



CLINICAL PRACTICE GUIDELINE Bacterial Infections Specific to Pregnancy

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1. Revision History

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1.0			

2. Key Recommendations

- 1. The Irish Maternity Early Warning System (IMEWS) with the customised Sepsis 6 Tool should be used to monitor women admitted to the maternity wards (http://bit.do/IMEWS).
- 2. Staff need to be particularly vigilant about the risk of infection following rupture of the amniotic membranes and/or during the peripartum period.
- 3. Appropriate microbiological cultures should be taken before commencing the recommended antibiotic regimen.
- 4. If an infection is suspected, appropriate antibiotics should be administered ideally within one hour without awaiting the results of microbiological cultures.
- 5. The dose of some drugs, such as gentamicin, is based on weight. It is recommended that the woman is weighed accurately at her first antenatal visit. The dosage is based on this weight and not her weight at the time of antibiotic administration because weight gained during pregnancy is mainly water.
- 6. If a woman has already developed an infection, therapeutic antibiotics and not prophylactic antibiotics are required.
- 7. Even in cases where the source of the pregnancy-specific infection appears clear, consideration should be given to taking a blood culture if a pyrexia ≥38°C persists because of the risk of associated bacteraemia.
- 8. The development of fetal heart rate abnormalities in women at risk of infective chorioamnionitis should raise concerns because it suggests that the fetus has become infected.
- 9. If a diagnosis of chorioamnionitis is suspected, treatment with antibiotics should be started as a matter of urgency once microbiological samples have been taken.
- 10. In cases of suspected chorioamnionitis, microbiological culture of the fetal and maternal aspects of the placenta/membranes is recommended. Histological examination of the placenta and umbilical cord is also recommended.
- 11. If a woman presents postpartum with symptoms and signs suggestive of a perineal infection, close vaginal inspection should be accompanied by microbiological culture. With the woman's consent, careful vaginal and rectal examination should be performed so that abnormalities such as fistula formation are identified.
- 12. When a breast abscess is suspected clinically, an ultrasound examination should be considered because it may identify multiple abscesses.
- 13. In women with an inflammatory breast mass that persists despite appropriate antibiotics, the possibility of a breast tumour should be considered and the woman referred urgently to a specialist breast clinic.
- 14. Should a woman with a presentation strongly suggestive of maternal infection demonstrate signs of sepsis as evidenced by the presence of the systemic inflammatory response syndrome customised for pregnancy, it is imperative that the National Clinical Guideline No.6: Sepsis Management is followed (http://bit.do/SepsisMangement).

3. Purpose and Scope

The purpose of this guideline is to improve the prevention and management of pregnancy-specific bacterial infections. The guideline is intended for healthcare professionals, particularly those in training, who are working in HSE-funded hospitals and primary care. It is designed to guide clinical judgement but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow the guideline if it is deemed to be in the best interests of the woman or her offspring. This guideline is not intended to comprehensively address antibiotic prophylaxis in obstetrics. It is intended to develop a suite of guidelines covering infections exacerbated by pregnancy in the next phase of this work. Existing and relevant national guidelines and reports on infection in pregnancy are listed in Appendix One.

4. Background and Introduction

Concern about maternal death due to sepsis has re-emerged in developed countries. In Ireland, there have been concerns about individual maternal deaths, and in the United Kingdom (UK) the last triennial Confidential Enquiry into maternal deaths reported an increase in direct maternal deaths due to sepsis, mainly from community-acquired group A beta-haemolytic streptococcus infection after delivery (GAS or Streptococcus pyogenes) (Cantwell *et al.*, 2011). In the United States of America, rates of maternal sepsis have been stable but rates of sepsis-related maternal deaths in hospital have increased (Bauer *et al.*, 2013). Consequently, national sepsis management guidelines were written and endorsed by the National Clinical Effectiveness Committee (NCEC) in November 2014 (http://bit.do/SepsisMangement). However, in order to help prevent sepsis in the maternity setting, the focus of this guideline is on the primary infection, specifically the prevention and management of pregnancy-specific bacterial infections.

