

Is sepsis in pregnancy different?

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Outline

- CASE PRESENTATION
- Epidemiology of sepsis in pregnancy
- Sepsis definitions
- Causes of sepsis in pregnancy
- Severity of illness scoring in pregnancy
- NOT a full review of sepsis and management

Case presentation

- 40 yr old woman, 32 weeks gestation
- Spontaneous rupture of membranes previous day
- Nausea, vomiting, abdominal pain x 24 hr
- Examination:
 - Confused, mumbling
 - T 38.5 HR 108 reg, RR 24, BP 92/50 (64)
 - Uterine tenderness
- Labs:
 - WBC 14.6; PLT 88,000; Na 142; Creat 100,
 - pH 7.32 CO₂ 28 O₂ 80, Bic 15, Sat 97% (on 40%)
- Urine dip: WBC+ RBC+

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**Chorioamnionitis
with septic shock**

Epidemiology of sepsis in pregnancy

- Netherlands (2004-2006): 21/100,000 deliveries
- UKOSS (2011-2012): 47/100,000 deliveries
- USA (2013-16): 38/100,000 deliveries

Kramer et al, Acta Obstet Gynecol Scand 2009; 88:647
Acosta et al. PLoS Med 2014; 11(7):e1001672
Hensley et al. JAMA 2019; 322:890-893

Incidence or diagnosis is increasing in many areas

Incidence in some LMIC may be far higher

SEPSIS IN PREGNANCY

UKOSS prospective study: 1 year (2011/2012):

- 365 severe sepsis
- 71 (19.5%) septic shock
- 5 (1.4%) died

Incidence: 15% increase since 1998

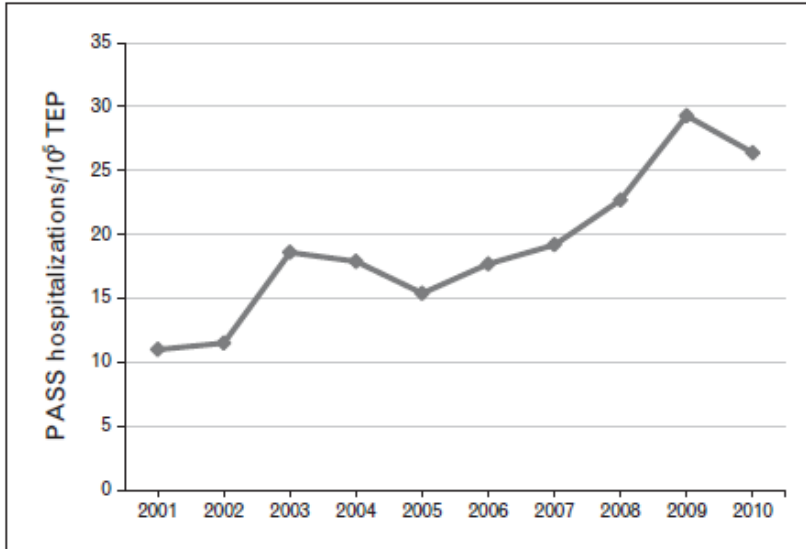
Timing:

- SIRS to severe sepsis <24 hr
- for Group A strep <9 hr

*Singer, Inada-Kim, Shankar-Hari. Lancet 2019. Oct 26th
Acosta et al. PLoS Med. 2014 Jul; 11(7): e1001672.*

