OXFORD MATERNAL AND PERINATAL HEALTH INSTITUTE

Maternal Health Task Force

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

Maternal Sepsis

The Geneva Foundation for Medical Education and Research

Abbreviations and acronyms

BMP	basic metabolic panel
bpm	beats per minute
CBC	complete blood count
C	Celsius
CRP	C-reactive protein
CPP	Chronic pelvic pain
CT	Computed tomography
e.g.	for example
IV	intravenous
IVIG	intravenous immunoglobulin
kg	kilogram
mg	milligram
mL	milliliter
mmol	millimole
MRSA	methicillin resistant staphylococci aureaus
PID	Pelvic Inflammatory Disease
PO	by mouth (per os)
PPROM	preterm prelabour rupture of membranes
STI	sexually transmitted infections
UTI	urinary tract infection

On successful completion of this module you should be able to

- Describe key barriers to the research and data collection on maternal sepsis and why this is important
- List key definitions related to maternal sepsis
- Discuss the epidemiology of maternal sepsis
- Identify common pathogens and infections that lead to sepsis
- Recognize risk factors for infection and sepsis in the antepartum and postpartum periods with specific referral to the postpartum period as a high risk time zone.
- Explain how to best prevent sepsis
- Summarize the methods for diagnosis of sepsis
- Discuss how to manage sepsis, severe sepsis and septic shock in pregnancy
- Identify vulnerable periods for acquiring infections
- Investigate and recognize sepsis in the postpartum period
- Describe which medications to use for different common infections

Research obstacles and data deficiencies

There is an urgent need for further trials and more data in resource-poor countries on the incidence, etiology, risk factors and treatment of maternal and neonatal sepsis in order to decrease maternal and neonatal deaths (Seale 2009).

The following issues are barriers to collecting data and conducting research on the topic:

•Definitions and terms vary from study to study, e.g. sepsis vs. puerperal sepsis vs. metritis vs. maternal infections (Van Dillen 2010)

•Maternal Sepsis is often undiagnosed or misdiagnosed because infection begins after hospital discharge without proper follow-up of cases (Van Dillen 2010).

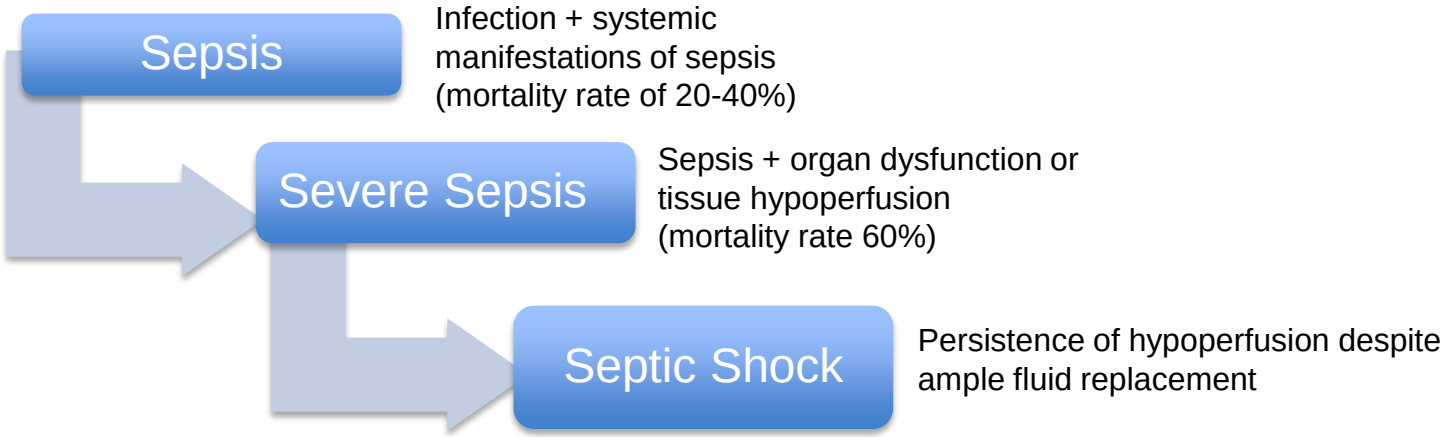
•Hospital-based studies in low-income countries do not reflect the general population of those countries (Van Dillen 2010).

•Lack of data from low-income countries makes the incidence difficult to determine. The available studies are mostly retrospective and do not include microbiological confirmation (Van Dillen 2010).

Seale AC, Mwaniki M, Newton CRJC, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009 Jul;9(7):428-38.

Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.

