Top 10 Pearls for the Diagnosis and Management of Maternal Sepsis with Case Review

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UCONN HEALTH

Disclosure of Relevant Financial Relationships - Shields

Vice-Chair, ACOG Clinical Practice Guidelines - OB Committee

Board examiner, OB/GYN specialty and MFM subspecialty certifying exam

Member, Varda 5, LLC, owns exclusive sublicense of Obstetric Life Support

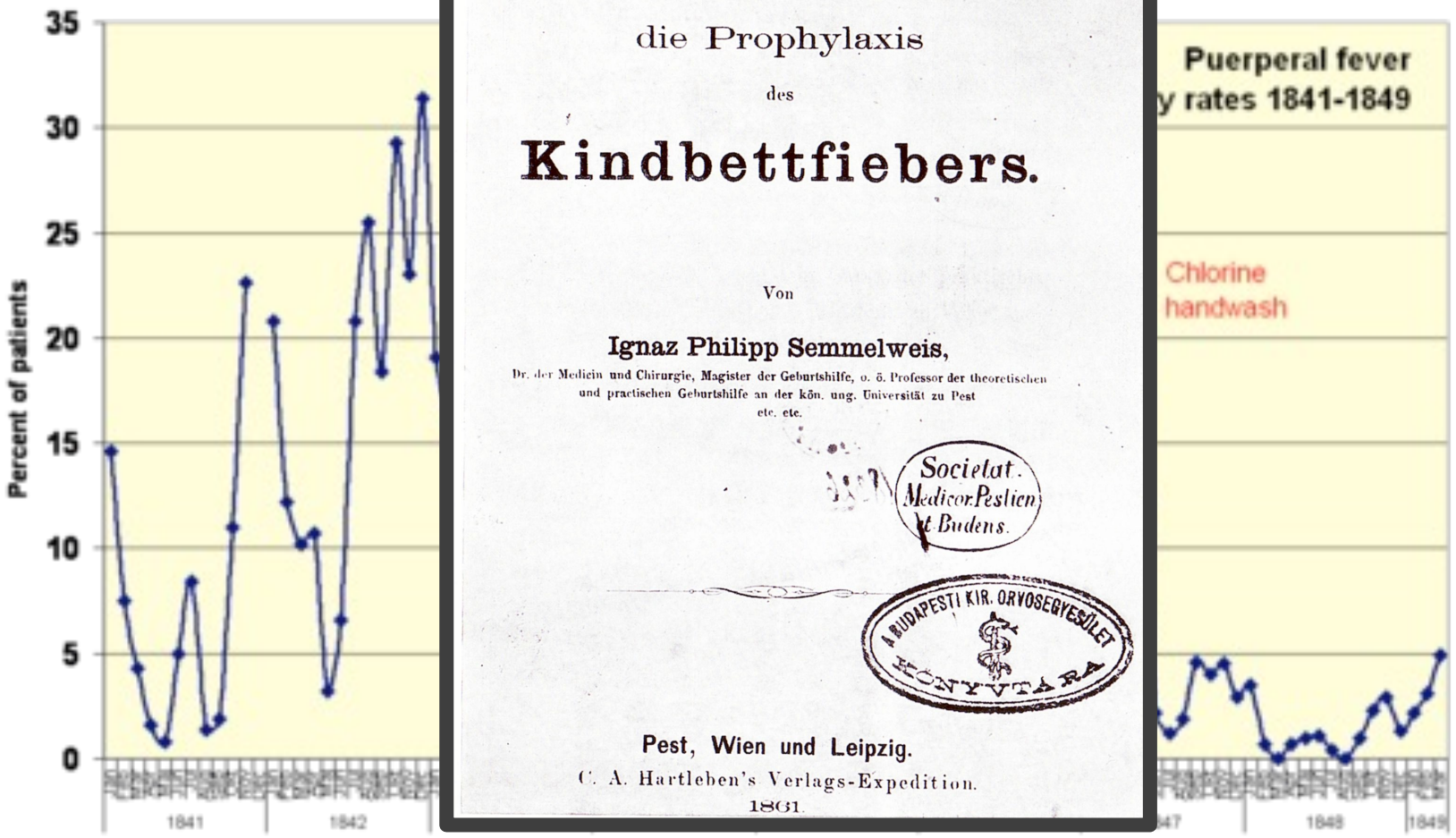
Baylor College of Medicine IP for maternal simulator

Disclosure of Relevant Financial Relationships -Tse

None

Objectives

Review	diagnostic challenges of sepsis during pregnancy and postpartum
Discuss	tools that assist with the early recognition of maternal sepsis
Examine	management principles that reduce maternal morbidity and mortality from complications of maternal sepsis
Review	case of maternal sepsis and discuss quality improvement considerations



Die Aetiologie, der Begriff

und

2633

die Prophylaxis

des

Kindbettfiebers.

Von

Ignaz Philipp Semmelweis,

Dr. der Medicin und Chirurgie, Magister der Geburtshilfe, o. ö. Professor der theoretischen und practischen Geburtshilfe an der kön. ung. Universität zu Pest etc. etc.

Pest, Wien und Leipzig.

C. A. Hartleben's Verlags-Expedition.

1861.

What is the definition of maternal sepsis?

A. At least one SIRS criteria and known or suspected infection
B. At least one clinical criteria and two SIRS criteria: T> 38°C <36°C, HR>90, RR>24, PaCO2< 32 mmHg, WBC> 14,000
C. Life-threatening, organ dysfunction caused by response due to infection
D. Persistent hypotensive from infection despite fluid resuscitation

Terminology	SSC Definition	Sepsis-3
SIRS	At least 2 of the following: T > 38°C < 36°C HR > 90 RR > 24 PaCO2 < 32 mmHg WBC > 14,000 or < 4,000	Not used
Sepsis	At least 2 SIRS criteria and known or suspected infection	**Sepsis is a life-threatening organ dysfunction caused by a dysregulated patient response to infection**
Severe Sepsis	Sepsis-induced hypotension SBP, < 90 mmHg MAP, < 70 mmHg, or an SBP reduction of 40 mmHg from baseline Serum lactate, > 2 mmol/L Signs of organ dysfunction (acute oliguria, for example)	Not used
Septic Shock	Sepsis-induced hypotension that persists despite adequate fluid resuscitation and requires vasopressors to support perfusion	**Sepsis-induced hypotension, or a serum lactate level > 2 mmol, that persists despite adequate fluid resuscitation and requires vasopressors to support perfusion.**

Sepsis diagnosed during pregnancy:

Maternal Sepsis

life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or post-partum period

What time in pregnancy is maternal sepsis responsible for most deaths?

A. Antepartum
B. Intrapartum
C. Postpartum up to 60 days
D. Postpartum > 60 days

Maternal Sepsis

- Responsible for 75,000 maternal deaths/year (globally)[1]
- Rare event: accounts for 0.3-0.6% of sepsis population in US[2]
    - 4/10,000 births → 3-4% with septic shock

So why should we prioritize this….

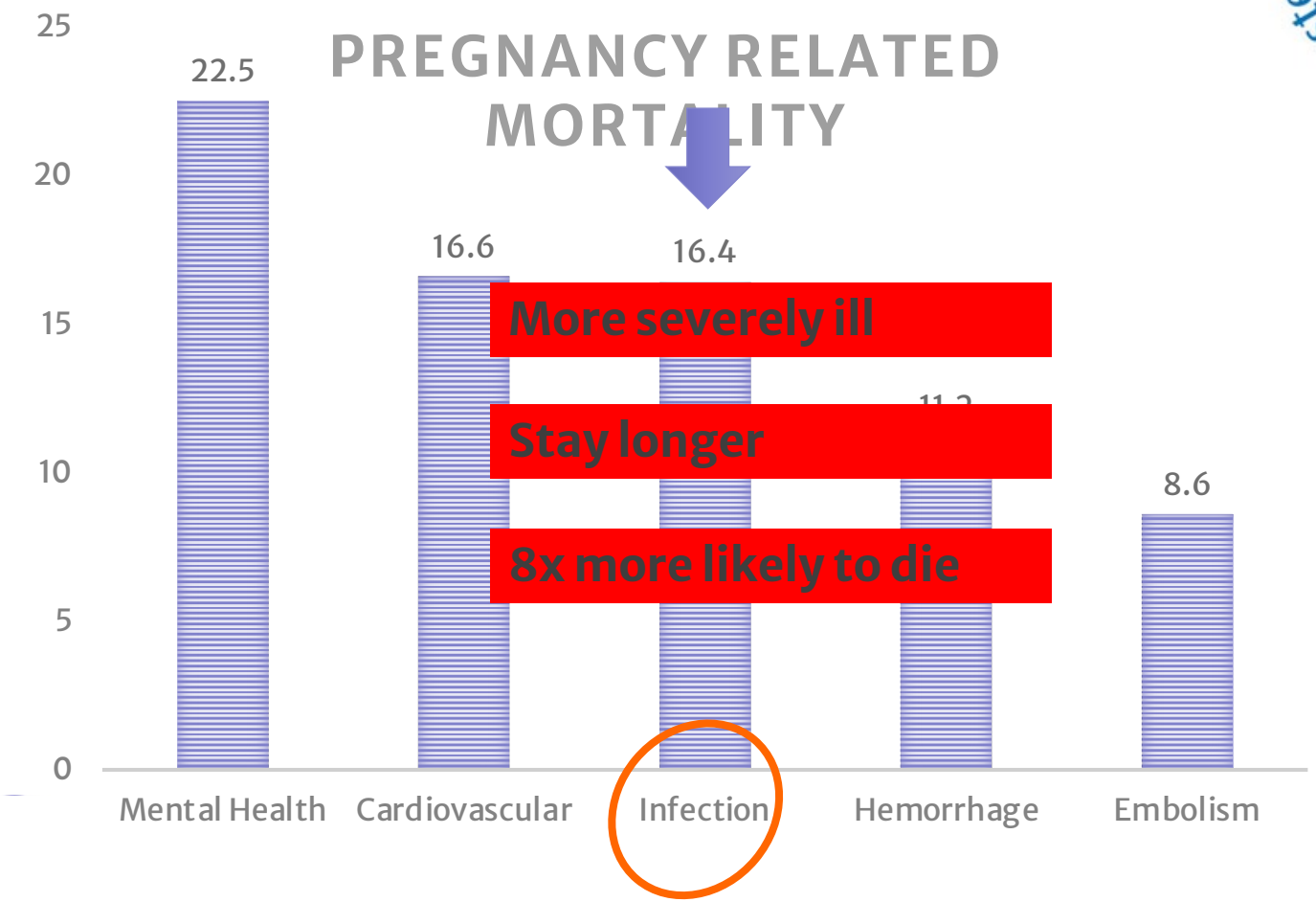
[1]*WHO 2014*
[2]*Barton JR Obstet Gynecol 2012*

Maternal Sepsis at Delivery and Postpartum

- Sepsis responsible for:
  - 24% of intrapartum deaths
  - 38.4% of postpartum maternal deaths

Liu LY Obstet Gynecol 2024

Causes of pregnancy-related death in the united states, 2020



CDC 2024

Maternal Sepsis

- For every maternal sepsis death, there is approximately **50** women who have life-threatening morbidity from sepsis (US)[2]
- Both maternal sepsis and sepsis-related maternal mortality appear to be increasing[3,4,5]

[1]*Barton JR Obstet Gynecol 2012*
[2]*WHO 2014*
[3]*Oud L J Clin Med Res 2015*
[4]*CDC 2021*

Risk Factors

Box 2. Risk Factors Associated With Maternal Sepsis

Patient factors

- Obesity
- Impaired immunity or immunosuppressant therapy
- Anemia
- Impaired glucose tolerance
- Vaginal discharge
- History of pelvic infection
- History of group B streptococcal infection
- Group A streptococcal infection in close contacts
- Age older than 35 y
- Disadvantaged socioeconomic background
- Congestive heart failure
- Chronic renal failure
- Chronic liver failure
- Systemic lupus erythematous

Obstetric factors

- Cesarean delivery
- Retained products of conception
- Prolonged rupture of membranes
- Multiple gestation
- Cervical cerclage
- Amniocentesis or other invasive procedure
- Complex perineal lacerations
- Wound hematoma

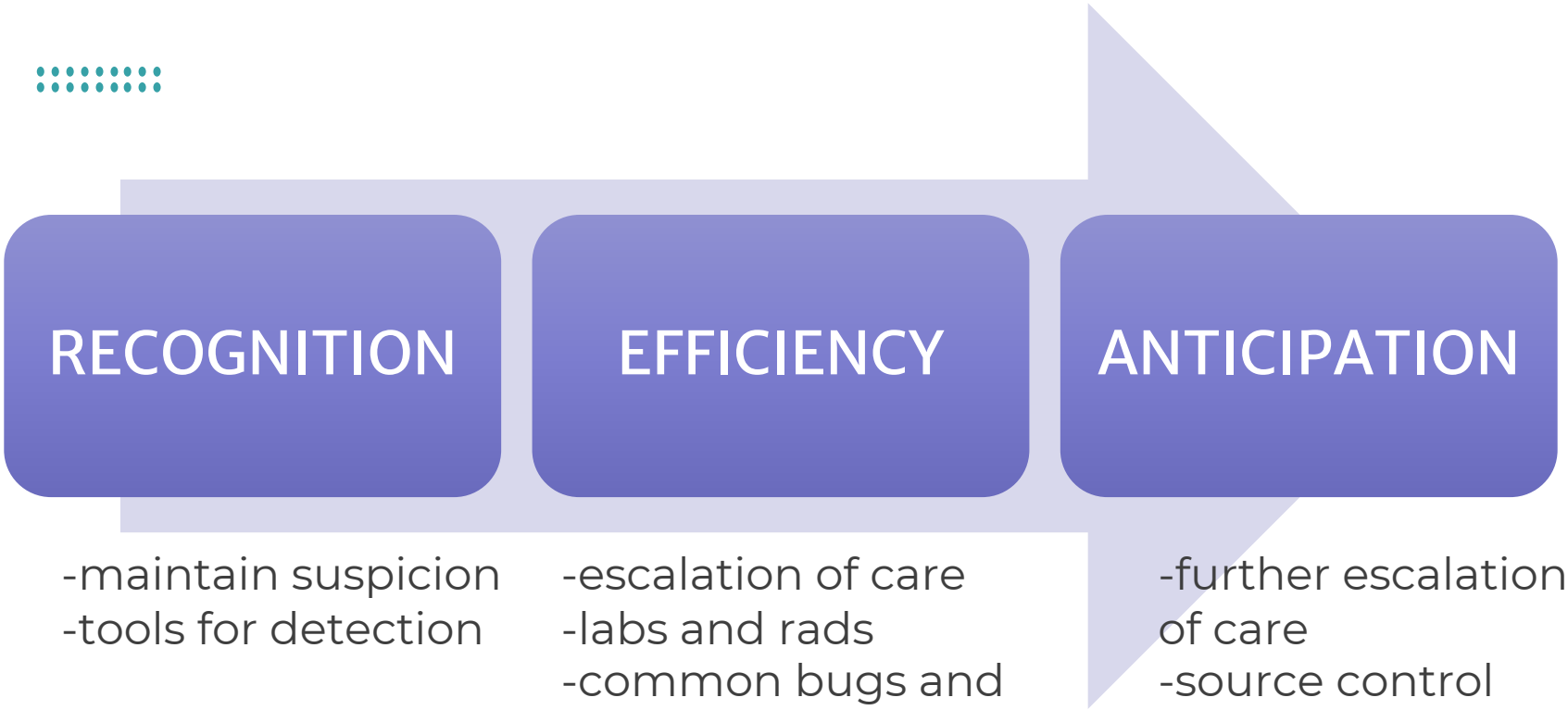
Adapted by permission from BMJ Publishing Group Limited. Buddeberg BS, Aveling W. Puerperal sepsis in the 21st century: progress, new challenges and the situation worldwide. Postgraduate Medical Journal 2015; 91:572–578. Copyright 2015.

