency are
  o Tachycardia
  o Tachypnoea and or desaturation in air
  o Increasing Systolic to Diastolic difference
  o Poor peripheral perfusion (cold extremities with prolonged capillary refill)
  o Alteration in conscious state eg confusion
  o Metabolic acidosis
Consortium of experts representing 11 international organisations (including ANZICS) used evidence and expert consensus to generate a series of recommendations.

Two “bundles” a resuscitation bundle & an ICU management bundle of tasks to be targeted to improve sepsis outcomes.

Paediatric pathway generated.....
1. Early intubation recommended

2. Fluids should be infused as 20ml/kg boluses over no more than 10 mins

3. BP not a reliable target in paeds but treatment should be titrated to clinical signs of adequate CO
   - HR in normal range
   - Improved CRT
   - Improved LOC
   - UO 1ml/kg/min

4. Inotropes started promptly if required (fluid refractory, >60ml/kg)

5. Hydrocortisone for catecholamine resistance

6. Transfuse child to Hb > 10g/dL
Paeds Surviving Sepsis Update 2008

1. First hour resuscitation target HR within normal range, normal BP and CRT < 2 secs
2. Prompt (alternate if necessary) vascular access crucial
3. Commence antibiotic as soon as possible (<1h)
4. Inotropes / vasopressors peripheral initially if required and CVL unavailable
5. ICU management should target either lactate correction or $S_vO2 > 70\%$
Establishing Access
2010 ILCOR “..IO should be considered early in the care of critically ill children whenever venous access is not readily available”
2005-2007, 291 patients across 90 hospitals (4/10^5 ED visits)
Range of primary diagnoses, 34% were in cardiac arrest…others
86% of IOs placed in “community hospital
37% mortality
No complications related to IO line noted

2008 Surviving Sepsis update “….in shock…if reliable venous access cannot be obtained in minutes”
What is the evidence for rapid fluid replacement?
91 children retrieved to Pittsburgh 1993-2001 for “septic shock”

For every hour of persistent shock there was a 2.3 fold increase in OR for mortality

<table>
<thead>
<tr>
<th>Therapeutic Intervention</th>
<th>All Patients (n = 91)</th>
<th>Shock Reversed (n = 24)</th>
<th>Persistent Shock (n = 67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical ventilation (n [%])</td>
<td>44 (48)</td>
<td>9 (38)</td>
<td>35 (52)</td>
</tr>
<tr>
<td>Intraosseous line (n [%])</td>
<td>8 (9)</td>
<td>1 (4)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Central venous line (n [%])</td>
<td>27 (30)</td>
<td>8 (33)</td>
<td>19 (28)</td>
</tr>
<tr>
<td>Fluid therapy (mL/kg)#</td>
<td>20.0 [9.2–49.2]</td>
<td>23.9 [12.2–44.7]</td>
<td>20.0 [8.2–57.5]</td>
</tr>
<tr>
<td>Appropriate fluid therapy (n [%])</td>
<td>41 (45)</td>
<td>24 (100)</td>
<td>17 (25)* P &lt; .001</td>
</tr>
<tr>
<td>Dopamine or dobutamine (n [%])</td>
<td>24 (26)</td>
<td>5 (21)</td>
<td>19 (28)</td>
</tr>
<tr>
<td>Epinephrine or norepinephrine (n [%])</td>
<td>15 (16)</td>
<td>2 (8)</td>
<td>13 (19)</td>
</tr>
</tbody>
</table>
Brazil 2008 90 children presenting with “septic shock”
Antibiotics within 1 hour presentation

- Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration
- Blood culture
- Culture other sites as clinically indicated
**RCH guideline fever $>38$ and unwell**

<table>
<thead>
<tr>
<th>Age</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 month corrected age</td>
<td>Full sepsis work up FBC/film, blood culture, urine culture (SPA), LP +/- CXR Admit for empirical antibiotics</td>
</tr>
<tr>
<td>1-3 months corrected age</td>
<td>Full sepsis work as above +/- LP, +/- CXR (if respiratory symptoms or signs) Admit for empirical antibiotics</td>
</tr>
<tr>
<td>&gt;3 months *</td>
<td>FBC/film, blood culture, urine culture (SPA up to 12 months of age) +/- LP/CXR Admit for observation +/- empirical antibiotics</td>
</tr>
</tbody>
</table>

* Without clear focus of infection
Contraindications to lumbar puncture

- LP should not be performed in a child
  - with impaired conscious state
  - with focal neurological signs
  - who is haemodynamically unstable

- In this circumstance treatment for meningitis/encephalitis can be commenced and an LP can be performed when the patient is stable and there are no other contraindications present
Empiric First Dose Antibiotics: Paediatrics