Definitions

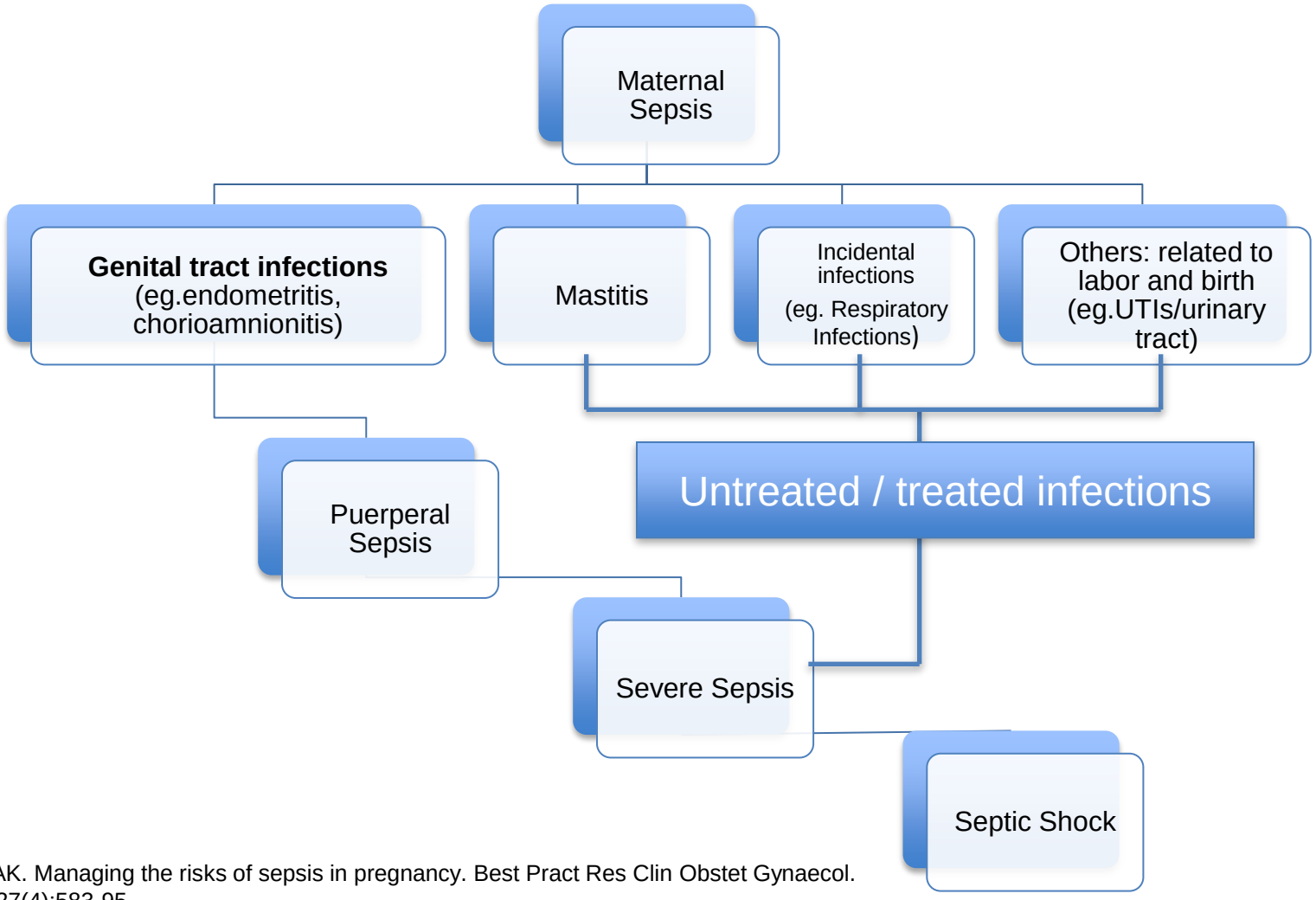


RCOG, 2012

Sepsis is thought to be the consequence of the body's inflammatory response to bacterial endotoxins and exotoxins. Cytokines and immunomodulators are produced by the body to fight infections and in large quantities their release causes a succession of critical events involving multiple organ systems. When an infection is untreated, this response can cause organ dysfunction, septic shock and death. (Karsnitz, 2013).

Karsnitz DB. Puerperal Infections of the Genital Tract: A Clinical Review. Journal of Midwifery & Women's Health. 2013 Nov 1;58(6):632-42.
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b). Royal College of Obstetricians and Gynaecologists. 2012.

Common causes of maternal sepsis



Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95.

Definition: Puerperal sepsis

Infection of the genital tract occurring at any time between the rupture of membranes or the onset of labor, and the 42nd day postpartum, in which a fever (oral temperature 38.5° C or higher on any occasion) and **1 or more** of the following signs and symptoms are present:

- Pelvic pain
- Abnormal vaginal discharge, e.g. presence of pus, abnormal smell/foul odour of discharge
- Subinvolution, i.e. delay in the rate of reduction of the size of the uterus (<2cm/day during the first 8 days).

Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95.

Definition: Puerperal infection

Puerperal infection is a more general term that includes sepsis, but also all extra-genital infections and incidental infections during the period around childbirth:

1. Infections of the genito-urinary (GU) system related to labour, delivery and the puerperium.
    - Infections related to the uterus and surrounding structures (endometritis)
    - Infections related to the urinary tract
2. Infections related to the birth process but not the GU system, e.g. breast abscess.
3. Incidental infections e.g. malaria, respiratory tract infections, which occur during the puerperium.

Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95.

Why is preventing maternal sepsis is a priority?

Prevention as well as early home visits and postnatal care of the newborn are key to preventing maternal and neonatal sepsis (Miller 2013) .

Maternal perspective:

- To reduce maternal morbidity and mortality.

Neonatal perspective:

- Millennium Development Goal 4.2 aims to reduce the infant mortality rate and attention must be made to preventing maternal infection for this rate to decrease (Seale 2010).
- Intra-amniotic infections cause neonatal sepsis, pneumonia and respiratory distress. It is also linked to long-term neurologic impairment in infants (Seale 2010).

Miller AE, Morgan C, Vyankandondera J. Causes of puerperal and neonatal sepsis in resource-constrained settings and advocacy for an integrated community-based postnatal approach. Int J Gynaecol Obstet. 2013 Oct;123(1):10-5.
Seale AC, Mwaniki M, Newton CRJC, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009 Jul;9(7):428-38.

Epidemiology

- New cases: Over 5 million/ year of maternal sepsis occur globally with an estimated 75,000 maternal deaths (Van Dillen 2013).
- Risk of maternal mortality:
  - In high-income countries: 2.1% of all maternal deaths.
  - In low-income countries: 11.6% of maternal deaths. e.g 2–2.7-fold higher in Africa, Asia, Latin America and the Caribbean than in developed countries (Van Dillen 2013)
- Risk of long-term morbidity is reported to be 0.1–0.6 per 1000 deliveries. It includes chronic PID, CPP, bilateral tubal occlusion and infertility (Arulkumaran 2013).
- Sepsis is one of the leading causes of preventable maternal mortality in both high-income and low-income countries (Van Dillen 2013).
- Especially in low-income countries**, prevention** of puerperal infection is the priority (Arulkumaran 2013)
- Though there is an interplay of factors leading to puerperal sepsis, the single most important risk factor for postpartum infection seems to be caesarean section. Trends in puerperal sepsis are likely to increase in future years as a result of increasing trends in caesarean section rates combined with rising incidences of nosocomial infections and antibiotic resistance (Dolea 2003).

Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902.
Dolea C, Stein C. Global burden of maternal sepsis in the year 2000: Evidence and Information for Policy (EIP). World Health Organization. 2003.
Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.

Newborn complications from maternal sepsis

Maternal sepsis has a significant impact on neonatal mortality, via vertical transmission of infection, with over one million infection-related neonatal deaths every year (Arulkumaran 2013).

Intra-amniotic infections cause neonatal sepsis, pneumonia and respiratory distress. They are also linked to long-term neurologic impairment in infants (Seale 2010).

Neonatal sepsis causes 26% of neonatal deaths, with an additional 10% of neonatal death arising from other preventable infections including diarrhea and tetanus (Miller 2013).

Millennium Development Goal 4.2 aims to reduce the infant mortality rate and attention must be made to preventing maternal infection for this rate to decrease (Seale 2010).

Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902.
Miller AE, Morgan C, Vyankandondera J. Causes of puerperal and neonatal sepsis in resource-constrained settings and advocacy for an integrated community-based postnatal approach. Int J Gynaecol Obstet. 2013 Oct;123(1):10-5.
Seale AC, Mwaniki M, Newton CRJC, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009 Jul;9(7):428-38.