A diagnosis of postpartum maternal sepsis was associated with:

- younger age
- Medicaid insurance
- lower socioeconomic status
- chronic medical conditions

Shields A Obstet Gynecol 2021
Liu LY Obstet Gynecol 2024

Top 10 pearls



RECOGNITION

Pearl #1:
FIRST, HEAR HER, ALWAYS MAINTAINING A HIGH INDEX OF SUSPICION FOR MATERNAL SEPSIS!

Challenges

In pregnancy:	Results in:
Younger and fitter population	Signs of sepsis/septic shock may be masked until the moment of cardiovascular collapse
External influences ❖ Blood loss ❖ Common infections ❖ Fluid administration ❖ Medications ❖ Delivery mode ❖ Anesthesia	Changes in hemodynamic status from external influences can mask signs of sepsis
Normal changes in maternal physiology	WBC count can be normally elevated in labor, resting heart rate may be higher
No obvious focus of infection	GU tract acts as point of entry

Snyder CC J Mat Fet Neonat Med 2013
Sriskandan S J R Coll Physicians Edinb 2011

Common Maternal Signs/Symptoms

Maternal Complaints

- Chills or sweats
- Shortness of breath*
- Palpitations*
- Abdominal/pelvic pain*
- Back pain*
- Abnormal vaginal discharge
- Cough/chest pain
- Flu-like symptoms
- Diarrhea*
- Rash

*Overlap with common symptoms of pregnancy

Signs

- **Fever - Temp >38°C**
- Tachycardia (HR > 110)
- Tachypnea (RR >24/min)

25% of pregnant women who die of sepsis never develop a fever!

Sriskandan S J R Coll Physicians Edinb 2011
Barton JR Obstet Gynecol 2012

Diagnosis of IAI – ACOG Clinical Update

- no definitively established confirmatory *clinical* criteria for diagnosing suspected intraamniotic infection exist
- Fever most common clinical sign
  - single oral T 39°C or higher
  - oral temperature of 38–38.9°C that persists after 30 min.
- Fever no long required to make diagnosis
  - IAI resulting in uterine fundal tenderness, foul-smelling or purulent vaginal discharge, and leukocytosis may occur without maternal fever

ACOG CPU April 29, 2024

Common Obstetric Signs/Symptoms

During pregnancy
- Leaking of vaginal fluid
- Decreased fetal movement
- Preterm contractions

Postpartum:
- Abdominal pain
- Abnormal vaginal discharge
- Vaginal pain

Barton JR. Obstet Gynecol 2012

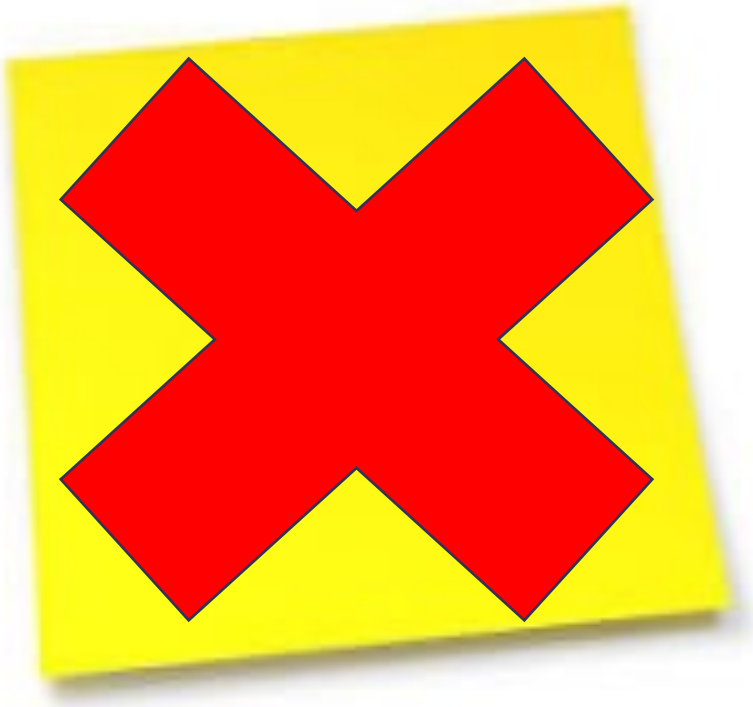
Common lab abnormalities

- Most common lab abnormality:
  → **leukocytosis (WBC > 15,000/mm3)**

- Normal range but with left shift
  "Use the diff to make a diff!"

- Leukopenia or neutropenia
  → advanced sepsis/septic shock due to bone marrow suppression
  → viral sepsis

RECOGNITION



Pearl #2:
Implement a rapid bedside tool for detection of maternal deterioration

Early Recognition: Current State

Delays in care →

lead to maternal death in up to 63% of cases!

Reasons for delays:

- ✓ Failure to recognize abnormal vital signs
- ✓ Absence of fever
- ✓ No obvious source of infection

Cantwell BJOG 2015
Bauer M. Anesth Analg 2013
Sriskandan S. J R Coll Physicians Edinb 2011
Snyder CC J Mat Fetal Neonat Med 2013

What are the best tools to screen for maternal sepsis after 20 weeks?

A. quickSOFA
B. CMQCC initial screen
C. UKOSS obstetric SIRS
D. non-pregnancy adjusted SIRS

Tools Used to Predict Mortality in Sepsis

quickSOFA

- systolic blood pressure of 100 mm Hg or less
- respiratory rate of 22/min or greater
- altered mentation

→ 2 or greater associated with a mortality rate > 10%

- highest predictive validity for in-hospital mortality (AUC 0.81)
- **NOT VALIDATED FOR PREGNANCY!!**
  - **82 validated maternal sepsis cases → sensitivity only 50%**

Levy MM. SCCM and Eur Soc of Int Med 2018
Bauer M. Anesth Analg 2020

Bedside tools used to screen for maternal sepsis

Several published early warning systems specifically designed for use in maternity care

Most not validated, some only for specific conditions (e.g. chorioamnionitis)

Tendency to over detect sepsis/septic shock

- low PPV

Edwards SE AJOG 2015
Albright AJOG 2014
Albright AJOG 2017
Bowyer Aust N Z J Obstet Gynaecol 2017
Yayja AJOG Global Rep 2023

		Pregnancy-adjusted screening tools		Screening tools focused more broadly on maternal morbidity		
Criterion	SIRS	CMQCC	UKOSS	MEWC	MEWT (red)	MEWT (yellow)
	Any two	Any two	Any two	Any one	Any one	Any two
WBC (10^9 cell/L)	< 4 or > 12	< 4 or > 15	< 4 or > 17	< 4 or > 15		
Heart rate (beats/min)	> 90	> 110	> 100	< 50 or > 120	>130	< 50 or > 110
Respiratory rate (breaths/min)	> 20	> 24	> 20	< 10 or > 24	>30	> 24 or < 10
Temperature (°C)	< 36 or > 38	< 36 or > 38	< 36 or > 38	< 36 or > 38		< 36 or > 38
Pulse Oximetry (%)				< 95	<90	< 93
Blood Pressure (mm Hg)				<90 or >160/100	>160/110	<85/45
Mean arterial pressure (mm Hg)					<55	
Exclusions for this study	None		None	None	Urine output, maternal agitation, confusion, or unresponsiveness; Patient with preeclampsia reporting a non-remitting headache or shortness of breath	Nurse concern

- Comparison of 5 screening tools for maternal sepsis during delivery hospitalization > 20 weeks
- 59 hospitals from 12 states
- 1,761 patients with sepsis during delivery hospitalization
- Two cohorts:
  A: 647 excluding chorio/endometritis
  B: 1069 with chorio/endometritis

Main. Obstet Gynecol 2024

Results

COHORT 1: Cases *excluding* chorioamnionitis and endometritis cases						
	Sepsis by Diagnosis Codes			Sepsis with End Organ Injury by Diagnosis Codes		
Screening System	False Positive Rate (95% CI) (in patients without sepsis codes, n=2,588)	Sensitivity (95% CI) (n=647 sepsis cases)	C statistic (95% CI)	False Positive Rate (95% CI) (In patients without sepsis codes, n=912)	Sensitivity (95% CI) (n=228 sepsis cases with end organ injury)	C statistic (95% CI)
CMQCC	6.9% (6.0-8.0)	90.6% (88.1-92.7)	0.92 (0.91-0.93)	9.2% (7.4-11.3)	96.9% (93.8-98.8)	0.94 (0.92-0.95)
SIRS	21.3% (19.7-22.9)	96.9% (95.3-98.1)	0.88 (0.87-0.89)	23.9% (21.2-26.8)	98.7% (96.2-99.7)	0.87 (0.86-0.89)
MEWC	38.3% (36.5-40.2)	96.9% (95.3-98.1)	0.79 (0.78-0.80)	43.9% (40.6-47.2)	98.2% (95.6-99.5)	0.77 (0.75-0.79)
UKOSS	9.6% (8.5-10.8)	92.0% (89.6-93.9)	0.91 (0.90-0.92)	11.6% (9.6-13.9)	96.1% (92.6-98.2)	0.92 (0.91-0.94)
MEWT (overall)	15.8% (14.4-17.3)	79.9% (76.6-82.9)	0.82 (0.80-0.84)	19.8% (17.3-22.6)	90.8% (86.3-94.2)	0.85 (0.83-0.88)

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C-statistics

COHORT 2: Cases *including* chorioamnionitis and endometritis cases						
	Sepsis by Diagnosis Codes			Sepsis with End Organ Injury by Diagnosis Codes		
Screening System	False Positive Rate (95% CI) (In patients without sepsis codes, n=13,542)	Sensitivity (95%CI) (n=1049 sepsis cases)	C statistic (95%CI)	False Positive Rate (95% CI) (In patients without sepsis codes, n=13,542)	Sensitivity (95%CI) (n=238 sepsis cases with end organ injury)	C statistic (95%CI)
CMQCC	60.2% (59.3-61.0)	93.6% (92.0-95.0)	0.67 (0.66-0.68)	60.2% (59.3-61.0)	93.7% (89.8-96.4)	0.67 (0.65-0.68)
SIRS	86.6% (86.0-87.1)	99.4% (98.8-99.8)	0.56 (0.56-0.57)	86.6% (86.0-87.1)	99.2% (97.0-99.9)	0.56 (0.56-0.57)
MEWC	92.3% (91.9-92.8)	97.7% (96.6-98.5)	0.53 (0.52-0.53)	92.3% (91.9-92.8)	97.9% (95.2-99.3)	0.53 (0.52-0.54)
UKOSS	67.5% (66.7-68.3)	95.2% (93.2-96.0)	0.64 (0.63-0.65)	67.5% (66.7-68.3)	95.0% (91.4-97.4)	0.64 (0.63-0.65)
MEWT (Overall)	45.7% (44.8-46.5)	78.5% (75.8-80.9)	0.66 (0.65-0.68)	45.7% (44.8-46.5)	87.4% (82.5-91.3)	0.71 (0.69-0.73)

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Bedside tools used to screen for maternal sepsis

- Maternal Sepsis Cases - convenience sample of 71 hospitals in 12 sates:
  - 525 antepartum: 2100 controls
  - 541 postpartum: 2164 controls
- Screens evaluated:
  - CMQCC initial screen
  - non-pregnancy adjusted SIRS
  - MEWC
  - UKOSS obstetric SIRS
  - MEWT

Bauer M Obstet Gynecol 2024

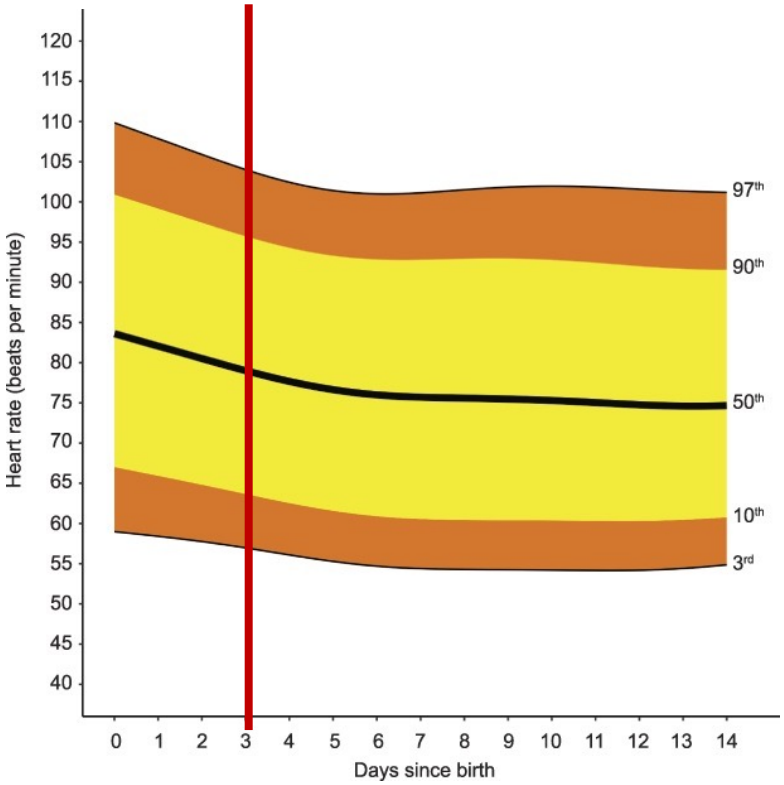
Bedside tools used to screen for maternal sepsis