4.1 Classification

While pregnant women are generally healthy, they are at risk of developing the same infections as the non-pregnant adult. In addition, their risk from some infections may be exacerbated by pregnancy or women may develop infections that are specific to pregnancy (Table 1).

Any one or more of these infections may progress to sepsis. The pregnancy-specific infections include chorioamnionitis, endometritis (with or without retained products of conception), perineal infections, wound infections and lactational mastitis. Delayed or inappropriate treatment of these infections may lead to bacteraemia or to sepsis and, subsequently, death. What all these infections have in common is that they are strongly associated with a breach in the woman's physical integrity, which is most likely to occur near the time of delivery. In the case of chorioamnionitis and endometritis, rupture of the amniotic sac and/or dilatation of the internal cervical os exposes the normally sterile uterine cavity to the normal vaginal microflora. In the case of perineal, wound and breast infections it is strongly associated with traumatic breakdown of the protective skin or vaginal wall.

Table 1: Classification of Infections and Pregnancy (Turner, 2014)

- A. Infections specific to pregnancy
 - 1. Chorioamnionitis
 - 2. Endometritis (with or without retained products of conception)
 - 3. Wound infection post caesarean section
 - 4. Perineal infection
 - 5. Lactational mastitis
- B. Infections exacerbated during pregnancy, for example,
 - 1. Urinary tract infection, including pyelonephritis
 - 2. Pneumonia
 - 3. Rubella
 - 4. Listeria
 - 5. Influenza
 - 6. Varicella
 - 7. Toxoplasmosis
 - 8. Herpes infection
 - 9. Parvovirus
 - 10. Cytomegalovirus (CMV)
- C. Infections incidental to pregnancy, for example,
 - 1. Viral hepatitis
 - 2. Human Immunodeficiency Virus (HIV)
 - 3. Sexually Transmitted Diseases (STDs)
 - 4. Tuberculosis
 - 5. Endocarditis

Chorioamnionitis is the most challenging of the pregnancy-specific infections. It is strongly associated with spontaneous rupture of the membranes and cervical dilatation. However, the site of infection is not visible and direct microbiological cultures are not feasible. The clinical evidence to support the diagnosis may be florid or extremely subtle. Chorioamnionitis may be defined clinically, histological or microbiologically (Tita and Andrews, 2010). Both inflammatory biomarkers and the white cell counts used for the early diagnosis of infection are altered physiologically by pregnancy (Carlin and Alfirevic, 2008). The pharmacokinetics of antibiotics during pregnancy may be greatly altered and, finally, consideration may have to be given to the fetal interest.

Similar challenges occur with endometritis except that consideration may also have to be given to the diagnosis and management of retained placental products. With both chorioamnionitis and endometritis the exposure of the vascular placental bed to colonies of vaginal microorganisms may lead quickly to maternal bacteraemia, which may be hard to evaluate because of the physiological changes in the woman's vital signs.

In contrast, perineal, wound and breast infections are easier to diagnose and manage. The site of infection is usually reddened, painful, swollen and visible. The site is easily accessible for microbiological culture. The infection is usually contained and, if treated appropriately, does not lead to maternal bacteraemia. These infections present after delivery when the physiological changes of pregnancy have started to return to normal. The white cell count also starts to normalise and, more importantly, the pharmacokinetics of antibiotics starts to normalise making sub-therapeutic drug levels less likely postpartum. The physiological changes in the woman's vital signs also start to revert back to normal.

Importantly, with all infections, the clinician needs to be cognisant of a woman with a presentation strongly suggestive of maternal infection who demonstrates signs of sepsis, as evidenced by the presence of the systemic inflammatory response syndrome (SIRS) customised for pregnancy (Appendix Two). In this case it is imperative that the National Clinical Guideline No.6: Sepsis Management is followed (http://bit.do/SepsisManagement).