Why are pregnant women are more vulnerable to sepsis and its sequelae?

Normal physiological changes in pregnancy (hyperdynamic circulation, tachycardia, diminished oxygen reserve, hypercoagulability) exacerbate the physiological changes brought on during sepsis to make sepsis life-threatening in pregnancy (Van Dillen 2010).

The most common causes of septic shock in pregnancy and postpartum include: **pyelonephritis, chorioamnionitis, and endometritis** (RCOG 2012).

These will be discussed in detail.

Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a). Royal College of Obstetricians and Gynaecologists. 2012.
Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.

Why are pregnant women more vulnerable to sepsis and its sequelae?

Postpartum events:

The postpartum period carries heightened risk for infections that can give rise to sepsis if not identified and treated promptly, due to the following factors:

- The placental site, a common place for infections to occur, is large, warm, dark and moist; the perfect conditions for bacteria to thrive.
- The placental site has a rich blood supply that leads directly to the main venous circulation. This is why septicemia and sepsis can occur quickly.
- Only the vagina (7–10 cm long) separates the entrance to the uterus from the vulva and perineum, making the uterus vulnerable to exogenous and endogenous bacteria.
- Tears to the cervix, vagina or perineum during the birth cause traumatized tissue that is prone to infection. Infection is usually localized initially, but can spread to underlying and surrounding tissues and into the bloodstream, causing septicaemia.

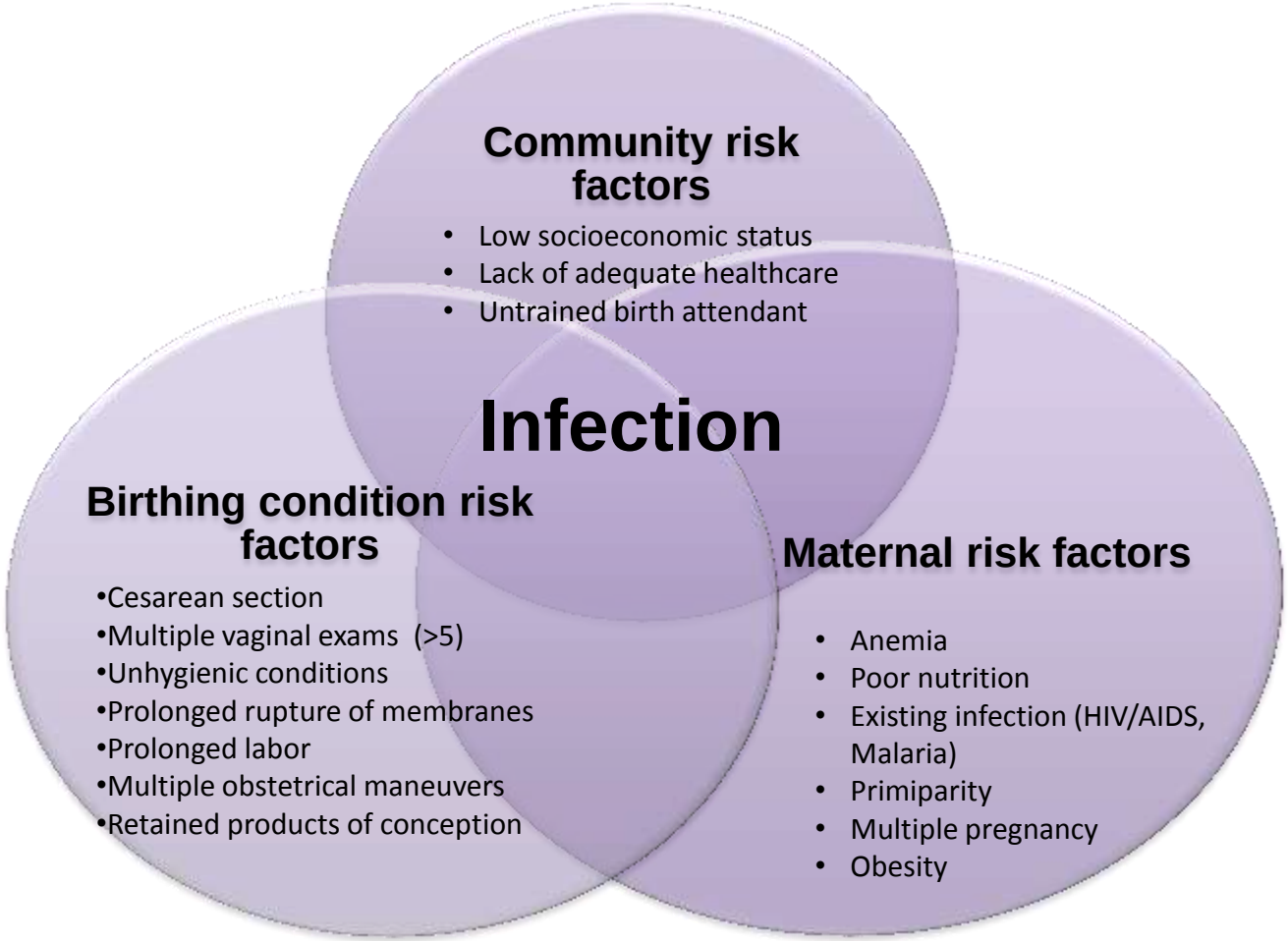
World Health Organization. Education Material for Teachers of Midwifery: Midwifery Education Modules- Managing puerperal sepsis. 2nd ed. Geneva: World Health Organization; 2008.

Low-income settings

- Mortality rates attributable to sepsis approach 33% in low-income settings (Arulkumaran 2013).
- Births in resource-constrained environments carry increased risk of exposure to pathogens due to a lack of effective infection prevention and management (Miller 2013).
- Health systems failures including limited access to adequate and timely therapy also contribute to the increase in maternal sepsis (Van Dillen 2010).
- There is little research into common causative microorganisms of puerperal sepsis in the community, making standardization of antibiotic management difficult (Miller 2013).
- Preventative measures as well as early home visits and postnatal care of the newborn are key to preventing maternal and neonatal sepsis (Miller 2013) .
- There is no high quality evidence that clean birth kits alone reduce newborn mortality or puerperal sepsis, though a few existing studies of combined interventions that included clean birth kits were associated with reduced puerperal sepsis and neonatal mortality (Hundley 2012).

Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902.
Hundley VA, Avan BI, Braunholtz D, Graham WJ. Are birth kits a good idea? A systematic review of the evidence. Midwifery. 2012 Apr;28(2):204-15.
Miller AE, Morgan C, Vyankandondera J. Causes of puerperal and neonatal sepsis in resource-constrained settings and advocacy for an integrated community-based postnatal approach. Int J Gynaecol Obstet. 2013 Oct;123(1):10-5.
Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.

Risk factors for maternal sepsis



Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.
The Global Library of Women's Medicine. The Safer Motherhood Knowledge Transfer Program: Maternal Sepsis- Prevention Recognition Treatment. The Global Library of Women's Medicine. Unknown date.

Common pathogens

Bacteria causing an infection can be:
• Endogenous: organisms that normally exist in the woman's genital tract, bowel or skin
Or
• Exogenous: arising from outside the woman, due to poorly treated existing infections, poor hand washing technique, vaginal exams or other environmental causes

Intrapartum	Postpartum
Group A beta-hemolytic streptococci (GAS) Escherichia coli Group B beta-hemolytic streptococci (GBS) Peptostreptococcus Bacteroides species. Note: most infections are polymicrobial and require multiple drugs	GAS (symptoms normally present <12 hours postpartum) Escherichia coli GBS Staphylococcus aureus Chlamydia trachomatis Clostridium

Adapted from:
Karsnitz DB. Puerperal Infections of the Genital Tract: A Clinical Review. Journal of Midwifery & Women's Health. 2013 Nov
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a).
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b).

Specific clinical syndromes associated with maternal sepsis

- Chorioamnionitis In Labor.
- PPROM –Preterm Prelabour rupture of membranes at <37 weeks.
- PROM- Prelabour rupture of membranes.
- Acute Pyelonephritis with pregnancy.
- Endometritis
- Mastitis and Breast Abscess
- Puerperal Wound Infection

Clinical syndromes: Chorioamnionitis in labor

- Definition: Inflammation of the amnion and/or chorion from ascending pathogens; usually affects the amniotic fluid, fetal membranes, placenta and/or uterus (Fahey 2008).
- Newborn complications of chorioamnionitis include: neonatal sepsis and pneumonia (Czikk 2011) with Neonatal mortality 1-4% for term infants and 10% for preterm infants (Fahey 2008).
- Perinatal complications: Chorioamnionitis presents a significant risk for PPROM, preterm birth, and cesarean section (Fahey 2008)
- Maternal complications: 5-10% of women with chorioamnionitis will develop bacteremia (Fahey, 2008)
- Chorioamnionitis increases maternal risk for postpartum hemorrhage, wound infections, pelvic abscesses and postpartum endometritis (Fahey 2008).

Diagnosis: commonly based on clinical symptoms: maternal fever (>38° C), maternal tachycardia (≥100-120 bpm), fetal tachycardia (≥160 bpm), uterine tenderness, purulent amniotic fluid and maternal leukocytosis (>15,000-18,000 cells/mm3). However, treating based on these symptoms alone often leads to over-diagnosis (Fahey 2008).

Czikk MJ, McCarthy FP, Murphy KE. Chorioamnionitis: from pathogenesis to treatment. Clin Microbiol Infect. 2011 Sep;17(9):1304-11.
Fahey JO. Clinical management of intra-amniotic infection and chorioamnionitis: a review of the literature. J Midwifery Womens Health. 2008 Jun;53(3):227-35.

Clinical syndromes:
PPROM – Preterm Prelabour Rupture of Membranes at <37 weeks

PPROM occurs in approximately 2% of pregnancies but is associated with 40% of preterm births. There is an association between ascending infection from the lower genital tract and PPROM which may lead to preterm births and its sequelae.

Diagnosis is best based on maternal history and a sterile speculum examination. Amniotic fluid pooling in the vagina is visible on speculum exams. Ultrasound examinations (demonstrating oligohydraminos) may be used to confirm the diagnosis.

Management:

Do's	Don'ts
• Observe the woman for signs and symptoms of chorioamnionitis, • Perform a cardiotogography to diagnose fetal tachycardia • Treat group Beta Streptococcus if it is isolated in cases of PPROM • Give antenatal corticosteroids to women between 24-34 weeks gestation • Consider delivery from 34 weeks of gestation. • Give Erythromycin for 10 days following diagnosis of PPROM.	• Perform unnecessary digital examinations. • Perform weekly high vaginal swabs, CBC, or C-reactive protein. • Carry out Amniocentesis for diagnosis of uterine infection • Give Tocolytic agents • Prescribe Co-amoxiclav as it increases the risk of neonatal necrotizing enterocolitis.

Royal College of Obstetricians and Gynaecologists. Preterm Prelabour Rupture of Membranes (Green-top Guideline No. 44). Royal College of Obstetricians and Gynaecologists. 2006, amended 2010.

Clinical syndromes:
PROM- prelabour rupture of membranes

Antibiotics **should not** be routinely given to pregnant women with rupture of membranes prior to labour at term (≥36 weeks in this reference) unless they shows signs of infection.

Wojcieszek AM, Stock OM, Flenady V. Antibiotics for prelabour rupture of membranes at or near term. Cochrane Database Syst Rev. 2014;10:CD001807.

Clinical syndromes:
Postpartum maternal sepsis

Postpartum infections account for 46-47% of maternal sepsis and most arise from:
•Endometritis
•Mastitis
•Perineal and abdominal wounds
•Urinary tract infections

Risk factors include: obesity, diabetes, anaemia, invasive procedures during labour and birth, prolonged rupture of membranes, GAS infections, wound hematoma, caesarean section, retained placental pieces, history of pelvic infections, cervical cerclage

Long-term **morbidity** may include:

•chronic pelvic inflammatory disease
•chronic pelvic pain
•bilateral tubal occlusion
•infertility

Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95.

Clinical syndromes: Endometritis

Etiology	Risk Factors	Symptoms and signs	Management	Complications
Inflammation of the uterine lining Symptoms present in first 5 days Note: women who would like an intrauterine device placed must be infection-free for 3 months prior to insertion	• Cesarean birth • Prolonged rupture of membranes • Increased vaginal exams • Retained placental parts • Postpartum hemorrhage • Group B streptococcus colonization • Chorioamnionitis	• Fever • Uterine tenderness • Purulent lochia • Subinvolution • Pelvic pain • Malaise	• History and physical exam • CBC with differential • BMP • Urine culture • Blood culture • Cervical and endometrial cultures should be done if GAS is suspected • Notify pediatric provider if GAS cultures are positive • Antibiotics	• Abscess • Hematoma • Necrotizing fasciitis • Septic pelvic thrombophlebitis • Pelvic infections

Karsnitz DB. Puerperal infections of the genital tract: a clinical review. J Midwifery Womens Health. 2013 Dec;58(6):632-42.