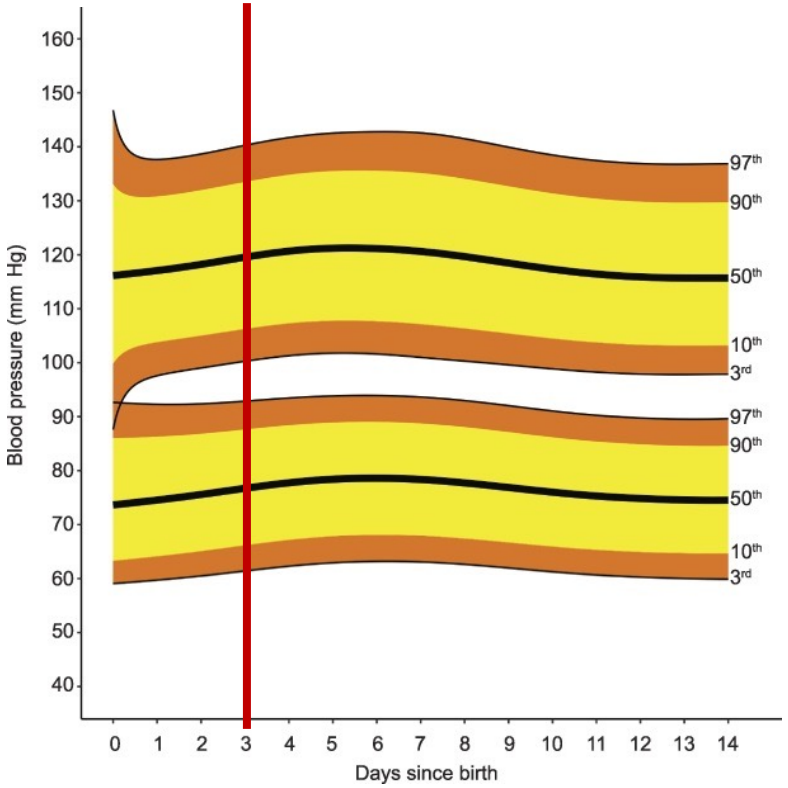
Results:

- Pregnancy-adjusted sepsis screen tools performed better between >20 weeks and during delivery hospitalization
- Non-pregnancy adjusted SIRS screening tools better <20 weeks or >3 days

Bauer M Obstet Gynecol 2024

Vital Signs in Postpartum





Green J Obstet Gynecol 2021

Should we implement a bedside screen for maternal sepsis?

- ✓ Implementation of a pregnancy-adjusted may decrease maternal risk.
- ✓ Use pregnancy-adjusted tools (CMQCC or UKOSS) between 20 weeks gestation and 3 days postpartum.
- ✓ Understand limitations of tools in use.
- ✓ Avoid use of a single screening step.
- ✓ Use non-obstetric sepsis screening tool < 20 weeks and > 3 days postpartum.

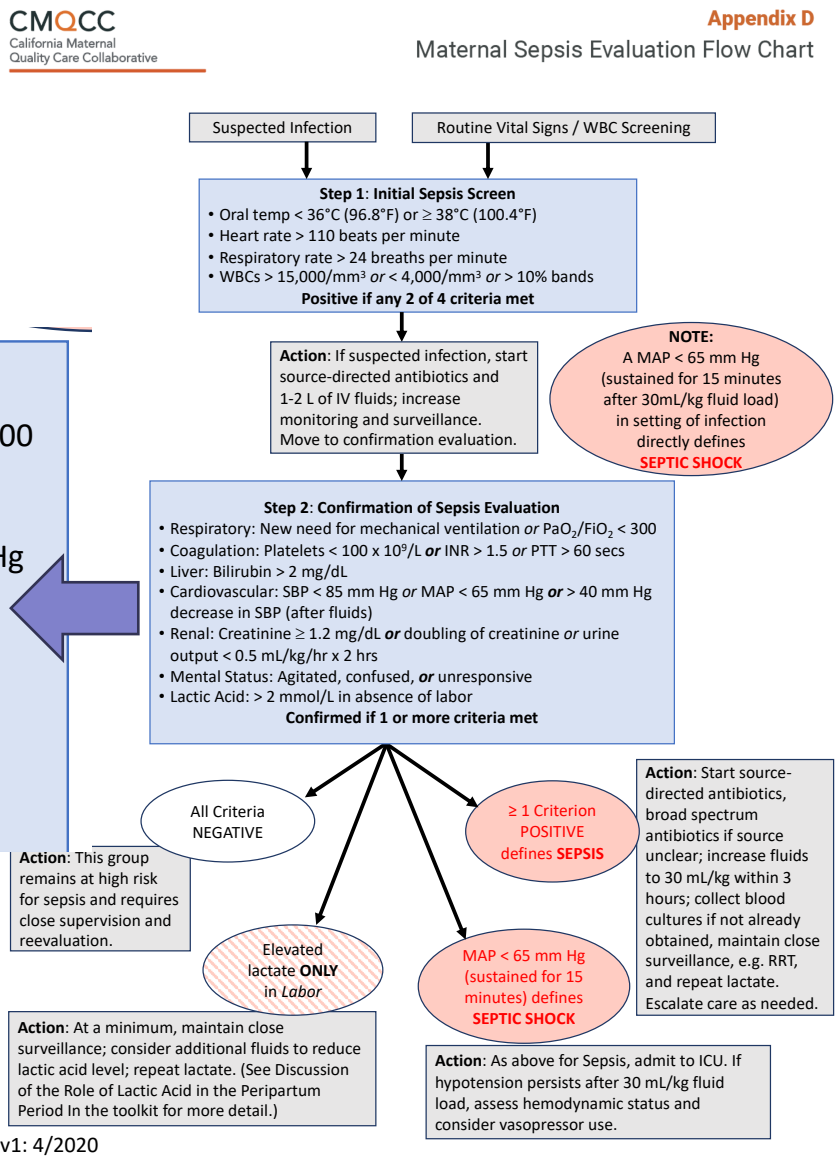
Sample SEPSIS EVALUATION flowchart

CMQCC sepsis flowchart 2020

Step 2: **Confirmation of Sepsis Evaluation**

- Respiratory: New need for mechanical ventilation *or* $PaO_2/FiO_2 < 300$
- Coagulation: Platelets < 100 x 10^9/L ***or*** INR > 1.5 *or* PTT > 60 secs
- Liver: Bilirubin > 2 mg/dL
- Cardiovascular: SBP < 85 mm Hg *or* MAP < 65 mm Hg ***or*** > 40 mm Hg decrease in SBP (after fluids)
- Renal: Creatinine ≥ 1.2 mg/dL ***or*** doubling of creatinine *or* urine output < 0.5 mL/kg/hr x 2 hrs
- Mental Status: Agitated, confused, ***or*** unresponsive
- Lactic Acid: > 2 mmol/L in absence of labor

Confirmed if 1 or more criteria met



Pearl 3. implement sepsis bundles to facilitate rapid escalation of care

Bedside Evaluation for Organ Dysfunction – Primary Survey

REVIEW VITALS

LOOK FOR EVIDENCE OF HEMODYNAMIC INSTABILITY

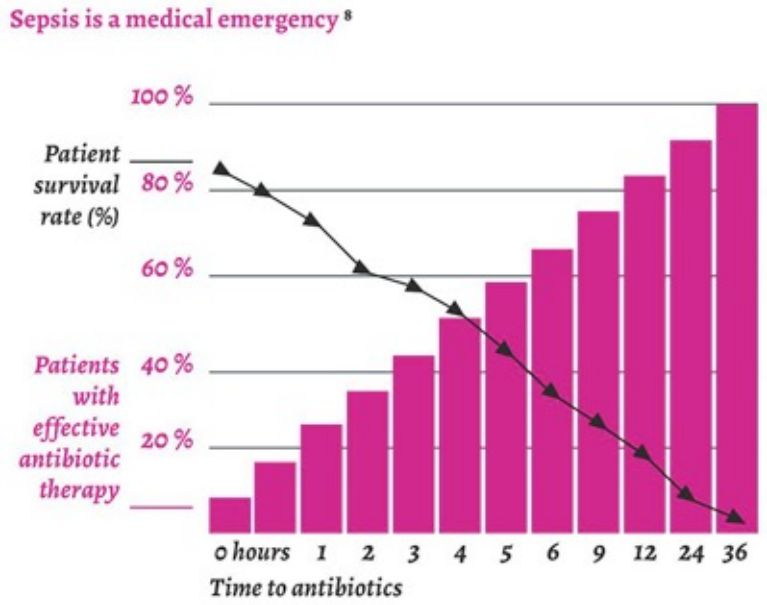
- MEAN ATERIAL PRESSURE < 65 MMHG
- RESPIRATORY RATE > 24
- ABNORMAL MATERNAL HEART RATE
- OXYGEN SAT <95%
- OLIGURIA
- MENTAL STATUS CHANGES
- DYSPNEA

} **Call Rapid Response Team!**

Move fasting during "golden hour" to save lives!

Early recognition and implementation of therapy reduces morbidity and mortality associated with sepsis (1C)

- Each hour delay in therapy ~ 8% increase in risk of death from sepsis!
- Early antimicrobial therapy within the first hour of diagnosis ~ 80% survival to hospital discharge.



True even for OB: Bauer et al reviewed 82 maternal sepsis cases

*****mortality rate 8.3% if antibiotics given within 1 hour versus 20% if > 1 hour**

Kumar A Crit Care Med 2006

Bauer M Anesth Analg 2019

Move fasting during "golden hour" to save lives!

Rapid response teams specifically trained in sepsis decrease in-hospital mortality by **2-3%**

Kumar A Crit Care Med 2006

SSC: hour 1 Bundle

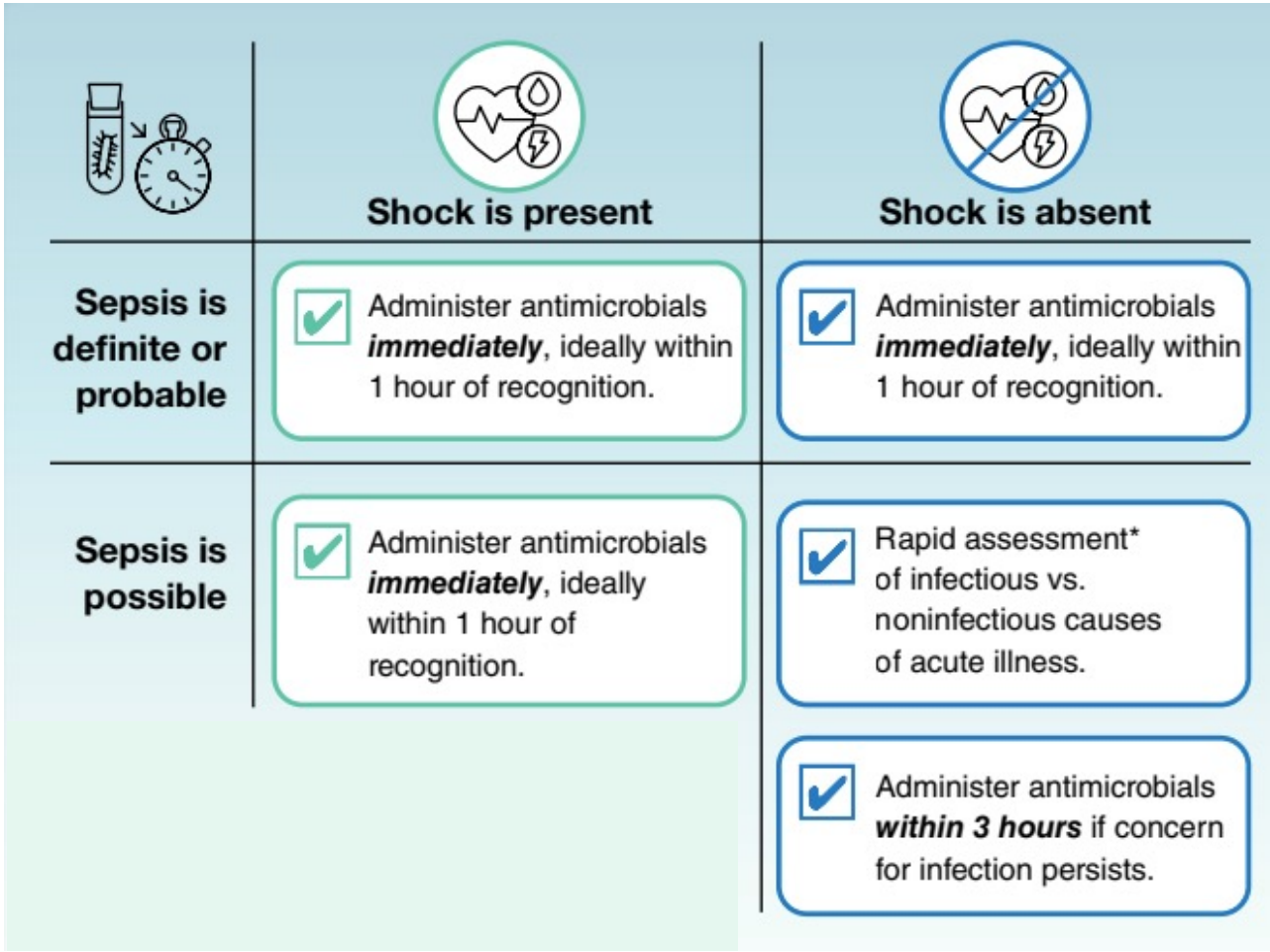
- **Administer broad spectrum antibiotics (strong/moderate)**
- **Rapidly administer 30 cc/kg crystalloids for hypotension, or lactate ≥ 4 mmol/L (strong, low)**
- **Obtain blood cultures prior to administration of antibiotics (best practice)**
- Measure lactate level. Re-measure if initial lactate is > 2 mmol/L (weak/low)
- Apply vasopressors if hypotensive during or after fluid resuscitation to maintain MAP = 65 mmHg (strong, moderate)

Levy MM. SCCM and Eur Soc of Int med 2006

DO NOT DELAY ANTIBIOTIC ADMINISTRATION TO COLLECT CULTURES!