4.2 Guidelines

Outside pregnancy, the Surviving Sepsis Campaign (SSC) has led to the introduction of Early Warning Scores (EWS), Sepsis Care Bundles (including the Sepsis 6 Box) and high quality prescriptive clinical guidelines that focus on improving the early diagnosis and effective management of sepsis (Dellinger *et al.*, 2013). Special consideration by SSC was also given to sepsis in children because they differ physiologically from adults. However, special consideration has, to date, not been given by the SSC to the prevention and management of maternal sepsis both in developing and developed countries.

A national standardised Irish Maternity Early Warning System (IMEWS) was implemented in April 2013, and a Sepsis 6 Tool customised for pregnancy was introduced in August 2014 (Appendix Two, http://bit.do/IMEWS_Chart). This guideline has been appraised by the National Clinical Effectiveness Committee (NCEC) and was endorsed by the Minister for Health in November 2014. It is important to note that, as with all clinical guidelines, the use of IMEWS and Sepsis 6 Tool are meant to compliment clinical judgment and not replace it (Maguire et al., 2014). New multidisciplinary training programmes and clinical audits have been established. Work is ongoing on the development, dissemination and implementation of national guidelines for the prevention and management of infection generally and for the prevention and treatment of individual infections during pregnancy.

4.3 Prevalence

The incidence of maternal infections and sepsis is difficult to compare nationally and internationally because of the differences in definitions, diagnostic criteria, obstetric practices and interventions, vaccination and prophylactic antibiotic policies, populations studied and in healthcare resources. Some maternal infections may be diagnosed and treated in an acute hospital setting but others may be diagnosed and treated solely in primary care. Thus, hospital studies may understate the overall prevalence of some pregnancy-specific infections such as mastitis, wound infections post caesarean section and perineal infection.

Maternal bacteraemia due to pregnancy-specific infections is uncommon before labour in a developed country. Over four years in a large Dublin maternity hospital, there were 58 out of 37,584 (0.15%) cases of bacteraemia. Only two cases of antepartum bacteraemia of genital tract origin were associated with preterm spontaneous rupture of membranes (SROM) with one of these developing septic shock (O'Higgins $et\ al.$, 2014). No case of bacteraemia was associated with wound, breast or perineal infections. Even in cases where the source of the pregnancy-specific infection is clear, however, consideration should be given to taking a blood culture if a pyrexia $\geq 38^{\circ}\text{C}$ occurs because of the risk of associated bacteraemia.

In a large American study of nearly 45 million obstetric hospitalisations for delivery between 1998-2008, sepsis complicated one in 3,333 deliveries, severe sepsis one in 10,823 and sepsis-related death occurred in one in 105,384 (Bauer et al., 2013). Of the cases of severe maternal sepsis (n=3,177), chorioamnionitis was present in 18.4%, endometritis in 8.6% and wound infection in 4.7% of cases. The majority of cases were due to infections exacerbated but not specific to pregnancy. Severe sepsis associated with mastitis or perineal infections was not reported (Bauer et al., 2013). This highlights that intrauterine infection either before or after delivery carries the highest risk of maternal sepsis due to infections specific to pregnancy, and that there is no room for complacency.

4.4 Antibiotic Therapy

The prescribing of antibiotics during pregnancy is informed by two particular considerations: firstly, whether or not the antibiotics will harm the fetus; and secondly, the altered pharmacokinetics of antibiotics during pregnancy (Anger and Piquette-Miller, 2008). Considerations about harm to the fetus and, in particular, teratogenicity are greatest in the first trimester. Considerations about alterations in pharmacokinetics begin early in the first trimester with the knowledge that these changes increase as pregnancy advances up to and including the intrapartum and postpartum periods (Frederiksen, 2001; Briggs and Wan, 2006). These considerations are important because withholding an antibiotic inappropriately or antibiotic under-dosing may increase the clinical risks associated with infection during pregnancy.

