There must have been a safer way for her to have our baby!
Most common cause of direct maternal deaths

CMACE 2006-2008
1.13 per 100,000
Sepsis

- Common cause of mortality and morbidity worldwide
- Leading cause of death in the ICU in the USA
- Maternal sepsis is a small fraction of total sepsis cases
- High income countries – small proportion of maternal deaths
- 10% of maternal deaths in Africa and Asia
- In South Africa HIV-related infection is the leading contributor to maternal mortality
SAMM due to sepsis
Serious Acute Maternal Morbidity

- Data is scarce
- Reported incidence of SAMM in western countries vary from 0.1 to 0.6 per 1000 deliveries
- For every maternal mortality there are 10 to 60 SAMM’s!!
- Are these cases of “pat on the back” - We prevented mortality
- Or more likely we diagnosed treated too late??
The Leading Cause of Direct Maternal Death in the UK

- Worldwide, infection and complications of sepsis are among the most common causes of severe maternal morbidity and mortality.

- In the UK deaths from sepsis have risen rather than declined in recent time.

- This is in contrast to the other major causes of direct maternal mortality.

- Community acquired β-haemolytic streptococcus Group A infection has been postulated as the cause.
Overview

- Early identification of maternal sepsis
- Physiological changes that make pregnant women more susceptible
- Current recommendations for diagnosis and treatment
Definitions

- Bacteraemia – viable bacteria in blood
- Infection - inflammatory response to the presence of micro-organisms in normally sterile tissue
- Systemic Inflammatory Response Syndrome (SIRS) - an inflammatory response diagnosed by 2 or more variables
Variables in SIRS

- Fever or Hypothermia (Core Temp <36°C or >38 °C)
- Tachycardia (Heart rate > 90 beats/min)
- Tachypnoea (RR >20 breaths/min)
- WCC >12 x 10⁹/l or <4 x 10⁹/l

NB above criteria relate to non pregnant patients

Average WCC in 3rd trimester is 8.5 x10⁹/l

WCC range in pregnancy is 5.1 -12.2 x10⁹/l

Post delivery WCC is 20-30 x10⁹/l
Sepsis

- SIRS in the presence of infection
- Severe Sepsis - sepsis with associated organ dysfunction, hypotension or hypoperfusion
- Septic Shock - sepsis + refractory arterial hypotension despite adequate fluid resuscitation
Definitions in consensus report in 1992

- Consensus report by the American College of Chest Physicians and the Society of Critical Care Medicine

- An international sepsis definition conference in 2001 resulted in expansion of the lists of signs and symptoms of sepsis to reflect clinical bedside experience

- See handout
Puerperal sepsis

- ICD – temperature rise above 38°C maintained over 24 hour or recurring during the period from the end of the first to the end of the 10th day after childbirth or abortion

- WHO – infection of the genital tract occurring at any time between the onset of rupture of membranes or labour and the 42nd day post partum in which fever and one or more of the following are present – pelvic pain, abnormal vaginal discharge, abnormal smell/foul odour of discharge and delay in the rate of reduction of the size of the uterus
Features of Severe Sepsis

- Hypotension
- Arterial hypoxaemia
- Raised lactate
- Acute oliguria (urinary output <0.5ml/kg/hr)
- Deranged renal/liver function
- Altered mental status
- Coagulation abnormalities
- Hyperglycaemia in absence of diabetes
Shock

- A state of compromised tissue perfusion that causes cellular hypoxia leading to tissue hypoxia and vital organ dysfunction
- Perfusion is insufficient to meet metabolic demands of tissues and anaerobic metabolism occurs
- Unsustainable, and if not corrected will progress to cellular dysfunction, cell death and organ damage
Physiological changes of pregnancy in relation to sepsis and septic shock

- Many of the normal physiological changes of pregnancy lead to increased susceptibility to infection
Normal CVS