Clinical syndromes: Mastitis

Most cases of mastitis occur in the first 6 weeks postpartum but it can occur at anytime during lactation. It affects anywhere from 3-20% of lactating women.

Definition: Mastitis is the inflammation of the breast that **may or may not involve a bacterial infection**.

There may be a spectrum of mastitis from engorgement to non-infective mastitis to infective mastitis to abscess. The most common pathogen for infective mastitis is *S. aureus*.

Risk Factors include: (most risk factors are related to milk stasis)

- Damaged nipples (especially if colonized with Staphylococcus aureus)
- Infrequent feedings
- Missed feedings
- Poor attachment of the baby to the nipple leading to inefficient milk removal
- Illness in mother or baby
- Oversupply of milk
- Rapid weaning
- Tight pressure on the breast from tight bras or seatbelts
- Maternal stress and fatigue
- White spot on the nipple or blocked duct

Diagnosis

Signs and symptoms include:

- a tender, hot, swollen, wedge-shaped area on the breast
- Fever of 38.5° C or greater
- Flu-like aches
- Systemic illness

Amir LH. The Academy of Breastfeeding Medicine Protocol Committee. Breastfeeding Medicine. 2014 Jun 1;9(5):239-43.

Clinical syndromes: Mastitis

Diagnosis

Laboratory tests are usually not necessary but WHO suggests breast milk culture and sensitivity if:

- There is no response to antibiotics in 2 days
- The mastitis recurs
- It is hospital acquired mastitis
- The patient is allergic to the usual therapeutic antibiotics
- The case is severe or unusual

Management

- The key is effective and frequent milk removal
- Rest, fluids, good nutrition
- Heat packs before feeding to help with milk flow and cold packs after feeding for pain
- Anti-inflammatory agents
- IV antibiotics for acutely ill women or with no improvement of symptoms after 12-24 hours
- Complications

Breast abscess: a well-defined portion of the breast that remains hard, red and tender despite appropriate interventions. It occurs in about 3% of women with mastitis.

- Breast ultrasound to identify collection of fluid
- Needle aspiration to drain fluid—send for culture
- Continue breast feeding
- Administer antibiotics

Amir LH. The Academy of Breastfeeding Medicine Protocol Committee. Breastfeeding Medicine. 2014 Jun 1;9(5):239-43.

Clinical syndromes:
Puerperal wound infection

In resource-poor countries wound infection rates following childbirth can be as high as 20%.
These infections usually begin at the site of an episiotomy, perineal laceration or caesarean section.

Risk Factors include:
•prolonged rupture of membranes
•compromised skin integrity
•poor suturing or incision repair techniques
•insufficiently achieving hemostasis during repairs

Signs and symptoms:
•pain or discomfort at a perineal or abdominal wound site
•purulent wound discharge
•wound dehiscence or inflamed wound edges
•edematous perineum
•hip pain
•low-grade fever

Management of perineal wound infections includes
•removal of sutures with wound debridement and cleansing
•sitz baths
•broad-spectrum antibiotics.
Secondary wound repair is necessary in third or fourth degree lacerations.

Abdominal wounds may need to be debrided and reclosure performed in the case of wound dehiscence.
Broad spectrum antibiotics should be started.

Complications include abscess, wound extension, septic pelvic thrombophlebitis and necrotizing fasciitis.

Karsnitz DB. Puerperal infections of the genital tract: a clinical review. J Midwifery Womens Health. 2013 Dec;58(6):632-42.

Diagnosis of sepsis: (International surviving sepsis campaign)

Item	Diagnostic feature
Clinical Localizing features	• Fever or rigors • Diarrhea or vomiting (may be sign of early TOXIC shock) • Abdominal/pelvic pain and tenderness. • Offensive vaginal discharge (strong odor suggests anaerobes; serosanguinous suggests streptoccocal infection) • Subinvolution of the uterus *in postpartum period*. • Productive cough • Urinary symptoms
General features	• Fever (>38˚ C) or Hypothermia (core temp <36˚ C) • Tachycardia (>90 beats/minute) • Tachypnoea (>20 breaths/minute) • Impaired mental state, altered conscious level • Considerable edema or positive fluid balance (> 20ml/kg over 24 hours) • Hyperglycaemia in the absence of diabetes (plasma glucose >7.7mmol/l)

Adapted from:
Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut J-F, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent J-L. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008 Jan;34(1):17-60.
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a).

Diagnosis of sepsis: (International surviving sepsis campaign) (cont'd)

Item	Diagnostic feature
Inflammatory	Leukocytosis (WBC count >12,000/ml). Leukopenia (WBC <4000/mL). Normal WBC count with greater than 10% immature forms. Plasma C-reactive protein >2 SD above the normal value. Plasma procalcitonin >2 SD above the normal value.
Organ dysfunction	Arterial hypoxaemia (PaO2/FIO2 < 300). Acute oliguria (urine output <0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation). Creatinine rise >0.5 mg/dL or 44.2micromol/L. Coagulation abnormalities (INR >1.5 or aPTT >60 s) Ileus (absent bowel sounds). Thrombocytopenia (platelet count <100,000/mL), Hyperbilirubinaemia (plasma total bilirubin > 4 mg/dl or 70 mmol/L)

Adapted from:
Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut J-F, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent J-L. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008 Jan;34(1):17-60.

Diagnosis of sepsis: (International surviving sepsis campaign) (cont'd)

Item	Diagnostic feature
Tissue hypoperfusion	Hyperlactaemia >1 mmol/L. Decreased capillary refill or mottling
Haemodynamic	Arterial hypotension (SBP <90 mmHg, MAP <70 mmHg, or an SBP decrease >40 mmHg in adults or more than 2 SD below normal for age.

Note that these features are for diagnosis of sepsis in general and not specific to maternal sepsis

Adapted from:
Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut J-F, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent J-L. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008 Jan;34(1):17-60.