The physiological changes due to pregnancy may affect the absorption, distribution, metabolism and clearance of antibiotics. Alterations in body composition, organ functions and biological processes in both the maternal and the feto-placental compartments may follow different trajectories over time with gestational age (Anger and Piquette-Miller, 2008; Abduljalil *et al.*, 2012). It is acknowledged that information on pharmacokinetic changes due to pregnancy remains limited and, as a result, doctors are often reluctant to deviate from the standard antibiotic dose for non-pregnant adults.

However, glomerular filtration rates may increase 40-65% which increases the elimination of antibiotics such as ampicillin, cephalosporins and gentamicin. The volume of the placenta increases during pregnancy and the transfer of antibiotics by the placenta can be complete, incomplete or exceeding (Pacifici, 2006). Antibiotics transferred completely include ampicillin and methicillin. Antibiotics transferred incompletely include gentamicin and vancomycin (Pacifici, 2006).

During the first half of pregnancy, the volume of amniotic fluid is the major component of intrauterine volume. From 11 weeks gestation fetal urine contributes to the volume and fetal swallowing plays a part in the elimination of amniotic fluid (Abduljalil *et al.*, 2012). In the second half of pregnancy fetal urine is the major source of production of amniotic fluid and fetal swallowing the major source of elimination. Rupture of the sac changes the dynamics of amniotic fluid, which may decrease tissue levels of antibiotics in the uterine cavity if the liquor volume decreases.

There are practical implications for antibiotic prescribing during and immediately after pregnancy. The choice of antibiotics will be influenced by patient characteristics, the source of the infection, local antibiotic sensitivities and the woman's previous and current microbiological cultures. However, the dose of some drugs such as gentamicin, are based on weight and it is mandatory that the woman is weighed accurately at her first antenatal visit. The dosage is based on this weight and not her weight gain at the time of antibiotic administration because weight gain during pregnancy is mainly water.

5. Methodology

Medline, EMBASE and Cochrane Database of Systematic Reviews were searched using terms which included maternal infection, sepsis, septicaemia, septic shock, bacteraemia, mastitis, chorioamnionitis, endometritis, perineal infection, wound infection, biomarkers for infection, leucocytosis, and puerperal infection. Searches were limited to humans and restricted to the titles of English language articles published between August 1984 and August 2014. Relevant meta-analyses, systematic reviews, intervention and observational studies were reviewed. Guidelines on infection and pregnancy from other national and international professional bodies were also reviewed.

The principal guideline developers were Dr Patrick Maguire, Ms. Mairead McGuire, Dr Karen Power and Professor Michael Turner working under the auspices of the HSE Clinical Programme in Obstetrics and Gynaecology. Feedback was received from consultation with Dr. Ulrich Bartels (Obstetrician and Gynaecologist, Mayo General Hospital, Castlebar), Dr. Michael Brassil (Obstetrician and Gynaecologist, Portiuncula Hospital, Ballinasloe), Dr. Joseph Clarke (General Practitioner), Ms. Karen Cliff (Midwife, Our Lady of Lourdes Hospital, Drogheda), Dr. Liz Dunn (Obstetrician and Gynaecologist, Wexford General Hospital), Dr. Vida Hamilton (National Clinical Lead for Sepsis), Dr Robert Cunney (Microbiologist, Health Protection Surveillance Centre and Temple Street University Hospital), Ms. Siobhan Hourigan (Midwife, HSE), Dr. Keelin O'Donoghue (Obstetrician and Gynaecologist, Cork University Maternity Hospital), Dr. Clare O'Loughlin (Specialist Registrar, Cork University Maternity Hospital) and the Clinical Advisory Group of the HSE Clinical Programme in Obstetrics and Gynaecology.