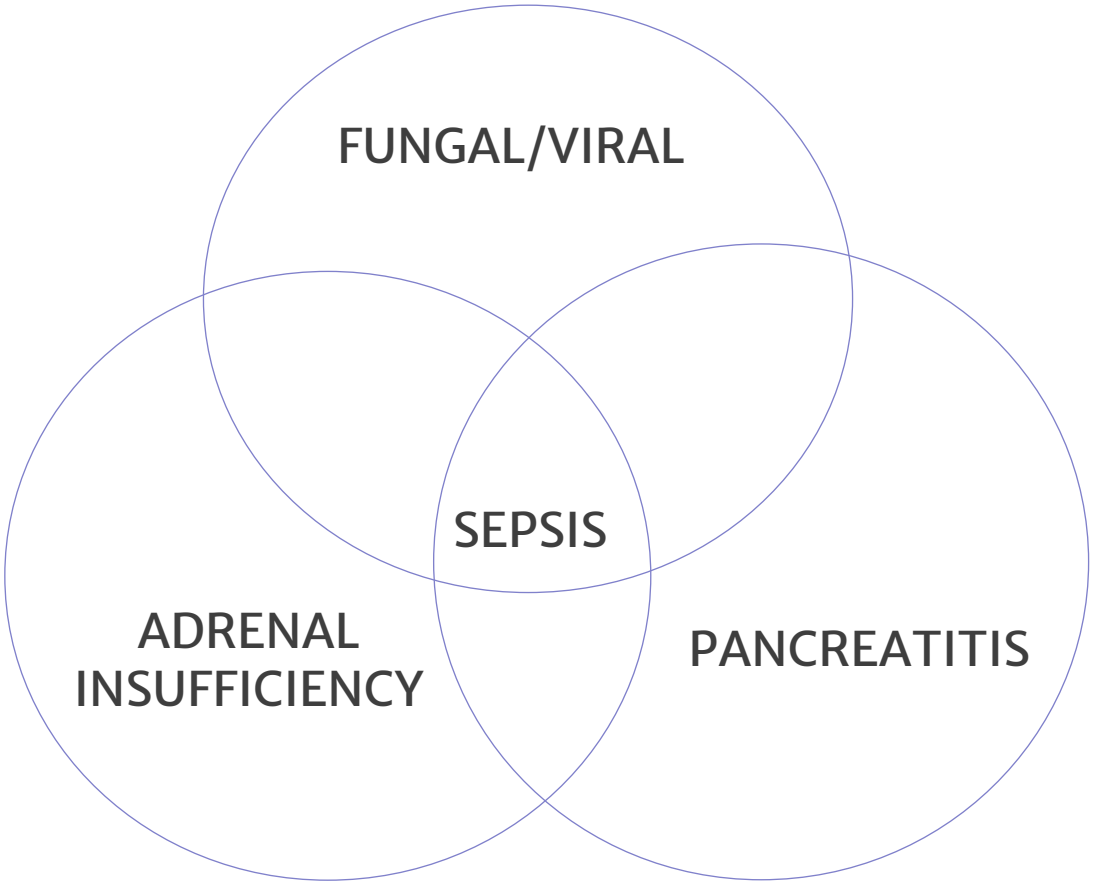
Pearl #4

Antimicrobial timing: 2021 update



Critical Care Medicine: October 4, 2021

What are we missing?



Secondary Survey

AFTER STABILIZATION: DETAILED HISTORY AND PHYSICAL

- PRESENTING SYMPTOMS
- CURRENT OR PRIOR INFECTIONS
- INTERVENTIONS OR PROCEDURES
- CURRENT MEDS
- MEDICATION ALLERGIES
- PHYSICAL

Bedside Evaluation for Organ Dysfunction – Secondary Survey

TABLE 2
Organ damage caused by sepsis

System	Description of damage
Central nervous system	Altered mental status
Cardiovascular system	Hypotension from vasodilation and third-spacing; myocardial dysfunction
Pulmonary system	ARDS
Gastrointestinal system	Paralytic ileus
Hepatic system	Hepatic failure or abnormal transaminases
Urinary system	Oliguria or acute kidney injury
Hematologic system	Thrombocytopenia or disseminated intravascular coagulopathy
Endocrine system	Adrenal dysfunction and increased insulin resistance

ARDS, acute respiratory distress syndrome.

Society for Maternal-Fetal Medicine. Maternal sepsis. Am J Obstet Gynecol 2023.

General: lethargy, mental status changes

Skin: cool skin, cyanosis, discoloration, pallor or rash, jaundice, bleeding from IV sites

CV: delayed cap refill, JVD, arrythmia, murmurs

Resp: Dyspnea, use of accessory muscles, rales or rhonchi, decreased breath sounds

Abd: TTP, rebound/guarding, distention, absent or diminished bowel sounds, wound erythma

Back: CVAT

Reproductive: breast engorgement, leaking of fluid, abnormal vaginal discharge, preterm contractions, fetal tachycardia

Shields Obstet Gynecol 2021
SMFM Consult #67 2023

Bedside Evaluation for Organ Dysfunction – Secondary Survey

CBC with differential

Leukocytosis/left shift, leukopenia, neutropenia

Lactate

Marker of decreased cellular perfusion

- 2 → increased risk of ICU admission
- 4 -> increased risk of death

Blood cultures

50% positive if before antibiotics

Draw from 2 sites

Urinalysis and Culture
Most common etiology in pregnancy
Straight cath

Comprehensive Metabolic Panel
Elevated liver enzymes, hyperbilirubinemia, Elevated creatinine, hyperglycemia

Coagulation studies
Elevated INR, PTT
Low fibrinogen

Arterial blood gas
Acidemia, hypercarbia, hypoxia

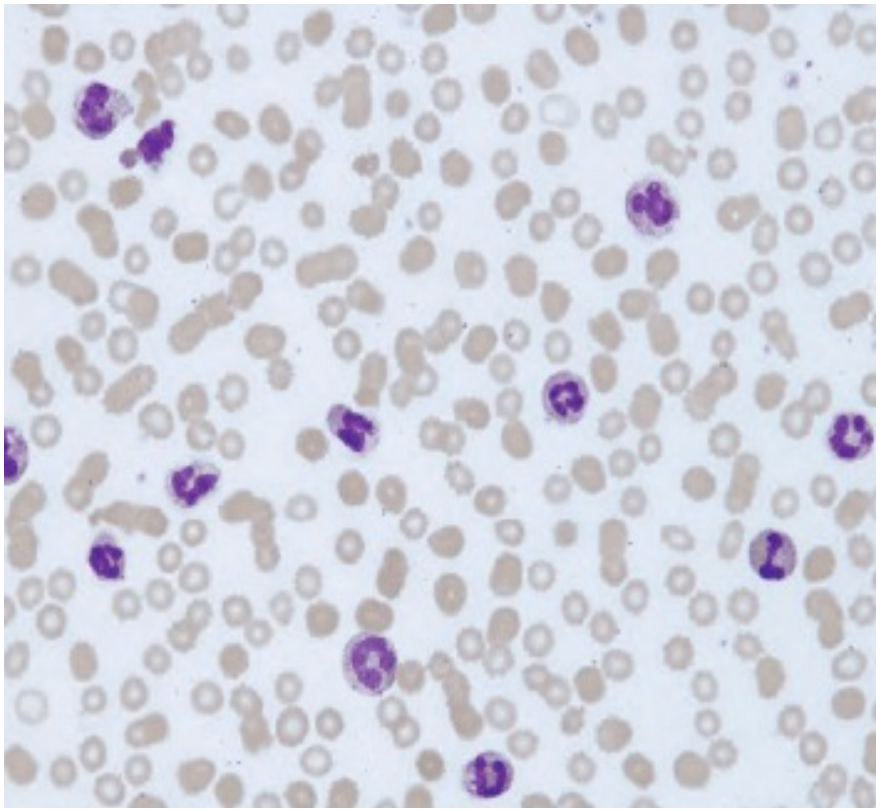
Other cultures
Sputum, wound, surgical site, body fluids
Most result in 2-3 d, AF/CSF may take 1-2 wks

Rapid molecular testing
Viral pathogens - presenting with respiratory complaints, flu-like symptoms, rash, hepatitis

Peripheral blood smear
Look for signs of infection

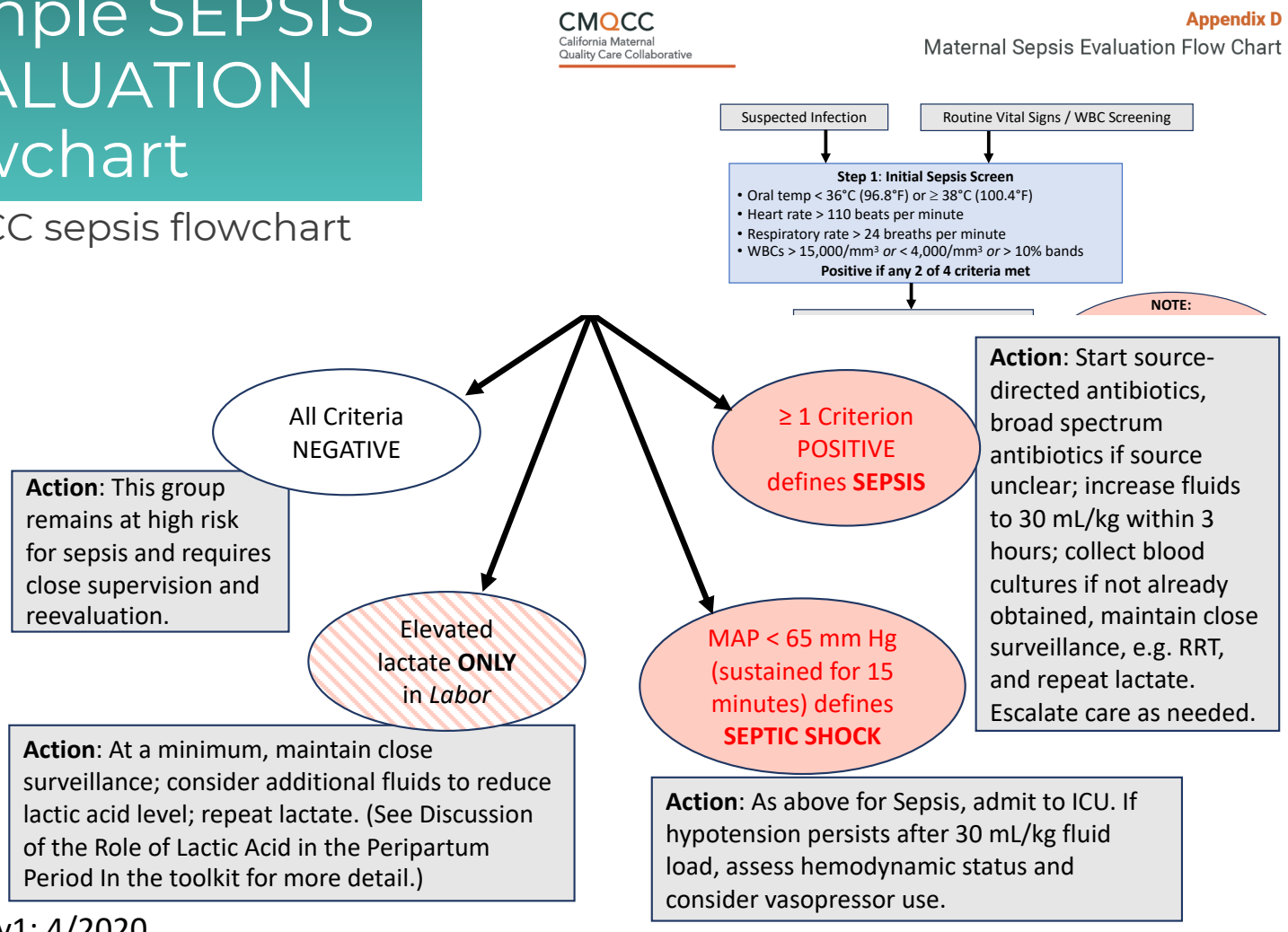
Peripheral smear

- Toxic granulation
- Dohle bodies
- Cytoplasmic vacuoles
- Intracellular bacteria
- Neutropenia (rarely)