Key interventions for prevention of maternal sepsis

Early recognition, diagnosis and prompt treatment decreases complications and the risk of sepsis that can arise from genital tract infections (Karsnitz, 2013). The following priority interventions are recommended:

- Treat PPROM (RCOG 2010)
- Maintain asepsis during birth (Karsnitz 2013)
- Perform rigorous hand washing during birth (Karsnitz 2013)
- Make minimal use of invasive procedures (Karsnitz 2013)
- Teach all pregnant and recently postpartum women signs and symptoms of genital tract infections (RCOG 2012).
- Be vigilant for endometritis during the postpartum period (Karsnitz 2013)
- Ensure an early home visit or postnatal care facility for woman and baby (Karsnitz 2013)

Karsnitz DB. Puerperal infections of the genital tract: a clinical review. J Midwifery Womens Health. 2013 Dec;58(6):632-42.
Royal College of Obstetricians and Gynaecologists. Preterm Prelabour Rupture of Membranes (Green-top Guideline No. 44). Royal College of Obstetricians and Gynaecologists. 2006, amended 2010.
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a). Royal College of Obstetricians and Gynaecologists. 2012.

Other risk factors for puerperal infections

Given the increased risk of infection associated with the following interventions or conditions, antibiotic prophylaxis is recommended.

1. Manual Removal of the Placenta

There are no RCT to evaluate the effectiveness of prophylactic antibiotics in the management of manual removal of the placenta after a vaginal birth (Chongsomchai 2014).
However, the WHO recommends offering a single dose of ampicillin or first-generation cephalosporin after manual removal of the placenta. **Quality of evidence: very low; Strength of recommendation: strong** (WHO 2009)

2. Medical and surgical termination or pregnancy

Healthcare professionals should provide antibiotic prophylaxis against *C. trachomatis* and anaerobes for both medical **(Evidence grade C)** and surgical abortions **(Evidence grade A).** A single dose or short course of a tetracycline or nitroimidazole is recommended to prevent upper genital tract infections, however research into the optimal antibiotic is lacking (RCOG 2011).

Chongsomchai C, Lumbiganon P, Laopaiboon M. Prophylactic antibiotics for manual removal of retained placenta in vaginal birth. Cochrane Database Syst Rev. 2014;10:CD004904.

Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting an Induced Abortion (Evidence-based Clinical Guideline No. 7). Royal College of Obstetricians and Gynaecologists. 2011.

World Health Organization. WHO guidelines for the management of postpartum haemorrhage and retained placenta. World Health Organization. 2009.

Other risk factors for puerperal infections (cont'd)

3. Perineal Tears

The use of a broad-spectrum antibiotic is recommended for all obstetric anal sphincter repairs to reduce the incidence of infection and wound dehiscence.

4. Caesarean Sections

Prophylactic antibiotics should be given pre-operatively to women receiving a caesarean section. Ampicillin and first-generation cephalosporins are both effective in decreasing post-partum endometritis.

Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95.

Severe sepsis and septic shock

The Surviving Sepsis Campaign is a joint collaboration of the Society of Critical Care Medicine and the European Society of Intensive Care Medicine committed to reducing mortality from severe sepsis and septic shock worldwide by changing clinical behaviour: For more information see the surviving sepsis website which gives more specific treatment plans http://www.survivingsepsis.org/

They provide guidance on standard definitions and a multidisciplinary approach to treatment for sepsis based on a 2-phase approach.

1. The resuscitation phase
2. The management phase

Based on review of current best evidence, the Surviving Sepsis Campaign endorses the following "care bundles" for the treatment of severe sepsis and septic shock.

Note: This treatment is not specific to maternal sepsis

Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902.

Treatment of severe sepsis- Resuscitation bundle

Tasks to Be Performed within 6 Hours of Identifying Severe Sepsis

Obtain blood cultures (PRIOR to antibiotic administration)

Administer broad-spectrum antibiotic within 1 hour of recognition of severe sepsis and narrow therapy when organism is identified

Measure serum lactate (≥ 4mmol/l is indicative of tissue hypoperfusion)

In case of hypotension and/or a serum lactate>4mmol/l;

- Give initial minimum 20ml/kg of crystalloid or an equivalent.
- Give vasopressors for hypotension that is not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65mmHg

In the event of persistent hypotension despite fluid resuscitation (septic shock) and or lactate >4mmol/l

- Achieve a central venous pressure (CVP) of ≥8mmHg
- Achieve a central venous oxygen saturation (ScvO2) ≥70% or mixed venous oxygen saturation (SvO2)≥65%

IVIG has been used in pregnant women and is effective in treating shock due to streptococci and staphylococci

Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a). Royal College of Obstetricians and Gynaecologists. 2012.

Treatment of severe sepsis- Management bundle

Tasks to be performed as soon as possible and scored over 24 hours

Administer low-dose steroids per hospital policy

Administer drotrecogin alfa (activated) per hospital policy

Maintain glucose higher than lower limit of normal, but less than 150mg/dl (8.3mmol/l)

Maintain inspiratory plateau pressures at less than 30cmH_2O for mechanically ventilate patients

Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54.