6. Clinical Guidelines on Pregnancy-specific Infections

6.1 Chorioamnionitis

6.1.1. Background

Acute chorioamnionitis is an inflammation of the membranes and chorion of the placenta which may be associated with a funisitis where the inflammation extends to the umbilical cord (Tita and Andrews, 2010). It is strongly associated with premature spontaneous rupture of the membranes (SROM). The protective physical barriers of the amniotic sac, the cervical mucous plug and the internal cervical os are disturbed thus exposing the normally sterile intrauterine cavity to the normal vaginal microflora. Infective chorioamnionitis may, however, occur with intact membranes due to genital tract mycoplasmas or rarely it may follow haematogenous spread due, for example, to listeria monocytogenes (Gibbs and Duff, 1991; Eschenbach, 1993). Iatrogenic chorioamnionitis may also complicate cervical cerclage or invasive prenatal testing. Infective chorioamnionitis is more likely to occur preterm than at term and is strongly associated with a prolonged SROM-delivery interval.

Infective chorioamnionitis is a clinical diagnosis and there must be a strong clinical suspicion in circumstances where there is a possibility that the integrity of the amniotic sac has been compromised either spontaneously or iatrogenically. After a careful history and abdominal examination, it may be necessary to confirm that the membranes have ruptured (National Guideline No 24, Preterm Prelabour Rupture of the Membranes). If confirmation is required, it should only be done by speculum examination under the strictest of aseptic techniques. In short, great care needs to be exercised to avoid introducing polymicrobial contamination of the uterine cavity through the cervical os. Vaginal and rectal examination should be avoided particularly if the woman is not labouring. If a speculum examination is performed, a vaginal swab should be taken for culture and sensitivity.

Acute chorioamnionitis or intraamniotic infection is the most important of the pregnancy-specific infections because it occurs before delivery and, therefore exposes the fetus as well as the woman to serious complications, particularly if the diagnosis or treatment of infection is delayed. It is also a diagnostic challenge because symptoms or signs may be subtle and non-specific, laboratory investigations are sensitive but not specific, microbiological sampling is technically not feasible and it takes time to get definitive results.

6.1.2 Diagnosis

The diagnosis of clinical chorioamnionitis should be considered if there is a history of purulent or meconium-stained liquor, if there is a history of abdominal pains or tenderness or if there is a fetal or maternal tachycardia. The maternal vital signs should be recorded using the Irish Maternity Early Warning System (IMEWS) (http://bit.do/IMEWS) if the woman is admitted to the ward.

Microbiological confirmation of the diagnosis before delivery is challenging because it is difficult to get an uncontaminated intrauterine sample for culture and the organisms isolated may not be those responsible for the infection. There also may be difficulty culturing organisms, particularly mycoplasmas, if the woman has already received antibiotics such as prophylactic erythromycin. Sometimes the responsible organism may not be identified until swabs are taken from the baby or placenta after delivery. Thus, clinical chorioamnionitis may not be confirmed microbiologically. In cases of a maternal pyrexia $\geq 38^{\circ}$ C, a blood culture should be performed as about one in ten women with infective chorioamnionitis may have bacteraemia usually due to Group B Streptococcus (GBS) and *Escherichia coli* (Gibbs and Duff, 1991).

Compared with postpartum pregnancy-specific infections, laboratory investigations have their limitations in the early diagnosis of infective chorioamnionitis. Pregnancy is associated with a physiological leucocytosis (Abbassi-Ghanavati, Greer and Cunningham, 2009; Farah *et al.*, 2012). The white cell count may increase further in labour, or in women given steroids preterm to prevent Respiratory Distress Syndrome but this is usually transient (< 72 hours) (McKay and Cidlowski, 2003). Thus, a mild leucocytosis may not reflect infection and is not helpful in diagnosis.