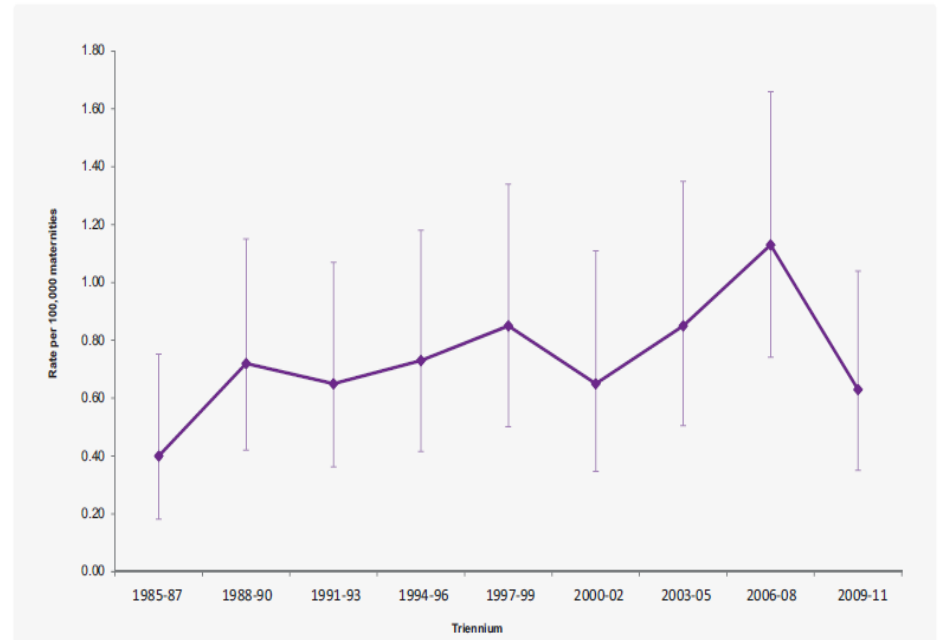
Epidemiology of sepsis in pregnancy

Longitudinal data from Texas



Oud & Watkins. J Clin Med Res. 2015;7:400-16.

Figure 2.5: Maternal mortality rates from genital tract sepsis 1985–2011



Source: CMACE, MBRRACE-UK

Sepsis definitions & pregnancy

Case presentation

SIRS criteria:

- fever
- tachycardia
- tachypnea
- WBC

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The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

2016

ation

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

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Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥ 22 /min

Altered mentation

Systolic blood pressure ≤ 100 mm Hg

SOFA score of 2 or greater identified a 2- to 25-fold increased risk of dying compared with patients with a SOFA score less than 2.¹²

NOT diagnostic criteria for sepsis

Are these definitions/scores appropriate in the pregnant patient?