Sample SEPSIS EVALUATION flowchart

CMQCC sepsis flowchart 2020



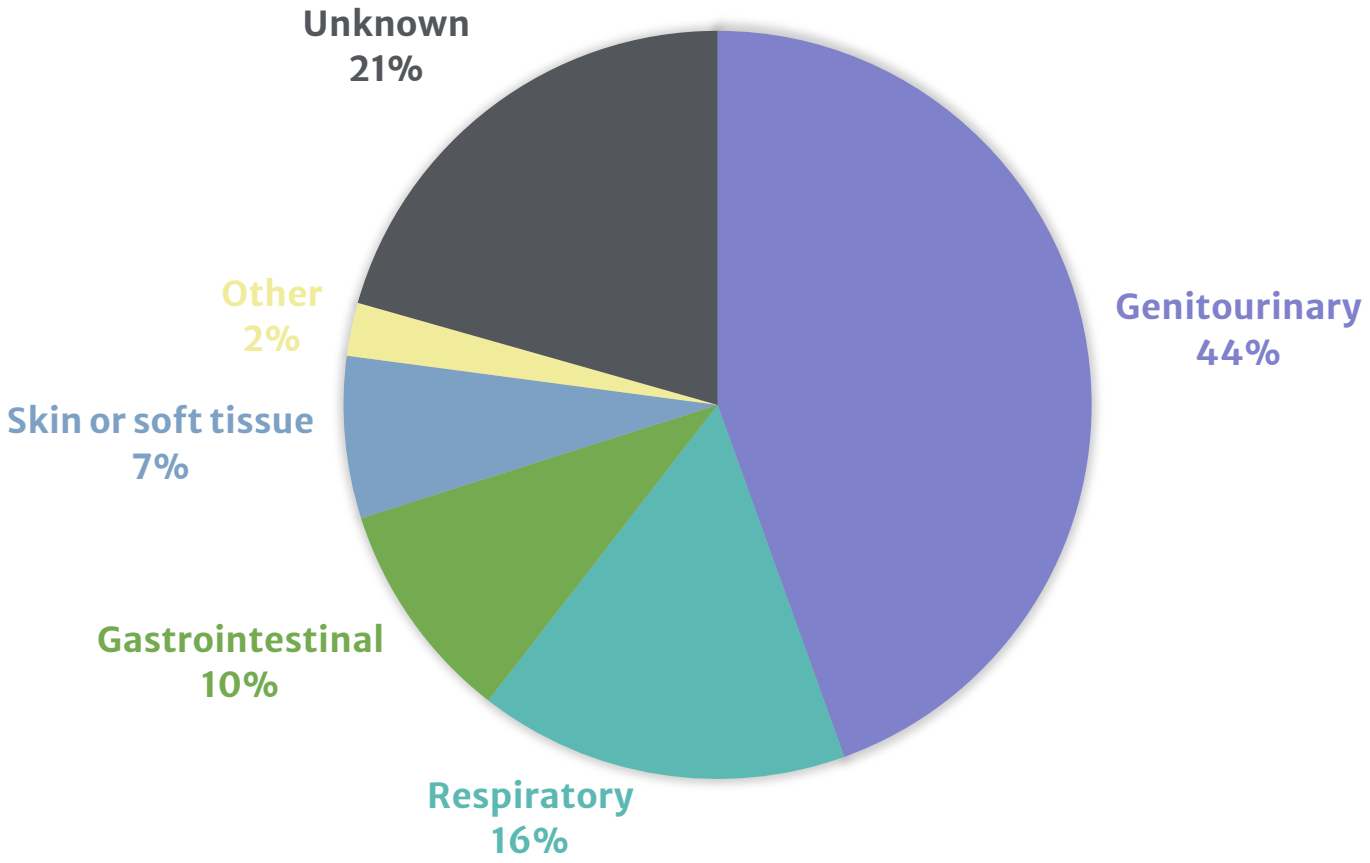
Imaging studies

Guided by bedside assessment

- Chest radiograph
- CT of chest, abdomen and pelvis
- Ultrasound

Pearl #5: "Wizard of Oz"

Most frequently encountered concurrent diagnoses in maternal sepsis in the United States from 1998 to 2008



Hensley MK JAMA 2019

What is the most common organism isolated from maternal sepsis?

A. E. coli
B. Group B streptococcus
C. Staph aureus
D. Group A streptococcus

Organisms isolated from each stage of pregnancy

Table 1. Organisms isolated at each stage of pregnancy

Organism	Antenatal	Intrapartum	Postnatal	All isolates
Escherichia coli	26	22	55	103
Group B *Streptococcus*	2	43	12	57
Anaerobes	4	8	11	23
Staphylococcus aureus	4	5	12	21
Enterococcus faecalis	2	5	6	13
Group A *Streptococcus*	0	2	10	12
Streptococcus milleri	1	4	4	9
Klebsiella pneumonia	1	2	2	5
Proteus mirabilis	0	3	2	5
Haemophilus influenzae	3	1	0	4
Streptococcus pneumoniae	1	0	3	4
Morganella morganii	0	0	3	3
Group C *Streptococcus*	0	1	2	3
Enterobacter species	1	0	2	3
Group G *Streptococcus*	0	0	2	2
Listeria monocytogenes	1	1	0	2
Moraxella species	0	0	2	2
Staphylococcus saprophyticus	0	1	1	2
Acinetobacter lwoffii	1	0	1	2
Streptococcus gallolyticus	0	1	0	1
Total	47	99	130	276

Antenatal

- *E. coli*

Intrapartum

- *E. Coli*
- *Group B streptococcus*

Postpartum

- *E. coli*
- *Group B streptococcus*
- *Staph aureus*
- *Anaerobes*
- *Group A streptococcus*

Knowles SJ. BJOG 2014

REVIEW ARTICLE FREE PREVIEW

Complications of Unsafe and Self-Managed Abortion

Lisa H. Harris, M.D., Ph.D., and Daniel Grossman, M.D.

- Uterine infection associated with spontaneous or induced abortion
- Symptoms: **fever, purulent discharge, boggy uterus**
- Common organisms: E. coli, streptococcus, staphylococcus, Clostridium welchii, B. Fragilis, Coliform bacillus
- Treatment: broad-spectrum antibiotics and uterine evacuation

Remember…GAS kills quickly!

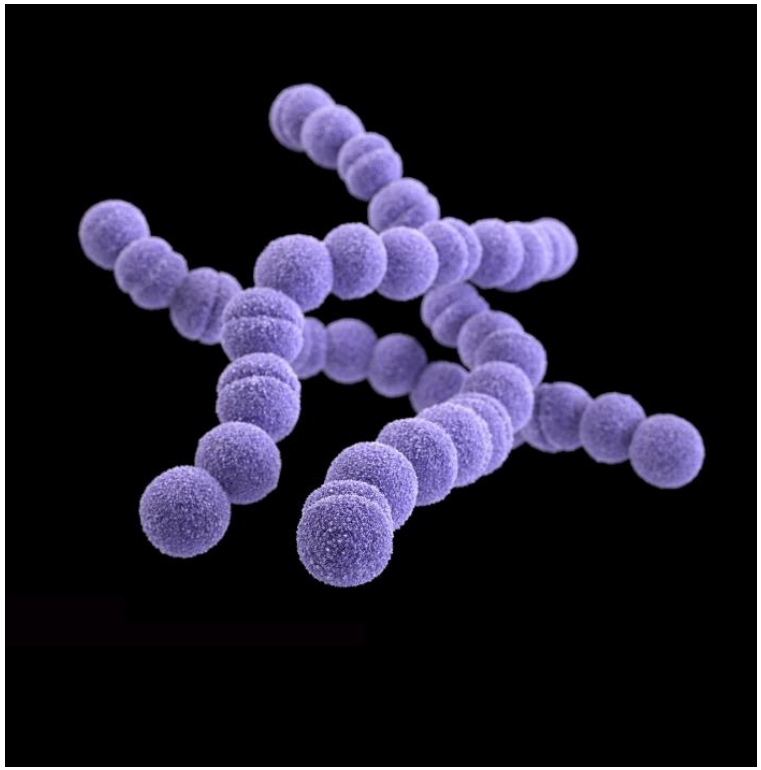


Image: CDC

Group A Streptococcus

GAS (*Streptococcus pyogenes*) is not a part of the normal microbiome of the urogenital tract

Present in only 0.03% of individuals

- Routine screening not useful

Most common postpartum

Rapid clinical deterioration

- In 75% < 9 hours between first signs of sepsis and septic shock
- In 50%, <2 hours

Responsible for >50% of maternal deaths worldwide!

Acosta CD et al PLoS Med 2014
Anteby EY. Infect Dis Obstet Gynecol 1999

Pearl #6: Choose antimicrobials tailored to the most likely diagnosis

Antimicrobial Therapy

Administer broad-spectrum antibiotic therapy after obtaining blood cultures, within the 1st hour

Choice of antibiotic(s) should be driven by

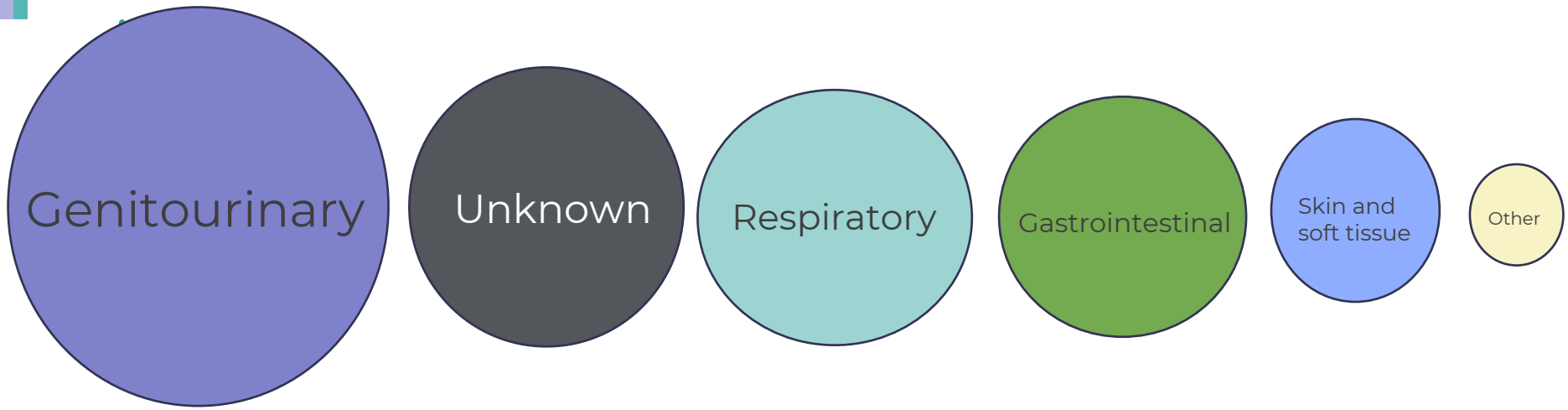
- likely source
- serious allergies
- recent treatment of infection
- surgical history
- local antibiogram

Dellinger RP. Surviving Sepsis Campaign. CCM Journal 2013

What is the recommended antibiotic regimen for maternal sepsis due to group A streptococcus?

A. Ampicillin + gentamicin
B. Carabapenem
C. Penicillin G + clindamycin
D. Vancomycin + piperacillin-tazobactam

Choosing Antimicrobials



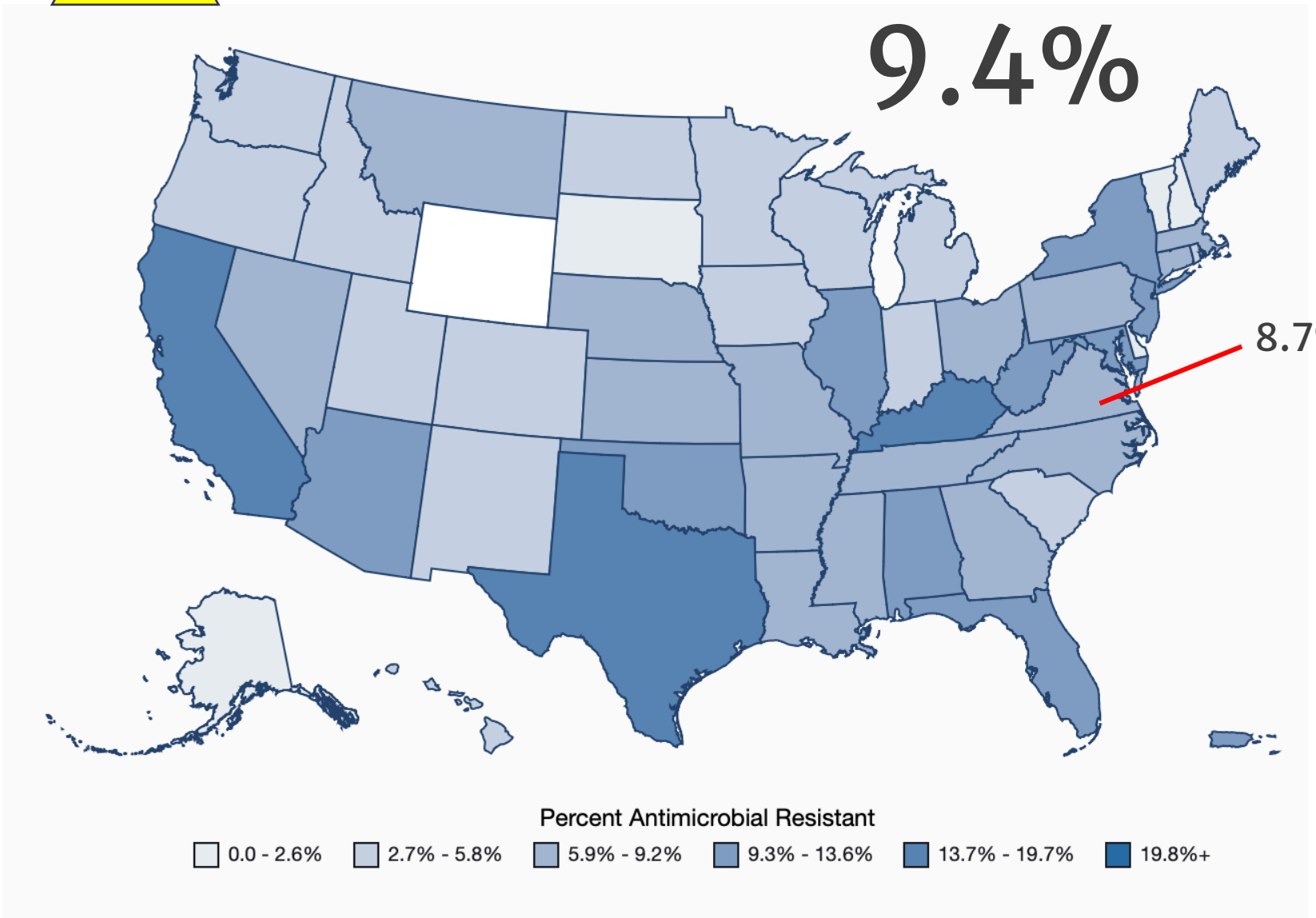
65%	16%	10%	7%
Ampicillin + Gentamicin + Clindamycin (or Metronidazole)	Cephalosporin (3rd/4th Gen) + Azithromycin	Cephalosporin ($3^{rd}/4^{th}$ Gen) + Metronidazole	Cephalosporin ($3^{rd}/4^{th}$ Gen) + Metronidazole If necrotizing: Vancomycin + Pipericilllin/ tazobactam