- Hyperdynamic with a decreased SVR
- Increased CO – 30 to 50% (increase in HR and SV)
- Blood volume increases by 40%
- The heart may be considered to be under increasing stress
- Decreased albumin
Sepsis induces
Decrease in SVR
Vasodilation and myocardial depression
May result in rapid haemodynamic collapse
Decrease in colloid osmotic pressure renders woman more vulnerable to pulmonary oedema should cardiac failure occur
Respiratory

- Increased minute ventilation
- Mild respiratory alkalosis
- Compensatory mild metabolic acidosis
- This reduces a woman’s ability to compensate for any acidosis that develops due to sepsis
- Especially if any respiratory failure
Renal system

- Ureteric dilatation
- Compression of ureters
- Increase risk of pyuria and pyelonephritis
Recognition of sepsis and septic shock

- Clinical
- Subtle signs
- Early signs are tachypnoea and tachycardia
- Followed by hypotension and low UO
- Classical features such as pale, clammy skin, cool peripheries and altered levels of consciousness are only evident once shock has progressed – Too late!
Maternal death enquiries and contributors to maternal death

- Repeatedly shown that there is a failure to recognise developing sepsis and septic shock
- Late and inadequate or inappropriate treatment of shock
- CMACE emphasises early recognition of the following signs and symptoms
Signs and symptoms

- Pyrexia/ hypothermia
- Persistent tachycardia (>100 beats/minute)
- Tachypnoea (RR > 20 breaths/min)
- Leucopenia (WCC < 4 x 10^9/l)
- Diarrhoea and/or Vomiting
- Lower abdominal pain
- Abnormal or absent fetal heart beat
Key recommendation of last 2 reports - MEOWS

- Early warning charts are standard in all hospitals in the UK
- 5 simple variables – mental function, heart rate, BP, temp and RR
- Hourly UO may be included
- Do not take into account CVS and respiratory changes in pregnancy but seems sensible to use at present
- Ongoing research into parameters that should be used
The MEOWS chart

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Normal</th>
<th>Red</th>
<th>Yellow</th>
</tr>
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<tbody>
<tr>
<td>HR</td>
<td>100-120</td>
<td>≥120</td>
<td>≥150</td>
</tr>
<tr>
<td>BP (Systolic)</td>
<td>110-130</td>
<td>≥130</td>
<td>≥160</td>
</tr>
<tr>
<td>BP (Diastolic)</td>
<td>70-90</td>
<td>≥90</td>
<td>≥120</td>
</tr>
<tr>
<td>Temperature</td>
<td>36.5-37.5</td>
<td>≥38</td>
<td>≥39.5</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>95-100</td>
<td>&lt;90</td>
<td>&lt;85</td>
</tr>
<tr>
<td>urine output</td>
<td>50-80 mL/h</td>
<td>&lt;50 mL/h</td>
<td>&lt;25 mL/h</td>
</tr>
</tbody>
</table>

**If EWS is triggered**
(1 red or 2 yellow measurements)

- Alert **midwife co-ordinator**. Contact **SHO** who will review the patient within 30 minutes. If they are unavailable contact **registrar** or **consultant**. He/she will formulate a management plan and seek senior advice if appropriate.

- Consider early **anaesthetic / critical care** involvement if appropriate.

- Initiate treatment as advised by medical staff. Monitor EWS observations every 15 minutes to assess response to treatment. Contact medical staff for re-assessment if further deterioration.

- Medical re-assessment within 2 hours of treatment

- **Patient improves**: Contact consultant and consider HDU/ICU referral.