qSOFA (Quick SOFA) Criteria

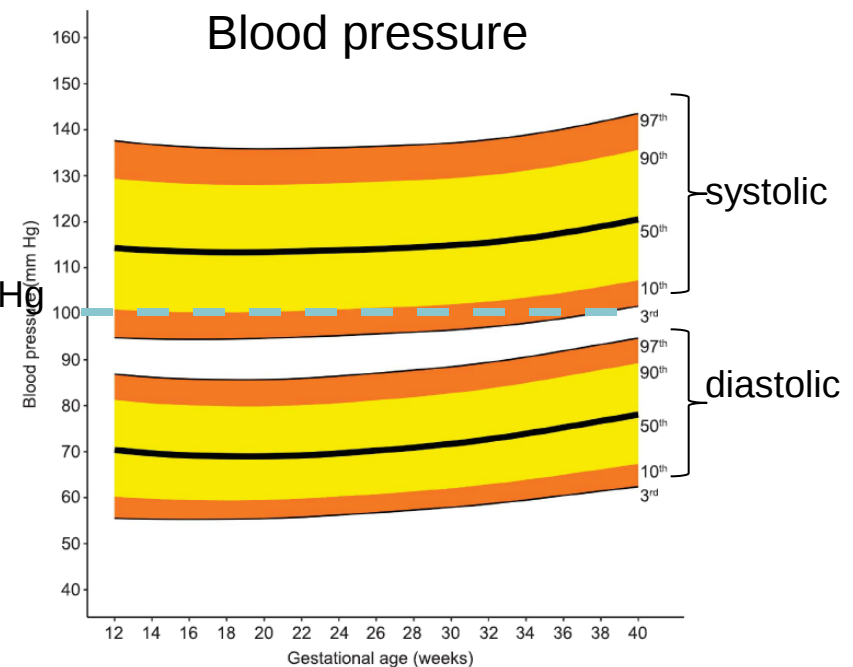
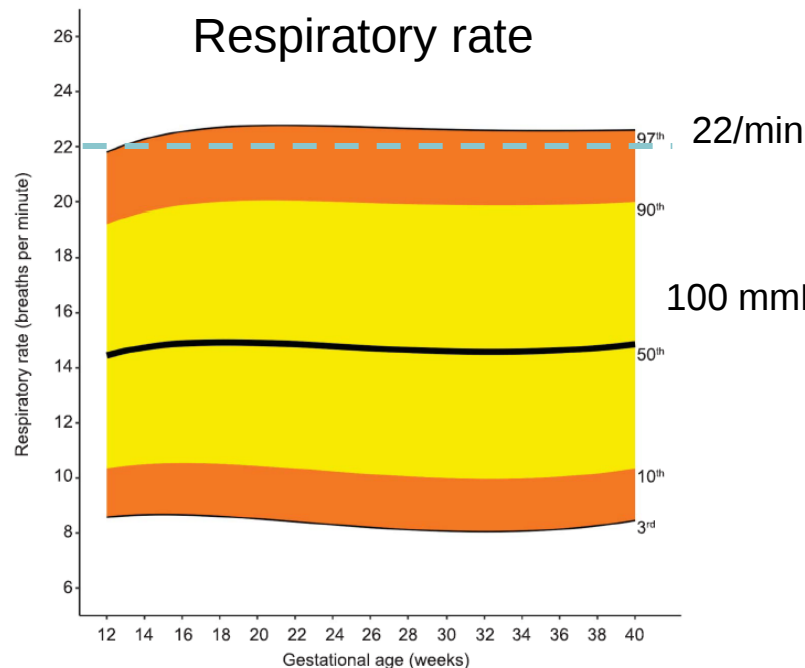
Respiratory rate $\geq 22/\text{min}$

Altered mentation

Systolic blood pressure $\leq 100 \text{ mm Hg}$

In pregnancy:

- RR not changed (V_t increased)
- mentation not affected
- BP slightly lower



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SOMANZ has proposed obstetrically modified omqSOFA

Respiratory rate $\geq 25/\text{min}$

Altered mentation

Systolic blood pressure < 90 mmHg



Bowyer et al, Aust NZ Obstet Gynaecol 2017; 57:540-551

Lactate in pregnancy:

- no difference in normal levels (< 2 mmol/L)
- slight elevation during labour (4 mmol/L)

Bauer et al. Am J Perinatol. 2018 Nov 5 (published online)

How different is the septic pregnant patient?

- Overlap with normal physiology & hemodynamics ($\downarrow$ BP, $\uparrow$ CO)
- Often a low index of suspicion
- Altered cell-mediated immune response
- Unfamiliar clinical syndromes
- Different microorganisms
- Perceived limitations to:
 - imaging
 - drug therapy

Altered cell-mediated immunity

↓ Th1 (CMI)

↑ Th2 (humoral), innate response?