Hensley MK JAMA 2019

Genitourinary Source

	Urosepsis	Intraamniotic Infection/Endomyometritis
Predominant Organism (s)	E. Coli Others: Enterobacteriaceae Klebsiella	E. Coli Others: Group A and B strep, anaerobes
1st line	Ampillicin + Gentamicin	Ampicillin + Gentamicin + Clindamycin (or Metronidazole)
Alternative	Carbapenem Pipericillin-tazobactam	Cefotaxime or Cetriaxone + Metronidazole
Pearls	ESBL - Carbapenem MRSA – Vancomycin or teicoplanin	Group A Strep (confirmed) – Penicillin G + Clindamycin

Multidrug resistant *E. coli*



CDC 2021

EXAMPLE

Antibiotic Regimens by Source of Infection

(excerpted from CMQCC Maternal Sepsis Toolkit)

ACOG
The American College of Obstetricians and Gynecologists
District II

SOURCE INFECTION	RECOMMENDED ANTIBIOTICS
Abdominal infections	Ceftriaxone, cefotaxime, ceftazidime, or cefepime plus metronidazole;
	Complicated case may require monotherapy with a carbapenem or piperacillin-tazobactam
Chorioamnionitis	Ampicillin plus gentamicin. Add anaerobic coverage with clindamycin or metronidazole if cesarean delivery required
Community-acquired pneumonia	Cefotaxime, ceftriaxone, ertapenem, or ampicillin plus azithromycin, clarithromycin, or erythromicin
Endomyometritis	Ampicillin, gentamicin, and metronidazole (or clindamycin); **Alternatively, may use cefotaxime or ceftriaxone plus metronidazole.**
Hospital-acquired pneumonia	Low risk patients: piperacillin-tazobactam, meropenem, imipenem, or cefepime
	High mortality risk patients: double coverage for pseudomonas (beta lactam plus an aminoglycoside or a quinolone) and MRSA coverage with vancomycin or linezolid
Skin and soft tissues (necrotizing)	Vancomycin plus piperacillin-tazobactam If Streptococcus Group A or Clostridium perfringens are present, use penicillin G plus clindamycin
Urinary tract infections	Gentamycin with ampicillin; **Alternatively, may use monotherapy with a carbapenem or piperacillin-tazobactam**

→Consult your hospital antibiogram

ACOG

Source: SMFM, 2019; Gibbs et al., 2020, CMQCC Maternal Sepsis Toolkit

De-escalation

- Reassess antimicrobial regimen daily
  - prevent the development of resistance
  - reduce toxicity
  - reduce costs
- De-escalation is anticipated in 3-5 days, when identification and susceptibility patterns available

Dellinger RP. Surviving Sepsis Campaign. CCM Journal 2013

Therapeutic Drug Monitoring

Clinical benefits have only been demonstrated for aminoglycosides

Monitor drug levels in patients

- septic shock
- liver or kidney impairment
- large Vd

Dellinger RP. Surviving Sepsis Campaign. CCM Journal 2013

Antimicrobial Therapy: Course Duration

- Course typically lasts 7-10 days
  - Some exceptions: source control issues, immunosuppressive states
- Antibiotic stewardship program/ID specialist
  - Up to 50% of patients with sepsis, septic shock have negative blood cultures

pearl #7

Fluid resuscitation should be initiated rapidly for patients with a blood lactate level greater than 4 mmol/L or mean arterial pressure < 65 mm Hg

What is the recommended fluid therapy in maternal sepsis?

A. Colloids
B. Isotonic crystalloids
C. Hydroxyethyl starches
D. Hypotonic crystalloids

Fluid Therapy

- Crystalloids initial fluid of choice in the resuscitation of sepsis and septic shock (grade 1B)
- Albumin may be used when patients require substantial amounts of crystalloids (grade 2C)
- Do not use hydroxyethyl starches (grade 1B)

Fluid Therapy – 2021 SSC Guidelines

For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg (ideal body weight) of IV crystalloid fluid should be given in the first 3 hours (downgraded from strong to week LOE)

- **In 70 kg patient → 2.1 liters in 3 hours**

Is this the right amount for pregnant people?

Fluid Therapy – Follow SSC guidelines in pregnancy?

Aggressive fluid administration
↓
third spacing
↓
left ventricular diastolic dysfunction from ventricular wall edema
↓
pulmonary edema, cerebral edema, bowel edema with increased intraabdominal pressure
↓
higher mortality

- Only ≅ 50% of hypotensive septic patients are fluid responders
- Increased risk for ARDS from urosepsis in pregnancy

SMFM RECOMMENDATION: 1-2 L in first 3 hours

Shields AD. Maternal Sepsis. SMFM 2023
NHLBI. NEJM 2023

Fluid Therapy Responsiveness

Continue fluid challenge as long as there is hemodynamic improvement

- Monitor improvement through dynamic measures (pulse pressure variation, passive leg raise, echo)
  - **Pulse pressure**

    arterial line waveform in patients in sinus rhythm on controlled mechanical ventilation
  - **Passive leg raise**

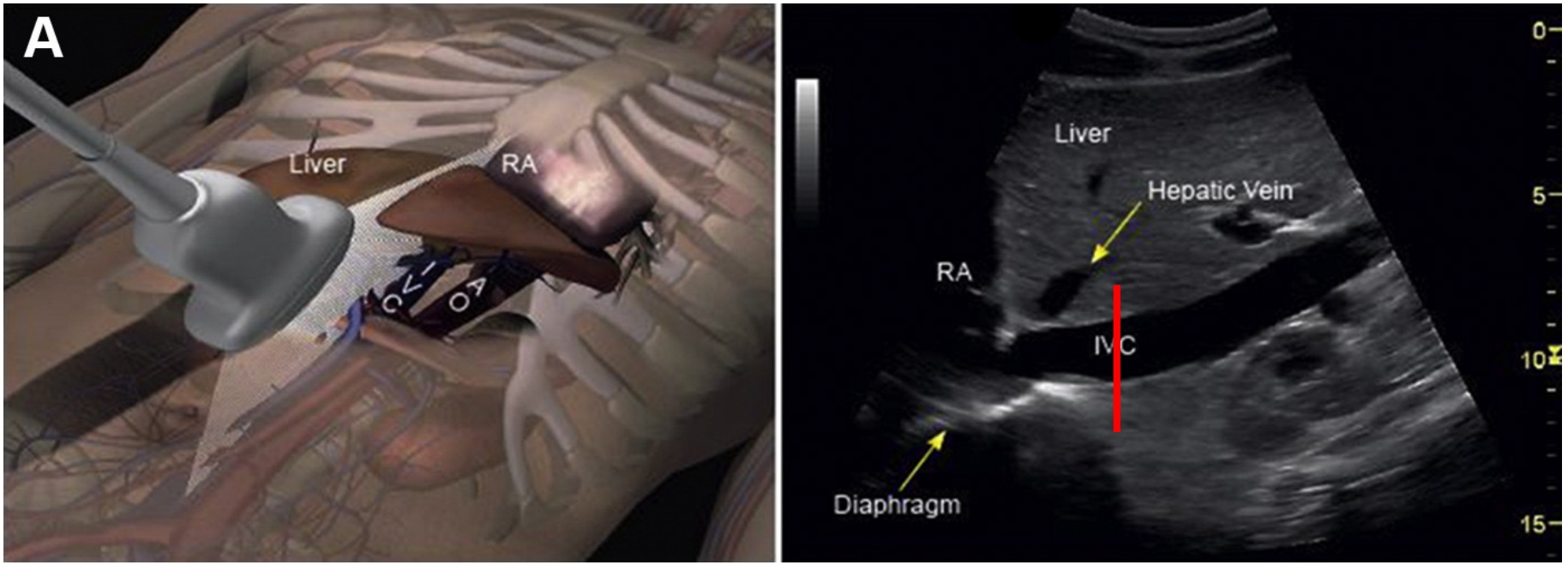
    spontaneously breathing or not in sinus rhythm

    raise leg 30-45° for 2-3 minutes → autotransfusion 300 cc of blood from legs to chest → increase in cardiac output
  - **POCUS: IVC diameter**

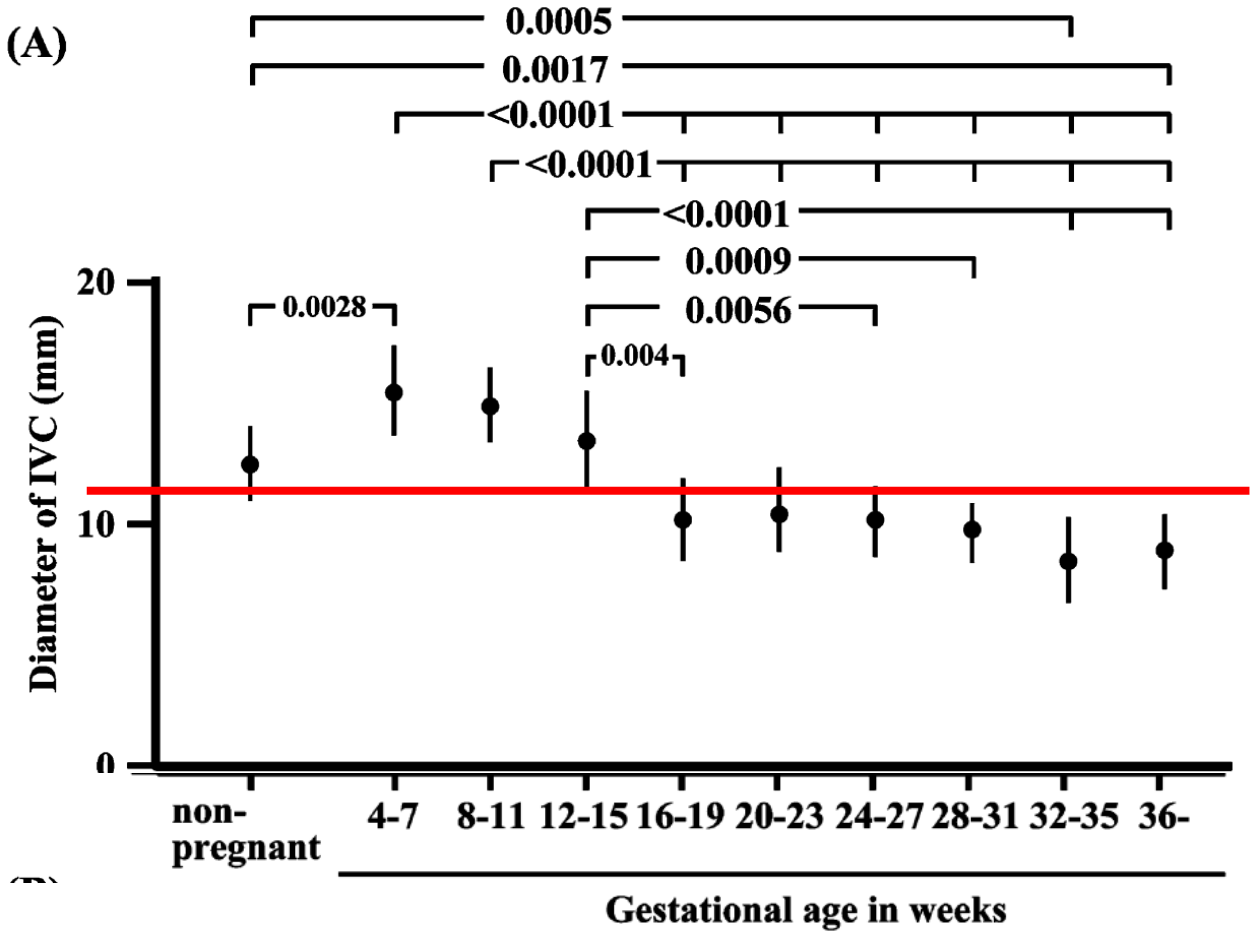
    < 1.5 cm with significant variation in caliber during resp cycle → **fluid responder**

    > 2 to 2.5 cm with minimal variability with the respiratory cycle → **vasopressors**

Fluid Therapy Responsiveness with POCU



IVC Diameter Measurements in Pregnancy



Ryo. J Perinat Med 2004

pearl #8

Escalation of care is critical to survival.

Rapid escalation of care

If septic shock suspected:

- higher risk of maternal death (50%) and multiorgan failure

Early consultation with ID and critical care and prompt transfer of care

Vasopressor support

Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C)

- Restore effective tissue perfusion
- Normalize cellular metabolism

Barton JR Obstet Gyneol 2012

What is the first-line vasopressor for treatment of maternal septic shock?