- **No improvement**: HDU/ICU referral required.
Management of severe sepsis and shock

- Aimed at stabilising the patient while diagnosing and treating the underlying cause
- Urgent and aggressive resuscitation
- More likely to be effective and severe sepsis avoided if started early
- Goal is to resuscitate and eliminate underlying infection
Surviving sepsis campaign

- Few studies with pregnant patients
- Seems sensible to use at present - endorsed by CMACE
- Protocolised approach
- Treatment directed towards achieving following goals in first 6 hours
Resuscitation goals

- Central Venous Pressure (CVP) - 8-12 mmHg
- Mean arterial pressure (MAP) - ≥ 65 mmHg
- Urine output ≥ 0.5 ml/kg/hr
- Central venous (superior vena cava) or mixed venous oxygen saturations ≥ 70 % or ≥ 65% respectively
Fluid therapy

- If patient hypotensive
- Warmed fluid challenge 1000ml crystalloid challenge
- Larger volumes may be required in septic shock but careful monitoring required due to susceptibility of fluid overload
- CVC to guide fluid resuscitation and inotropes but should not delay resuscitation
Antimicrobial therapy

- IV antibiotics as early as possible - always within the first hour
- Broad spectrum then tailor with results
- As postulated Group A Strep likely cause and the rise of this pathogen as a cause of death mirrors the increase of its prevalence in the general population
Antibiotic recommendations

Table 1. The following antibiotic recommendations are taken from the CMACE report 2006-2008

- **Where the organism is unknown and the woman is not critically ill** - co-amoxiclav 1.2g 8hrly + metronidazole 500mg 8hrly Or cefuroxime 1.5g 8hrly + metronidazole 500mg 8hrly or cefotaxime 1-2g 6 to 12hrly + metronidazole 500mg 8hrly

- **In cases of penicillin and cephalosporin allergy** - clarithromycin 500mg 12hrly + gentamicin or clindamycin 600mg to 1.2g 6-8hrly + gentamicin

- **In severe sepsis or septic shock** - piperacillin-tazobactam 4.5g 8hrly + gentamicin 3-5mg/kg daily or ciprofloxacin 600mg 12hrly + gentamicin 3-5mg/kg daily

- a carbopenem such as meropenem 500mg - 1g 8hrly may be added metronidazole 500mg 8hrly may be considered to provide anaerobic cover

- **If Group A streptococcal infection is suspected** - clindamycin (600mg to 1.2mg 6-8hrly) is more effective than penicillin as it inhibits exotoxin production

- **If there are risks for MRSA** - add teicoplanin 10mg/kg 12hrly for 3 doses then 10mg/kg daily or linezolid 600mg 12hrly
Blood Products

- If not actively bleeding and no invasive procedures planned - transfuse platelets if < 5 x10⁹/l regardless
- If significant risk of bleeding or if surgery or invasive procedures planned - transfuse platelets if <50 x10⁹/l
- Hb Target 7-9 g/dl - transfuse accordingly
Vasopressors

- Nor-adrenaline or Dopamine via CVC
- MAP > 65mmHg
- Low dose steroids may be added if shock remains poorly responsive to fluids and vasopressors
- Keep glucose less than 10 mmol/l (not too tight 4-6 associated with increase complications)
- Ventilation, renal support etc. as per ITU
- Consider DVT, stress ulcers etc. as per care bundle
Removing the Source

- Focus of infection identified and removed early
- Retained products
- Hysterectomy should be considered
GAS is typically community based. 5-30% of the population are asymptomatic carriers on skin or in throat.

Strep throat is one of the most common childhood infections and all the mothers who died from GAS sepsis either worked with or had young children.
Direct deaths: UK 1985-2008
Rates per million maternities

- Pregnancy induced hypertension
- Thromboembolism
- Haemorrhage
- AFE
- Sepsis
<table>
<thead>
<tr>
<th>Cause</th>
<th>2003-5</th>
<th>2006-8</th>
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</thead>
<tbody>
<tr>
<td>Thromboembolism</td>
<td>41</td>
<td>18</td>
</tr>
<tr>
<td>Pre-eclampsia / eclampsia</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>AFE</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Early pregnancy</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Anaesthetic</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
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</table>