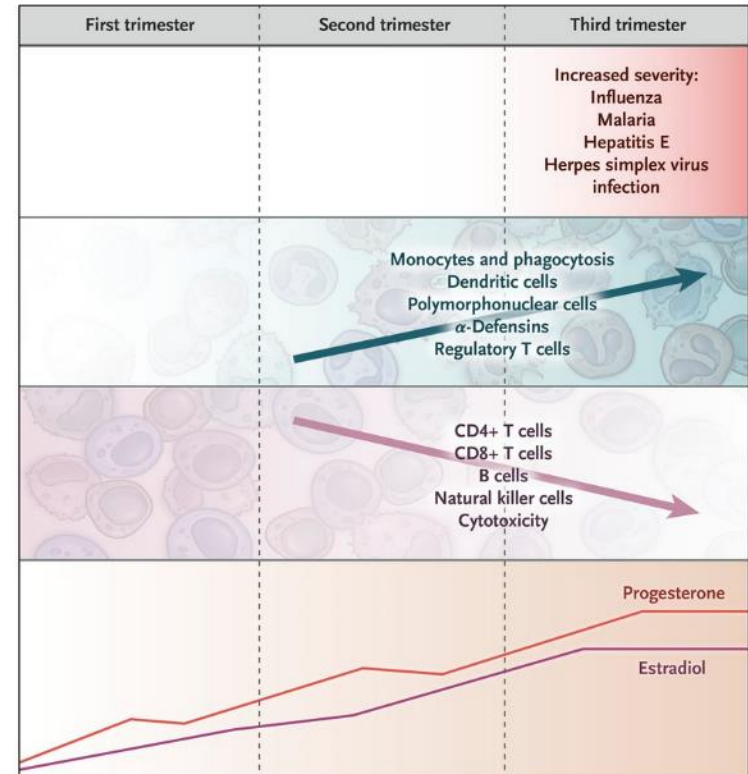
To allow tolerance to paternal antigens?

Increased risk or severity of:

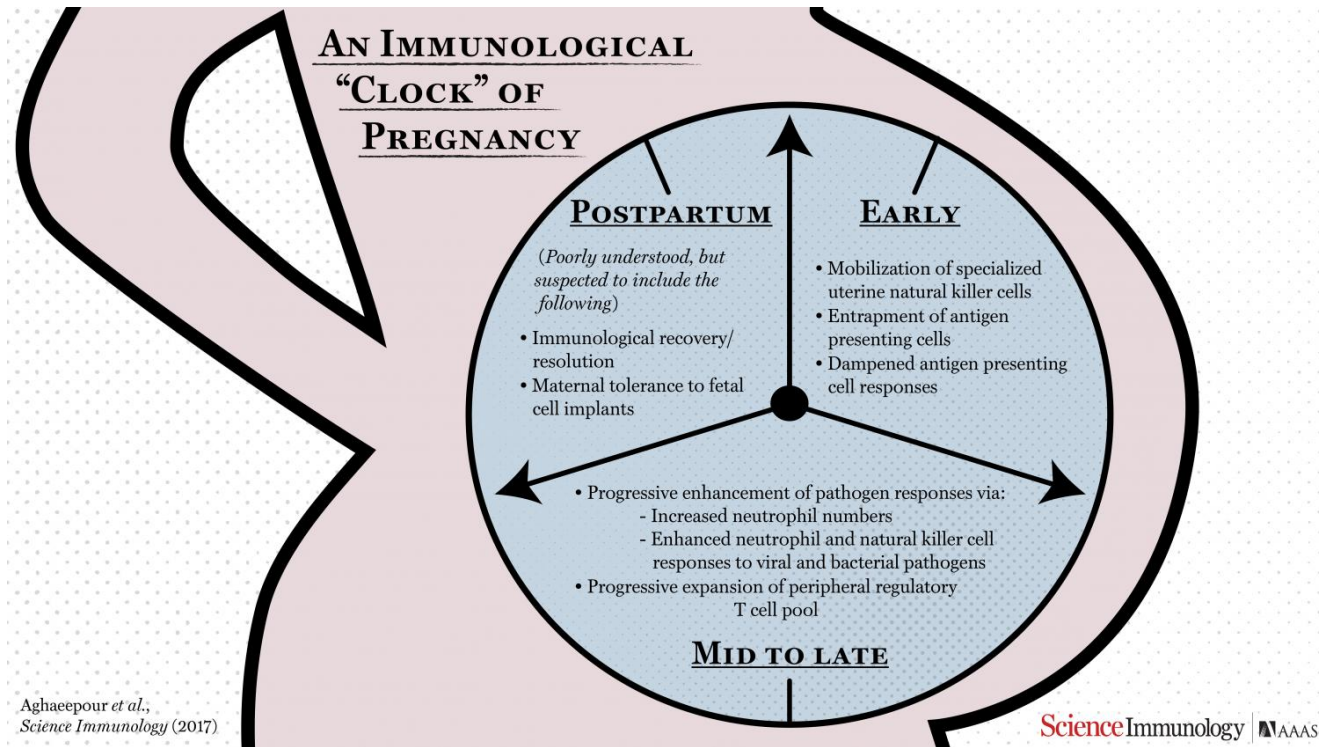
- influenza
- varicella
- coccidioidomycosis