A. Dobutamine
B. Dopamine
C. Epinephrine
D. Norepinephrine

Vasopressor support: First Line Agent

Norepinephrine

- Increases MAP by significant alpha-1 receptor-mediated vasoconstriction
- Improves hemodynamics and oxygen delivery
  - 93% compared with 31% with dopamine[1]
- Reduces lactate levels and is associated with improved urine output[2]
- Can reduce uterine blood flow

[1]Martin C. Chest 1993
[2]DeBacker Crit Care Med 2003

Vasopressor support: Alternatives

If BP inadequate with low to moderate norepinephrine add:

*Vasopressin 0.03 units/minute

- added to norepinephrine with intent of either raising MAP or decreasing norepinephrine dosage

*Dobutamine for sepsis-induced cardiomyopathy

*Avoid dopamine

- no longer used for renal-enhancing effect

Critical Care Medicine: October 4, 2021

Corticosteroids –SCCM Update 2024

- ✓ Septic shock
- ✓ ARDS
- ✓ Severe bacterial community-acquired pneumonia

Avoid:

High dose/short duration corticosteroids (> 400 mg/d hydrocortisone equivalent for less than 3 d) for adult patients with septic shock

Chaudhuri, D. Critical Care Medicine 2024

VTE prophylaxis

- Sepsis and pregnancy are both independent risk factors
- Incidence: 37.2%!
- Prevent with unfractionated heparin or low molecular weight heparin, and early ambulation when feasible

Treat Hyperglycemia

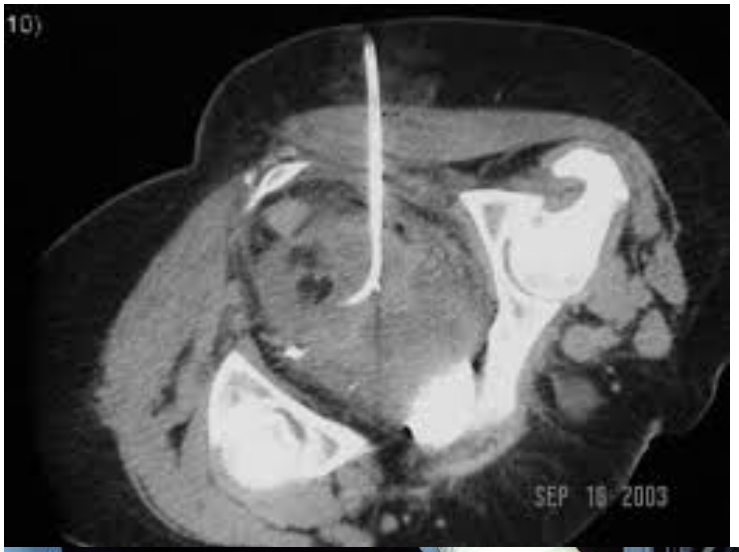
- Initial insulin therapy for a glucose value >180 mg/dL
  - increased mortality in critically ill sepsis patients
  - Pregnancy-specific data are lacking

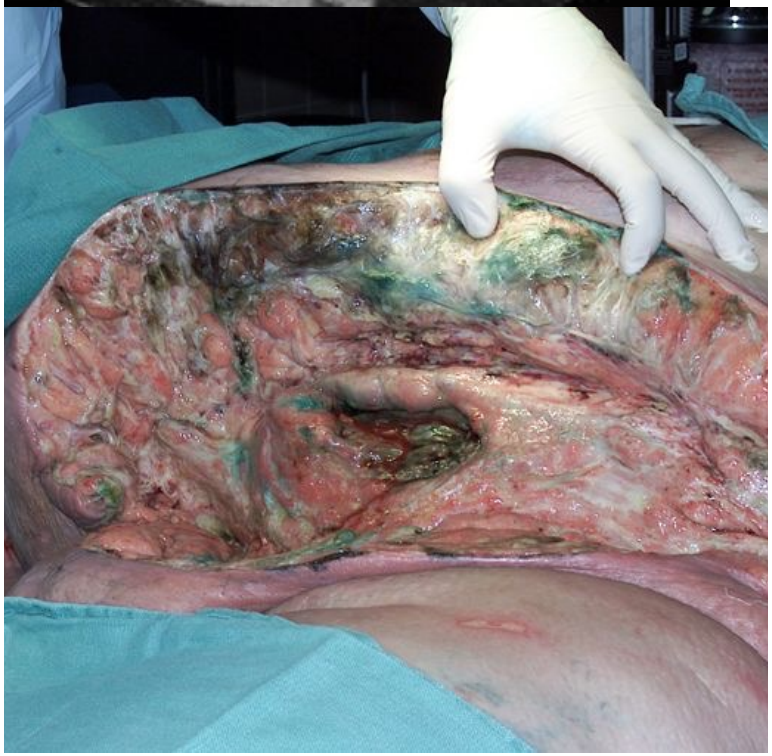
pearl #9

Once patient is stabilized, get to the source of the problem!

Source Control

- Rapid identification of a focus of infection amenable to source control measures
- Optimizing medications that concentrate in targeted anatomical areas (e.g., kidneys, pelvic abscess)
- Minimal target **6-12 hours** after diagnosis of sepsis

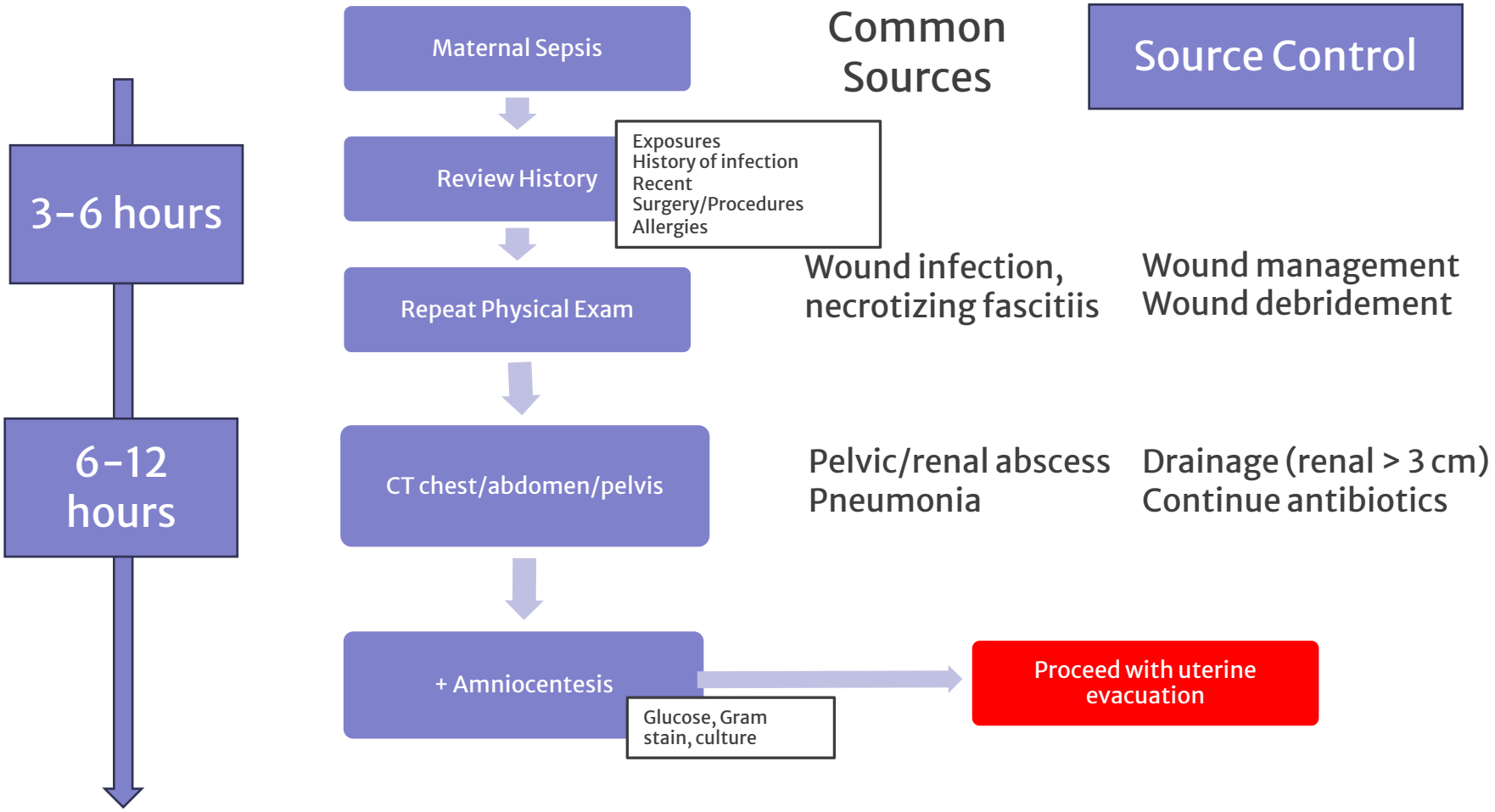




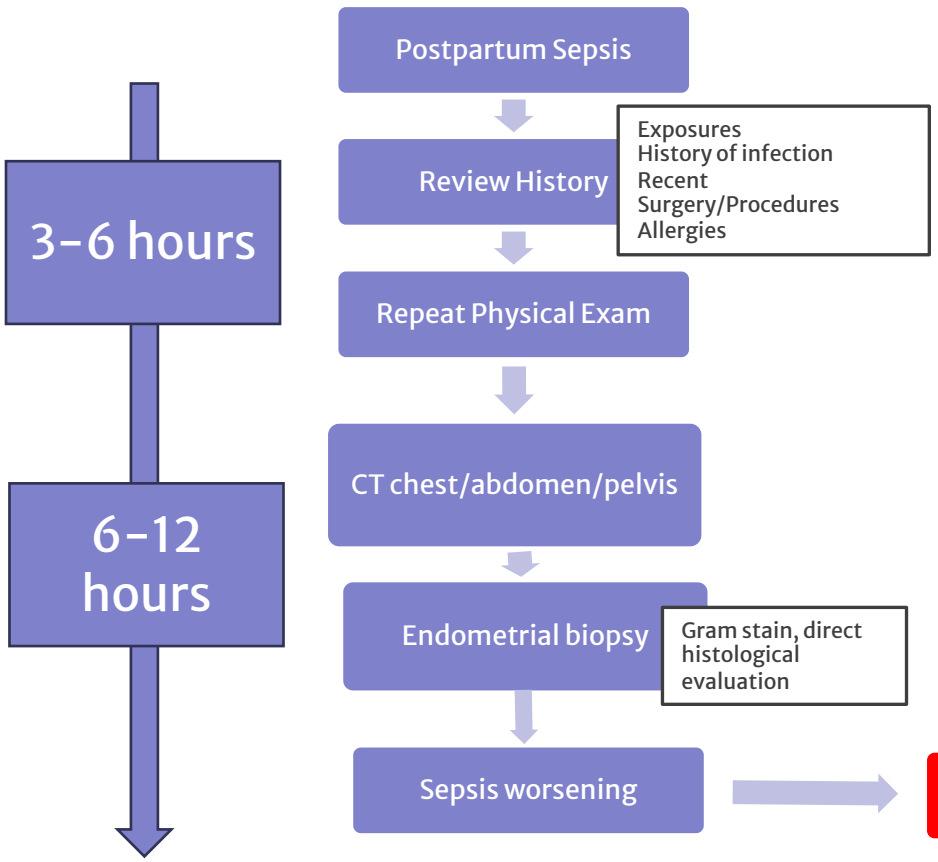
Source control – OB/GYN

Knight M Saving Lives, Improving Mother's Care 2009–2012

Source Control: When to evacuate uterus?



Source Control: When to do a hysterectomy?



Common Sources	Source Control
Wound infection, necrotizing fascitiis	Wound management Wound debridement
Pelvic/renal abscess Pneumonia	Drainage (renal > 3 cm) Continue antibiotics
Endomyometritis	Continue antibiotics

pearl #10

Anticipate and prevent adverse pregnancy outcomes.

Pregnancy Outcomes with Sepsis

Increased rates of

- Preterm labor
  - Preterm delivery (OR 2.7)
- Perinatal morbidity and mortality
  - IUFD/NND 10-12%, higher w/ GU origin
- Operative delivery
- Cesarean delivery (OR 2.6)
  - Up to 80% in women with septic shock

Kankuri E. Acta Obstet Gynecol Scan 2003
Synder CC J Mat Fet Neonat Med 2013

Antepartum Considerations

Preterm labor

- use magnesium sulfate if tocolysis desired to administer corticosteroids and source is known
- B-agonists may increase risk of ARDS

Delivery may be considered to improve maternal status

- Consider gestational age, maternal status, fetal status
- Stabilize mother before proceeding with emergent delivery as many times fetal status will improve

Barton JR. Obstet Gynecol 2012

Delivery Considerations

For most cases, mode of delivery is based upon obstetric indication

- If vaginal delivery planned → assist second stage
- Be prepared to perform E-CS at bedside
- In the event of cardiopulmonary arrest → Resuscitative cesarean delivery at location, no anesthesia required, by 4 minutes from arrest

Culture and administer antimicrobial prophylaxis of neonate if GAS is suspected or confirmed

Barton JR. Obstet Gynecol 2012

Recovery Considerations

If patient recovers from sepsis and remains pregnant:

- Consider antepartum fetal testing and serial growth assessment

If discharge home, especially if admitted to ICU, recommend physical, emotional, and cognitive support

Blauvelt CA. JAMA Netw Open 2021

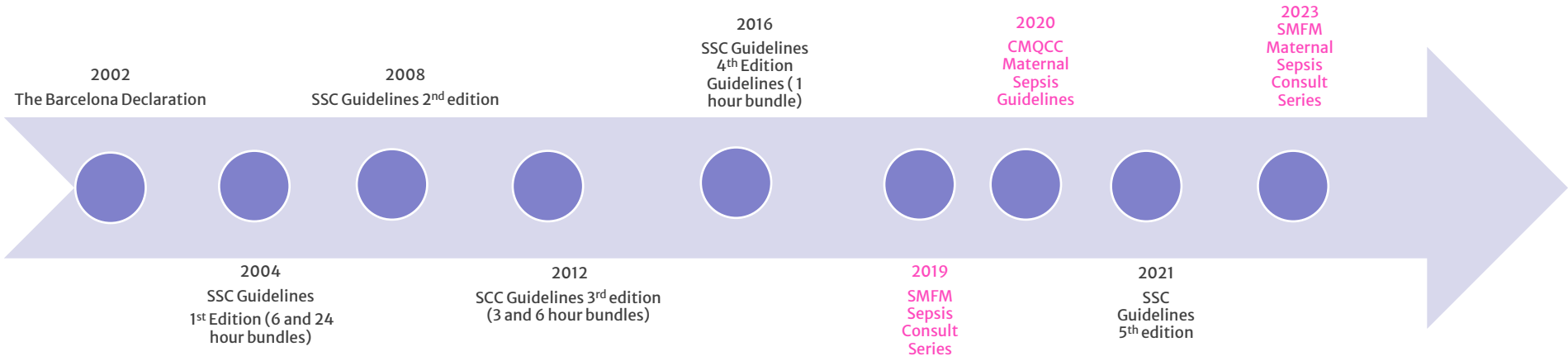
pearl #11 (bonus pearl!)

An ounce of prevention is worth a (pound) of sepsis cure!