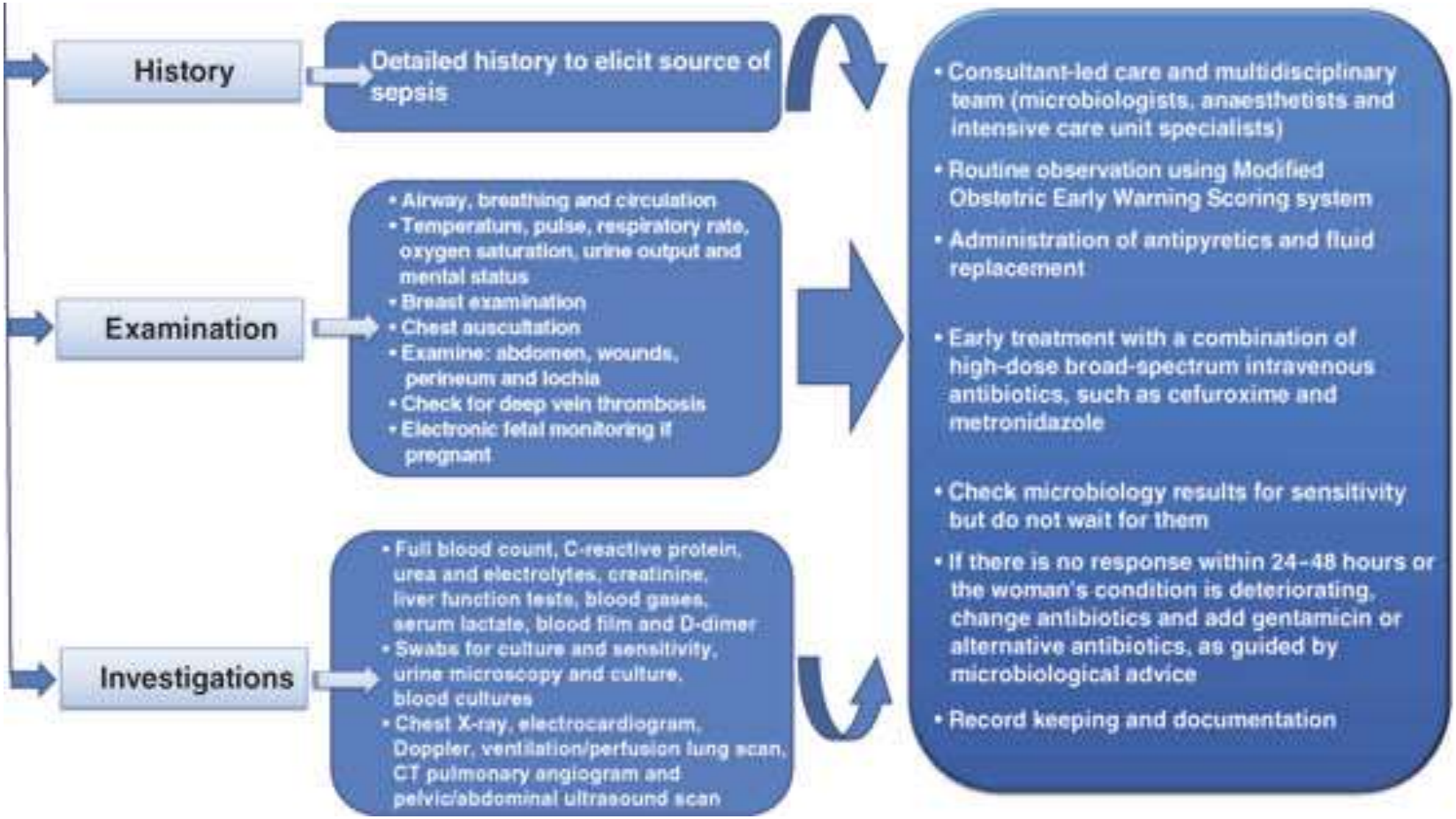
General management of maternal sepsis

- Assess general condition of woman (WHO 2008)
- Administer oxygen and perform resuscitation if necessary (WHO 2008)
- Collect blood cultures (before antibiotics are administered) (RCOG 2012)
- Begin antibiotic treatment (RCOG 2012)
    - High-dose broad-spectrum IV antibiotics initially
    - Narrow therapy when organism is identified
- Test serum lactate (RCOG 2012)
- Test for MRSA status via nose swab if status is unknown (RCOG 2012)
- Identify the source of sepsis and treat it: rule out retained placental fragments (RCOG 2012)
- Consider giving a tetanus toxoid if she was exposed to tetanus or has an unknown vaccination history (WHO 2008)
- While aggressive fluid replacement in septic patients is necessary, postpartum women are more vulnerable to pulmonary oedema with fluid overload than non-postpartum women (RCOG 2012).
- Breast feeding limits the use of certain antibiotics.

Note: Management is based on expert opinion and case reports (RCOG 2012)

Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a). Royal College of Obstetricians and Gynaecologists. 2012.
Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b).
World Health Organization. Education Material for Teachers of Midwifery: Midwifery Education Modules- Managing puerperal sepsis. 2nd ed. Geneva: World Health Organization; 2008.

General management of maternal sepsis
Management of suspected genital tract sepsis



Sinha P, Otify M. Genital tract sepsis: early diagnosis, management and prevention. The Obstetrician & Gynaecologist. 2012 Apr 1;14(2):106-14.

Neonatal sepsis management

Neonatal sepsis can occur as a result of maternal puerperal infection and should be treated promptly.

Definition:

- Early-Onset Neonatal Sepsis: occurs within 7 days of birth- 75% of neonatal deaths occur in this period. This is usually reflective of vertically acquired infection from the maternal genital tract (Seale 2010)
- Late-Onset Neonatal Sepsis: occurs after 7 days of birth and is usually reflective of environmental microorganisms (Miller 2013).

Risk Factors

- Lack of rigorous hand washing, strict hand washing is important to prevent spread of infection (ReproLine Plus 2014).

Diagnosis/Signs and Symptoms:

- Careful monitoring of the baby for signs and symptoms of sepsis is necessary especially if the mother has an infection (ReproLine Plus 2014).
  - Vital signs
  - Altered feeding patterns
  - Lethargy or poor muscle tone
  - Cry weak or inconsolable

Management/Treatment

- If the baby and mother are well enough, keep them together and the mother may breastfeed (ReproLine Plus 2014) .

If the mother is very ill, contact a newborn care provider. A close relative may care for the baby if the mother and baby must be separated (ReproLine Plus 2014).

Miller AE, Morgan C, Vyankandondera J. Causes of puerperal and neonatal sepsis in resource-constrained settings and advocacy for an integrated community-based postnatal approach. Int J Gynaecol Obstet. 2013 Oct;123(1):10-5.

ReproLine Plus. Managing Puerperal Sepsis [Internet]. Jhpiego and Johns Hopkins University. 2014 [cited 2015 March 05].

Seale AC, Mwaniki M, Newton CRJC, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009 Jul;9(7):428-38.

Antibiotic regimens

Diagnosis	Regimen
Chorioamnionitis Czikk MJ, McCarthy FP, Murphy KE. Chorioamnionitis: From Pathogen to Treatment. Clinical Microbiology and Infection. 2011 Sep;17(9):1304-1311.	IV ampicillin 2 grams every 6 hours AND IV gentamicin 1.5 mg/kg every 8 hours ADD IV clindamycin 900 mg every 8 IN case of CS Note: one additional dose after delivery
Group Beta streptococcus CDC. Recommendations and Reports. Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines for CDC, 21010.Nov 19, 2010/59 (RR10):1-32.	Penicillin G, 5 million units IV initial dose, then 2.5–3.0 million units every 4 hours until delivery (should be started >4 hours before delivery)
Endometritis Karsnitz DB. Puerperal infections of the genital tract: a clinical review. Journal of Midwifery & Women's Health, 2013;58(6): 632-642	Clindamycin 900mg IV AND Gentamicin 1.5mg/kg IV every 8 hours (moderate to severe cases)
PPROM RCOG.PPROM (Green-top Guideline No. 44). Royal College of Obstetricians and Gynaecologists. 2006; amended 2010.	Erythromycin 250mg PO every 6 hours for 10 days
Bacterial vaginosis Centers for Disease Control and Prevention. Website. Sexually transmitted diseases, treatment guidelines 2010.	Metronidazole 500mg PO twice a day for 7 days

Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b). Royal College of Obstetricians and Gynaecologists. 2012.