Placental tropism for certain organisms:

- *Listeria monocytogenes*
- *Falciparum malaria*



Altered cell-mediated immunity



Response to infection may vary with stage of pregnancy

Causes & Risk factors

Risk factors:

1. Non-obstetric

- altered cell-mediated immunity
- local effects (ie. urinary infections)
- obesity
- impaired glucose tolerance
- co-morbidity: liver/renal/heart/HIV
- history of pelvic infection or GBS

2. Obstetric

Causes & Risk factors

2 . Obstetric

- **Caesarean delivery** (esp after onset labor)
- assisted reproductive technology
- cervical cerclage
- preterm rupture of membranes
- prolonged labour
- retained products of conception
- peripartum hysterectomy

Causes & Risk factors

Specific syndromes	Microorganisms
pyelonephritis	enteric
choroamnionitis	vaginal/enteric Listeria (hematogenous)
postpartum endometritis	vaginal/enteric Enterococcus (cephalosporin prophylaxis)
necrotizing fasciitis	Group A streptococcus
puerperal ovarian vein thrombophleb	complication of earlier infection
septic abortion	vaginal/enteric C. perfringens (& tetani)
pneumonia	influenza, usual organisms

Enteric: E. coli, Enterococcus, Enterobacter, anaerobes

Vaginal: Grp B strep, mycoplasma, staphylococcus

Perceived limitations to
Radiological imaging
Drug therapy

Radiological Procedures

- Fetal risk

Gestational Period	Effect	Radiation dose (mGy)
Pre-implantation: 0-2 weeks	Death or no consequence	≥50-100
Embryogenesis: 2-8 weeks	Congenital anomalies	≥200
Early fetal: 8-15 weeks	Microcephaly Decrease in IQ (25 points)	≥200 ≥1000
Late fetal: 16-40 wks 16-25 weeks 25-40 weeks	Severe mental effects Carcinogenic risk: 1% 6%	≥250 50 50 - 500

Table 2. Estimated fetal dose from common imaging procedures.

Fetal dose range (mGy)	Examples of procedures
0.001–1.0	X-rays: beyond 10 cm of uterus including head, chest, breast, teeth, extremities X-rays: abdomen, pelvis, hip pulmonary angiogram CT: head or neck, pelvimetry, chest, computed tomography pulmonary angiogram (CTPA) Nuclear scan: Lung ventilation, liver/spleen, ventilation/perfusion (V/Q)
1.1–10	X-rays: Barium enema, intravenous pyelography, lumbar spine CT: lumbar spine, abdomen, coronary artery angiography Nuclear scan: renal, white cell, bone, cardiac.
11–50	CT: pelvis, pelvis and abdomen, pelvis and abdomen and chest Nuclear scan: PET/CT whole body scan, myocardial perfusion

Lowe 2019. Obstet Med (pub online April11
 National Radiological Protection Board, 1998
 Ratnapalan et al, CMAJ 2008; 179:1293

Radiological Procedures

Consider risk-benefit

- Don't avoid necessary studies, eg. CT angio
- Don't do unnecessary, eg. daily CXR, lateral
- Contrast is no longer considered a risk



Lowe 2019. Obstet Med (pub online April11
National Radiological Protection Board, 1998
Ratnapalan et al, CMAJ 2008; 179:1293

Drugs in Pregnancy

- Inotropic therapy:

- All inotropes potentially reduce placental perfusion
 - Fluid first, remember left lateral positioning
- Specific drugs:
 - Norepinephrine –reduce uterine blood flow, used for septic shock
 - Phenylephrine – used for hypotension 2° to spinal

- Antibiotics:

Very few limitations in pregnancy

Weigh risk-benefit in each situation

e.g. ciprofloxacin - animal studies suggest concerns

- limited data of concerns in humans

- pregnant CF pt, with Pseudomonas??