*Direct deaths: causes*
### Sepsis

<table>
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<tr>
<th></th>
<th>2000 -02</th>
<th>2003 -05</th>
<th>2006 -08</th>
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<tbody>
<tr>
<td>Sepsis in early pregnancy</td>
<td>2</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Puerperal sepsis</td>
<td>5</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>After surgical procedures</td>
<td>3</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Before or during labour</td>
<td>1</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Group A streptococcus</td>
<td>3</td>
<td>8</td>
<td>13</td>
</tr>
</tbody>
</table>
29 deaths 26 direct

- 3 were late direct and are not included in these numbers but are included in the discussion
- Age 15-41 years
- Stable relationships no social issues
- Normal BMI
- 9 x primi. 8 prior to 24 weeks. 12 x VD, 9 x CS
- 5 stillbirths. 16 babies survived
SICKLE CELL

- 2xSCD
- 1 xSCT
- Maternal mortality in SCD 1 in 220
Timing of Sepsis in pregnancy

- 8 Deaths in early pregnancy < 24 weeks
- 9 Deaths where sepsis developed before delivery (4xCS 5xVD)
- 7 Deaths where sepsis developed after vaginal delivery
- 9 Deaths after CS (4 cases it was performed as a result of pre-existing disease - see above)
- 8+9+7+5=29
Substandard care

- $\frac{18}{26} = 69\%$
- 12 outcome may have been different
SEPSIS VIGNETTE 1
A woman in mid-pregnancy called an out-of-hours GP

She was feverish, shivery and had a sore throat
- Dx – probable viral infection
- Few hours later, she developed abdo pain, D & V and reduced fetal movements
- GP returned. Dx abruption – rushed to hospital

On admission, critically ill:
- Tachycardia, breathlessness, cyanosis and confusion
- Dx septic shock.
- Correct multi-disciplinary treatment instituted immediately, including appropriate IV antibiotics and ITU support

Died a few hours after admission to hospital.
SEPSIS VIGNETTE 2
A woman with a 2\textsuperscript{nd} degree tear felt feverish for a few days after delivery, severe abdo pain and diarrhoea

- Accurately and quickly assessed by midwife – sepsis
- Condition deteriorated despite appropriate treatment including adequate antibiotic treatment
- Despite ICU she died a few hours later
- Blood cultures and perineal swabs grew GAS
SEPSIS VIGNETTE 3
A Woman with ruptured membranes for several days before CS for failure to progress in spont labour

- Oral amox and 1xIV co-amoxiclav at surgery
- After delivery cough and sore throat on discharge
- Cold, SOB + productive cough
- Midwife arranged review
- Ambulance arrived quickly but died in A&E
- GAS throat, lungs + uterus
Sepsis: recommendations
“Be aware of sepsis – beware of sepsis”

Education of pregnant and puerperal women
- Wash hands before and after visiting lavatory
- Signs and symptoms of infection

Identification and monitoring
- In the community, early signs of infection
- In hospital, MEOWS charts

Immediate antibiotic treatment
- Without waiting for investigation results

Guidelines on detection and management
- Local and, as a priority, national
Sepsis
Proposed new classification

1. Unsafe abortion
2. Ruptured membranes (genital tract sepsis)
3. Post-delivery (genital tract sepsis)
4. Community acquired sepsis in pregnancy
5. Severe postpartum sepsis related to the birth process but genital tract not involved
   eg. spinal anaesthesia, CS wound infection
6. Other, coincidental infections

All “Direct”, except 4 and 6 “Coincidental”
ANSWERS

• 1 (a) F (b) F (c) T (d) F
• 2 (a) F (b) T (c) T (d) T
• 3 (a) F (b) F (c) F (d) F

References

1) CMACE 2006-2008

2) Maternal Sepsis: epidemiology, etiology and outcome: Current opinion in Infectious Diseases: Jeroen van Dillen et al

3) Anaesthesia Tutorial of the week 235: C Cormack: World Federation of Societies of Anesthesiologists
QUESTIONS????????
The majority of sepsis occurring in the obstetric population is bacterial and sensitive to widely available antibiotics.

Mother and Baby doing well
Father a bit tired!!!