Antibiotic regimens (cont'd)

Diagnosis	Regimen
Infectious mastitis Betzold, C. An Update on the Recognition and Management of Lactational Breast Inflammation. Journal of Midwifery & Women's Health, 2007(updated 2010);52(6): 595-605.	Dicloxacillin 500 mg (po); four times/day or cephalexin 500 mg (po) four times/day (PCN allergic use clindamycin 300 mg four times/day) Note: Treat for 10-14 days
Breast abscess Betzold, C. An Update on the Recognition and Management of Lactational Breast Inflammation. Journal of Midwifery & Women's Health, 2007(updated 2010);52(6): 595-605.	Outpatient: Dicloxacillin 500 mg (po) four times/day or clindamycin 300 mg (po) four times/day Note: treat for 10-14 days Inpatient: Nafcillin 2.0.g every 4 hours IV or cefazolin 1.0 g every 6 hours IV or vancomycin 1.0 g every 12 hour IV.
Severe sepsis (broad spectrum) WHO. Managing puerperal sepsis. Education material for teachers of midwifery, Midwifery education modules – 2nd edition, 2008, Geneva.	Ampicillin 2g IV every 6 hours PLUS Gentamicin 5 mg/kg IV every 24 hours PLUS metrondazole 500mg IV every 8 hours. Note: antibiotics should be continued until afebrile 24 hours. If fever is still present after 72 hours, reconsider the antibiotic choice.

Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b). Royal College of Obstetricians and Gynaecologists. 2012.

References

- Amir LH. The Academy of Breastfeeding Medicine Protocol Committee. Breastfeeding Medicine. 2014 Jun 1;9(5):239-43. http://dx.doi.org/10.1089/bfm.2014.9984
- Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902. http://dx.doi.org/10.1016/j.bpobgyn.2013.07.004
- Bamfo JEAK. Managing the risks of sepsis in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013 Aug;27(4):583-95. http://dx.doi.org/10.1016/j.bpobgyn.2013.04.003
- Chongsomchai C, Lumbiganon P, Laopaiboon M. Prophylactic antibiotics for manual removal of retained placenta in vaginal birth. Cochrane Database Syst Rev. 2014;10:CD004904. http://dx.doi.org/10.1002/14651858.CD004904.pub3
- Czikk MJ, McCarthy FP, Murphy KE. Chorioamnionitis: from pathogenesis to treatment. Clin Microbiol Infect. 2011 Sep;17(9):1304-11. http://dx.doi.org/10.1111/j.1469-0691.2011.03574.x
- Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut J-F, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent J-L. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008 Jan;34(1):17-60. http://dx.doi.org/10.1007/s00134-007-0934-2

References

- Dolea C, Stein C. Global burden of maternal sepsis in the year 2000: Evidence and Information for Policy (EIP). World Health Organization. 2003. Available from: http://www.who.int/healthinfo/statistics/bod_maternalsepsis.pdf
- Fahey JO. Clinical management of intra-amniotic infection and chorioamnionitis: a review of the literature. J Midwifery Womens Health. 2008 Jun;53(3):227-35. http://dx.doi.org/10.1016/j.jmwh.2008.01.001
- Hundley VA, Avan BI, Braunholtz D, Graham WJ. Are birth kits a good idea? A systematic review of the evidence. Midwifery. 2012 Apr;28(2):204-15. http://dx.doi.org/10.1016/j.midw.2011.03.004
- Karsnitz DB. Puerperal infections of the genital tract: a clinical review. J Midwifery Womens Health. 2013 Dec;58(6):632-42. http://dx.doi.org/10.1111/jmwh.12119
- Miller AE, Morgan C, Vyankandondera J. Causes of puerperal and neonatal sepsis in resource-constrained settings and advocacy for an integrated community-based postnatal approach. Int J Gynaecol Obstet. 2013 Oct;123(1):10-5. http://dx.doi.org/10.1016/j.ijgo.2013.06.006
- ReproLine Plus. Managing Puerperal Sepsis [Internet]. Jhpiego and Johns Hopkins University. 2014 [cited 2015 March 05]. Available from: http://reprolineplus.org/learning-opportunities/course/managing-puerperal-sepsis/take-the-course#page-title
- Royal College of Obstetricians and Gynaecologists. Preterm Prelabour Rupture of Membranes (Green-top Guideline No. 44). Royal College of Obstetricians and Gynaecologists. 2006, amended 2010. Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg44/

References

- Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting an Induced Abortion (Evidence-based Clinical Guideline No. 7). Royal College of Obstetricians and Gynaecologists. 2011. Available from: https://www.rcog.org.uk/globalassets/documents/guidelines/abortion-guideline_web_1.pdf
- Royal College of Obstetricians and Gynaecologists. Bacterial sepsis in pregnancy (Green-top Guideline No. 64a). Royal College of Obstetricians and Gynaecologists. 2012. Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg64a/
- Royal College of Obstetricians and Gynaecologists. Bacterial sepsis following pregnancy (Green-top Guideline No.64b). Royal College of Obstetricians and Gynaecologists. 2012. Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg64b/
- Seale AC, Mwaniki M, Newton CRJC, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009 Jul;9(7):428-38. http://dx.doi.org/10.1016/S1473-3099(09)70172-0
- Sinha P, Otify M. Genital tract sepsis: early diagnosis, management and prevention. The Obstetrician & Gynaecologist. 2012 Apr 1;14(2):106-14. http://dx.doi.org/10.1111/j.1744-4667.2011.00083.x
- The Global Library of Women's Medicine. The Safer Motherhood Knowledge Transfer Program: Maternal Sepsis- Prevention Recognition Treatment. The Global Library of Women's Medicine. Unknown date. Available from: http://www.glowm.com/pdf/Maternal_Sepsis_WallChart_WEB.pdf

References

- Van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis. 2010 Jun;23(3):249-54. http://dx.doi.org/10.1097/QCO.0b013e328339257c
- Wojcieszek AM, Stock OM, Flenady V. Antibiotics for prelabour rupture of membranes at or near term. Cochrane Database Syst Rev. 2014;10:CD001807. http://dx.doi.org/10.1002/14651858.CD001807.pub2
- World Health Organization. Education Material for Teachers of Midwifery: Midwifery Education Modules- Managing puerperal sepsis. 2nd ed. Geneva: World Health Organization; 2008. Available from: http://apps.who.int/iris/bitstream/10665/44145/6/9789241546669_6_eng.pdf?ua=1
- World Health Organization. WHO guidelines for the management of postpartum haemorrhage and retained placenta. World Health Organization. 2009. Available from: http://whqlibdoc.who.int/publications/2009/9789241598514_eng.pdf