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis without source, immunocompetent</td>
<td>Gent + Fluclox</td>
</tr>
<tr>
<td>→ Meningococc or Pneumococc suspected</td>
<td>+ Ben Pen</td>
</tr>
<tr>
<td>→ Toxic Shock suspected</td>
<td>+ Lincomycin or Clindamycin</td>
</tr>
<tr>
<td>Severe Pneumonia</td>
<td>Cefotaxime ± Fluclox</td>
</tr>
<tr>
<td>UTI</td>
<td>Amp + Gent</td>
</tr>
<tr>
<td>CNS infection</td>
<td>Cefotaxime + Vancomycin</td>
</tr>
<tr>
<td>Line related</td>
<td>+ Vancomycin</td>
</tr>
<tr>
<td>MRSA colonised / suspected</td>
<td>+ Vancomycin</td>
</tr>
</tbody>
</table>

...by push over 3-5 mins in appropriate dose

Why the urgency of administration?
Association between timing of antibiotic administration and mortality from septic shock in patients treated with a quantitative resuscitation protocol*

300 adults with severe sepsis admitted to ED in US, mortality overall 19%

Table 5. Inhospital mortality: Shock recognition to initial antibiotics

<table>
<thead>
<tr>
<th>Time to Antibiotics</th>
<th>Number of Patients</th>
<th>Mortality (%)</th>
<th>Difference (%)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>Adjusted Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before shock recognition</td>
<td>119</td>
<td>11.8</td>
<td>12</td>
<td>2.35</td>
<td>1.12–4.53</td>
<td>2.59</td>
</tr>
<tr>
<td></td>
<td>After shock recognition</td>
<td>172</td>
<td>23.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 hr</td>
<td>101</td>
<td>25.8</td>
<td>-4.7</td>
<td>1.29</td>
<td>0.63–2.67</td>
<td>0.93</td>
<td>0.41–2.12</td>
</tr>
<tr>
<td>&gt;1 hr</td>
<td>71</td>
<td>21.1</td>
<td></td>
<td>1.11</td>
<td>0.42–2.98</td>
<td>0.69</td>
<td>0.21–2.22</td>
</tr>
<tr>
<td>≤2 hrs</td>
<td>145</td>
<td>24.1</td>
<td>-1.9</td>
<td>1.11</td>
<td>0.42–2.98</td>
<td>0.69</td>
<td>0.21–2.22</td>
</tr>
<tr>
<td>&gt;2 hrs</td>
<td>27</td>
<td>22.2</td>
<td></td>
<td>1.11</td>
<td>0.42–2.98</td>
<td>0.69</td>
<td>0.21–2.22</td>
</tr>
<tr>
<td>≤3 hrs</td>
<td>164</td>
<td>23.8</td>
<td>1.2</td>
<td>0.94</td>
<td>0.18–4.82</td>
<td>0.84</td>
<td>0.13–5.52</td>
</tr>
<tr>
<td>&gt;3 hrs</td>
<td>8</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Peripheral access for inotropes
73 of 1133 children retrieved to Children’s Hospital of Boston 2004-2006 treated with vasoactive agents by peripheral IV

- Primarily Dopamine monotherapy (90%) or Dop + Ad (7)
- 11/73 (15%) developed infiltration – all resolved without significant intervention
- In those in whom infiltrates developed infusions were running on average for longer (1069 ± 235mins V 600 ± 132mins) and were carrying a higher dose of inotrope (median 15 Vs 10µg/kg/min Dopamine)

2008 Surviving Sepsis recommendation: if required, peripheral inotrope should be infused with a carrier solution (“piggy-backed”) & prompt weaning or transition to CVL on arrival at tertiary centre
Are corticosteroids indicated?
477 children, 104 centres, 18 countries with severe sepsis requiring mech vent + inotrope randomised to receive APC (an anticoagulant) or not
Largest sepsis trial ever done in children
Terminated early by Lilly (“for futility”)
JZ reexamined database and looked at glucocorticoid administration (not controlled by protocol)
193 received steroids, 284 did not
Baseline characteristics (organ injury, illness severity) equal
No difference in mortality or evidence of morbidity in survivors
Initial Management of Sepsis

1. Recognise or suspect early sepsis

2. First hour resuscitation target HR within normal range, normal BP and CRT < 2 secs
   
   (20ml/kg fluid bolus up to 60ml/kg within the first 15 minutes followed by inotropes if refractory)

3. Prompt vascular access, IO if necessary

4. Commence antibiotic as soon as possible (<1h) with appropriate cultures before hand

5. Inotropes / vasopressors peripheral initially if required and CVL unavailable
References