Sepsis – Management

- Early recognition & management!
 - SOFA score
 - NEWS/ MEWS/OEWS

BJOG. 2011;118 Suppl 1:1-203

Date									
Time									
Systolic BP									
<80	3								
80 - 89	2								
90 - 139	0								
140 - 149	1								
150 - 159	2								
>160	3								
Respiratory rate									
<10	3								
10 - 17	0								
18 - 24	1								
25 - 29	2								
>30	3								
Heart rate									
<60	3								
60 - 110	0								
111 - 149	2								
>150	3								
FiO₂ to keep Sat >96%									
room air	0								
24 - 39%	1								
>40%	3								
Temperature									
<34	3								
34.1 - 35.0	1								
35.1 - 37.9	0								
38.0 - 38.9	1								
>39.0	3								
Consciousness									
alert (GCS = 15)	0								
not alert (<15)	3								

Sepsis – Management

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BJOG. 2011;118 Suppl 1:1-203

abn ≥ 0.9 eg. $\frac{100/\text{min}}{110/70}$

S.I. of >1 = HR $>$ SBP

>1.7 urgent eg. $\frac{155/\text{min}}{90/60}$

- Shock index: HR/sysBP
- Modified shock index: HR/MAP

Althunayyan et al. J Infect Public Health. 2019

Sepsis – Management

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BJOG. 2011;118 Suppl 1:1-203



Cradle device

Nathan HL et al. BMJ Innov
2018;4:192–198.

- Shock index: $HR/sysBP$
- Modified shock index: HR/MAP

Althunayyan et al. J Infect Public Health. 2019

Sepsis – Management

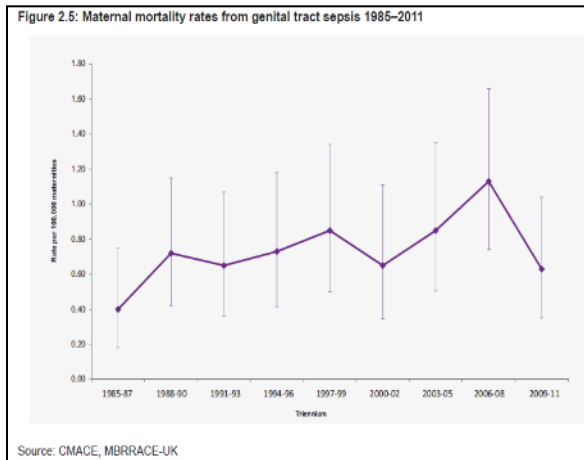
Sepsis in Obstetrics (SOS) score:

- to identify patients for ICU admission

Variable	High abnormal range				Normal	Low abnormal range			
Score	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature (°C)	>40.9	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	<30
Systolic Blood Pressure (mmHg)					>90		70-90		<70
Heart Rate (beats per minute)	>179	150-179	130-149	120-129	≤119				
Respiratory Rate (breaths per minute)	>49	35-49		25-34	12-24	10-11	6-9		≤5
SpO ₂ (%)					≥92%	90-91%		85-89%	<85%
White Blood Cell Count (/μL)	>39.9		25-39.9	17-24.9	5.7-16.9	3-5.6	1-2.9		<1
% Immature Neutrophils			≥10%		<10%				
Lactic Acid (mmol/L)			≥4		<4				

Albright et al. Am J Obstet Gynecol 2014;211:39.e7-8

SUMMARY



UK Sepsis Trust Clinical Toolkits

The key actions for diagnosis and management of sepsis are:

- Timely recognition
- Fast administration of intravenous antibiotics
- Quick involvement of experts – senior review is essential

Saving Lives, Improving Mother's Care 2014 (Knight, Kenyon et al. 2014)



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