Quality Improvement In The Management of Maternal Sepsis

UCONN HEALTH

Surviving Sepsis Timeline



Case Review #1

G1P0 at 36w2d admitted with PPROM who subsequently developed sepsis secondary to pyelonephritis

<u>Opportunities for improvement</u>

- Delay in diagnosis
- Delay in treatment
- Lactate repeated >6 hours
- Lack of awareness of vital sign changes
- Inadequate treatment

Society for Maternal•Fetal Medicine

Maternal Sepsis Challenges And Opportunities For QI

- Recognition
  - Pregnancy specific early warning systems
  - Provider and nursing awareness and knowledge
  - Patient education
- Protocolized maternal care
  - Maternal specific sepsis bundles
    - Fluid administration
    - Lactate
    - Antibiotics
    - Infectious sources

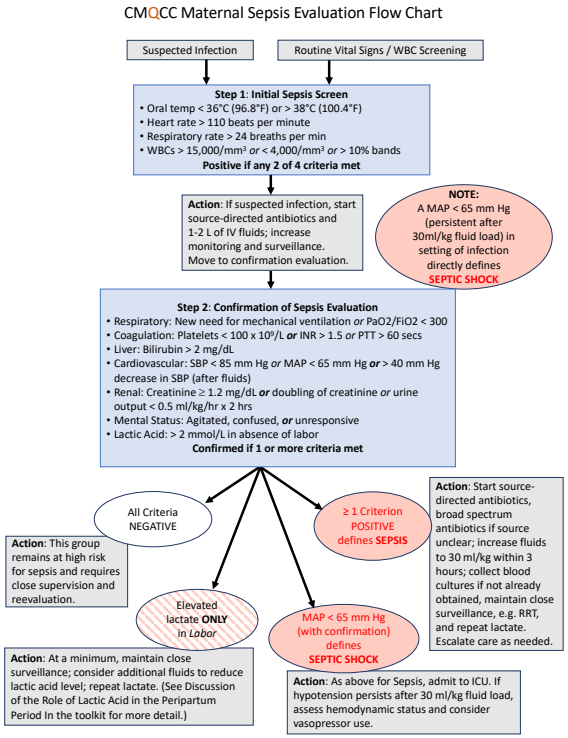
Society for Maternal•Fetal Medicine

Maternal Sepsis Challenges And Opportunities For QI

- Multidisciplinary care
  - Utilization of RRT
  - Involvement of obstetrics team
  - ICU transfer
  - Communication
- Equitable care
  - Black, Indigenous, and Hispanic people are disproportionally affected

Society for Maternal•Fetal Medicine

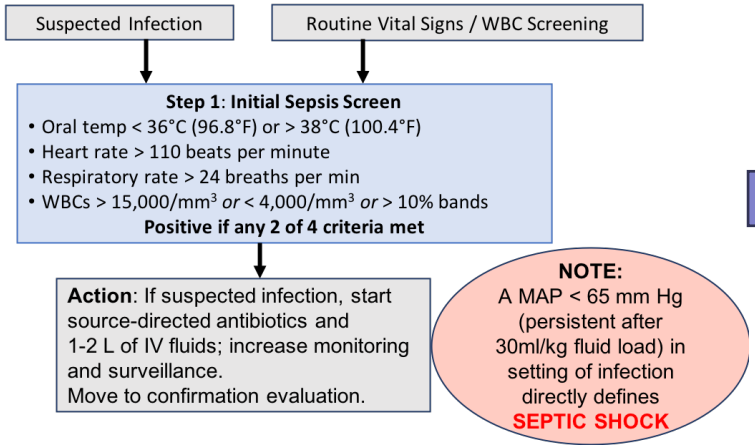
Maternal Sepsis Care Protocol at UCONN

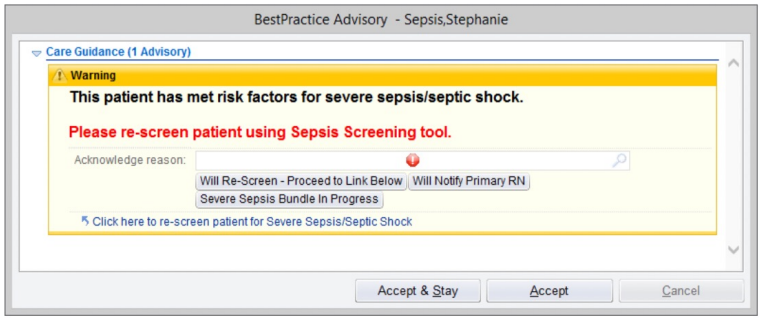


Epic

Society for Maternal•Fetal Medicine

Step 1 - Screening

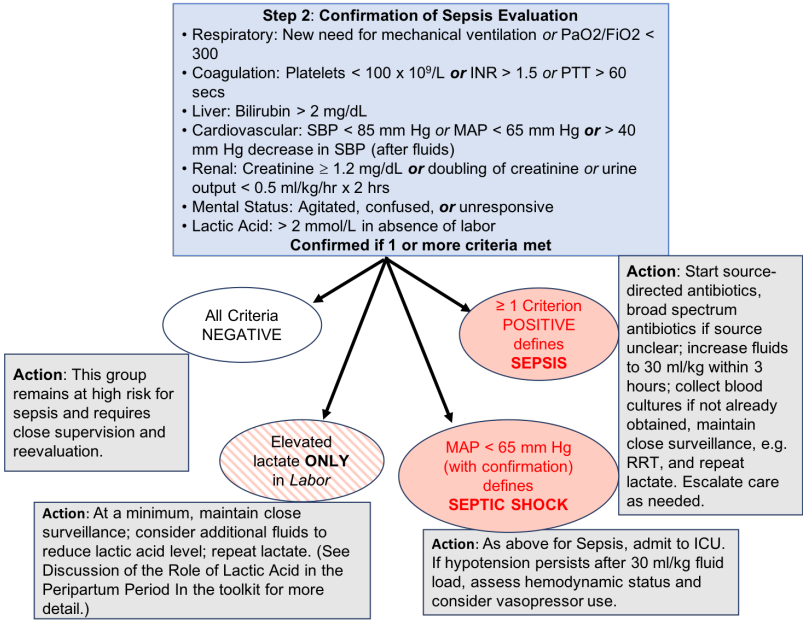


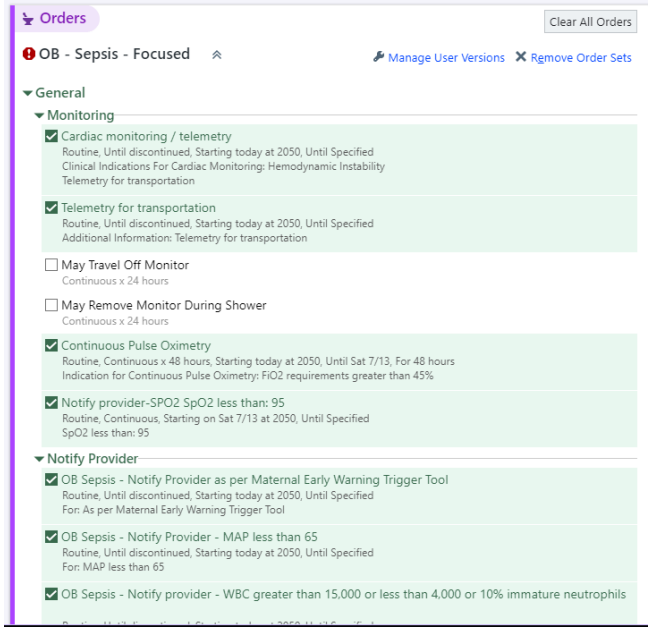


Sepsis BPA on Epic

Society for Maternal-Fetal Medicine

Step 2 – Diagnosing and Treating





Epic Order Set

Society for Maternal•Fetal Medicine

Barriers To Quality Care

Physicians

- Education and training
- Floor acuity
- Inexperience with maternal sepsis
- Treating two patients (maternal and fetal)

Staff

- Alert fatigue
- Education and training
- Non-protocolized care
- Potential for rapid deterioration
- Lack of familiarity with maternal sepsis
- Delays in obtaining medications, fluids, orders, labs

Pharmacy

- Determining if antibiotics are compatible with pregnancy or lactation
- Approval for antibiotics

Patients

- Not aware of symptoms
- Don't feel heard
- Inequitable care
- Access to hospital with appropriate level of care

Society for Maternal·Fetal Medicine

How can we help?

**Hear Her! Foster trust and mutual respect with your patients.

https://www.cdc.gov/hearher/index.html

**Implement care bundle to facilitate early recognition.

https://www.cmqcc.org/resources-toolkits/toolkits/improving-diagnosis-and-treatment-maternal-sepsis-errata-712022

*Involve consultants early (e.g., ID and critical care) and advocate for interdisciplinary care.

Questions?

UCONN HEALTH

References

Acosta CD, Kurinczuk JJ, Lucas DN, Tuffnell DJ, Sellers S, et al. (2014) Severe Maternal Sepsis in the UK, 2011–2012: A National Case-Control Study. PLoS Med 11(7): e1001672. doi:10.1371/journal.pmed.1001672

Acosta CD, Knight M, Lee HC, Kurinczuk JJ, Gould JB, Lyndon A. The Continuu of Maternal Sepsis Severity: Incidence and risk Factors in a Population-Based Cohort Study. 2013;8(7):1-8.

Albright CM, Ali TN, Vrishali L, Rouse DJ, and Anderson BL. Lactic Acid Measurement to Identify Risk of Morbidity from Sepsis in Pregnancy. Am J Perinat 2014; 210(1). DOI:10.1055/s-0034-1395477.

Anteby EY, Yagel S, Hanoch J, Shapiro M, Moses AE. Puerperal and intrapartum group A streptococcal infection. Infect Dis Obstet Gynecol 1999;7:276-82.

Barton JR xxx Obstet Gynecol 2012:120;3:689-703

Bauer ME, Lorenz RP, Bauer ST, Rao K, and Anderson FW. Maternal Death due to sepsis in the state of Michigan, 1999-2006. Obstet Gynecol 2015;126:747–52.

References

Chaudhuri, Dipayan MD, MSc, FRCPC[1,2]; Nei, Andrea M. PharmD, FCCM[3]; Rochwerg, Bram MD, MSc, FRCPC, FCCM[1,2]; Balk, Robert A MD, MCCM[4]; Asehnoune, Karim MD[5]; Cadena, Rhonda MD, FNCS, FCCM[6]; Carcillo, Joseph A. MD[7]; Correa, Ricardo MD[8]; Drover, Katherine BHSc[9]; Esper, Annette M. MD, MSc[10]; Gershengorn, Hayley B. MD, ATSF, FCCM[11,12]; Hammond, Naomi E. RN, BN, MN, MPH PhD[13,14]; Jayaprakash, Namita MB, MD, BcH, BAO[15,16]; Menon, Kusum MD, MSc[17,18]; Nazer, Lama PharmD, FCCM[19]; Pitre, Tyler MD[1,2]; Qasim, Zaffer A. MD[20]; Russell, James A. MD[21]; Santos, Ariel P. MD, MPH, FCCM[22]; Sarwal, Aarti MD, FCCM, FAAN, FNCS RPNI[23]; Spencer-Segal, Joanna MD, PhD[24]; Tilouche, Nejla MD[25]; Annane, Djillali MD, PhD (Chair)[26,27,28]; Pastores, Stephen M. MD, MACP, FCCP, FCCM (Chair)[29]. 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia. Critical Care Medicine ():10.1097/CCM.0000000000006172, January 19, 2024. | DOI: 10.1097/CCM.0000000000006172

Dellinger RP, et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. Crit Care Med J 2013;41(2): 580-637.

References

Edwards SE, Grobman WA, Lappen JR, Winter C, Fox R, et al. Modified obstetric early warning scoring systems (MOEWS): validating the diagnostic performance for severe sepss in women with chorioamnionitis. 2015;212:536e1-8.

Eppes CS, Clark SC. Extended-spectrum β-lactamase infections during pregnancy: a growing threat Am J Obstet Gynecol, 2015;213 (5): 650-652.

Kankuri E, Kurki T, Carlson P, Hiilesmaa V. Incidence, treatment and outcome of peripartum sepsis. Acta Obstet Gynecol Scan 2003;82:730-35.

Kenn S, Weber-Carstens S, Weizsaecker K, Bercker S. Prone positioning for ARDS following blunt chest trauma in late pregnancy. Int J Obstet Anesth 2009;18(3):268-71.

Knowles SJ, O'Sullivan NP, Meenan AM, Hanniffy R, Robson M. Maternal sepsis incidence, aetiology and outcome for mother and fetus: a prospective study. BJOG 2015;122:663-671.

References

Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, Suppes R, Feinstein D, Zanotti S, Taiberg L, Gurka D, Kumar A, Cheang M. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96.

Lappen JR, Keene M, Lore M, Grobman WA, Gosset DR. Exisiting models fail to predict sepsis in an obstetric population with intrauteirne infection. Am J Obstet Gynecol 2010;203:573.e1-5.

Levy MM, Dellinger RP, Townsend SR, et al; Surviving Sepsis Campaign:The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis. Crit Care Med 2010; 38:367–374

Maguire PJ, O'Higgines AC, Power KA, Daly N, McKeating A, Turner MJ. Maternal bacteremia and the Irish maternity early warning system. Int J Gynecol Obstet 2015;129:142-5.

National Vital Statistics Report (NVSR) "Deaths: Final Data for 2013" (NVSR Volume 64, Number 2).

Oud L, and Watkins P. Evolving trends in the epidemiology, resource utilization, and outcomes of pregnancy-associated severe sepsis: a population-based cohort study. 2015;7(6):400-416.

Silva E, Pedro Mde A, Sogayar AC, Mohovic T, Silva CL, Janiszewski M, Cal RG, de Sousa EF, Abe TP, de Andrade J, de Matos JD, Rezende E, Assunção M, Avezum A, Rocha PC, de Matos GF, Bento AM, Corrêa AD, Vieira PC, Knobel E; Brazilian Sepsis Epidemiological Study. Brazilian Sepsis Epidemiological Study (BASES study). Crit Care. 2004;8(4):R251-60

References

Snyder CC, Barton JR, Habli M, and Sibai BM. Severe sepsis and septic shock in pregnancy: indications for delivery and maternal and perinatal outcomes. J Mat Fetal Neonat Med 2013; 26(5): 503–506.

Sriskandan S. Severe peripartum sepsis. J R Coll Physicians Edinb 2011;41:339-46.

Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified early warning score in medical admissions. QJM 2001;94:521-6.