Likewise, inflammatory biomarkers vary during pregnancy particularly in obese subjects. Thus, the role of C-Reactive Protein (CRP) in the early diagnosis of maternal infection is unproven (van de Laar et al., 2009). Raised lactate levels have been shown to be prognostic in sepsis outside pregnancy but their role in the management of maternal infections remains to be determined (Dellinger et al., 2013). The development of fetal heart abnormalities in women at risk of infective chorioamnionitis should raise concerns because it suggests that the fetus has become infected.

Pyrexia alone may be due to non-infective causes. Fever is a recognized side-effect of misoprostol (Lumbiganon *et al.*, 2002). The use of an epidural for pain relief in labour may be associated with a pyrexia (Fusi *et al.*, 1989; McGrady and Litchfield, 2004). This is particularly challenging because women with infective chorioamnionitis are more likely to be nulliparous and to experience dystocia, which is the same cohort of women likely to require epidural analgesia.

6.1.3 Prevalence

An estimated 1-4% of all births in the United States are complicated by chorioamnionitis but the prevalence frequently depends on the criteria used, the population studied, the hospital management of ruptured membranes and the gestational age at delivery (Tita and Andrews, 2010). The development of clinical chorioamnionitis carries risks of maternal sepsis, and of adverse fetal consequences both short-term and long-term.

In one study chorioamnionitis complicated 40-70% of preterm births with premature SROM or spontaneous labour (Yoon *et al.*, 2001). This compares with a reported 12% for primary CS at term when it is strongly associated with a prolonged SROM-delivery interval (Rouse *et al.*, 2004). A particular challenge is the timing of delivery if the woman is not in labour. The evidence to guide practice is scant and thus, the management of each case should be

individualised. Consideration should be given to a multidisciplinary consultation, particularly with the neonatal staff, in circumstances where the baby is premature.

6.1.4 Antibiotic Therapy

Due to the strong association between PPROM and infective chorioamnionitis, clinical studies have examined the role of prophylactic antibiotics such as ampicillin and erythromycin. The systematic reviews have shown that prophylactic antibiotics reduce maternal and neonatal infection in women with preterm SROM compared with those treated expectantly (Tita and Andrews, 2010). However, prophylactic antibiotics have not been shown to be beneficial in women with intact membranes and they may increase the risk of cerebral palsy (Kenyon *et al.*, 2008).

There are no trials comparing the efficacy of different antibiotic regimens for chorioamnionitis. The combination of ampicillin 2g IV every 6 hours, or penicillin 5 x 10⁶ units (3g approx.) plus gentamicin 1.5mg/Kg every 8 hours remains the most extensively studied regimen for treating chorioamnionitis (Duff, 1993). These antibiotics have excellent activity against the leading two causes of neonatal sepsis, GBS and E. coli and result in therapeutic concentrations in the fetus. However, there is no licensed/authorised presentation of ampicillin either PO or IV available in Ireland (The Health Products Regulatory Authority, HPRA). Unauthorised ampicillin dosage forms can be imported from abroad through licensed wholesalers. However, the prohibitive cost and uncertain continuity of supply make it a non-viable and unsustainable option for standard regimens. Second generation (cefuroxime) and third generation (e.g. cefotaxime, ceftriaxone) cephalosporins as well as extended spectrum penicillins (piperacillin) also provide coverage against the usual pathogenic organisms causing chorioamnionitis. Like ampicillin and gentamicin they cross the placenta and have comparable maternal and cord blood levels (Maberry et al., 1992). While cephalosporin use has been studies in preterm premature rupture of membranes (PPROM), there are no studies evaluating them in chorioamnionitis. Some authors suggest that they can be used for women with chorioamnionitis who are allergic to penicillins but have not developed anaphylaxis (Fishman and Gelber, 2012). It has been suggested that in women with a history of anaphylaxis to penicillin, clindamycin 900mg every 8 hours could serve as an alternative (Soper, 2009). This regimen, however, has not been studied. Given increasing resistance of GBS and S. aureus to clindamycin, vancomycin may be a reasonable choice (Verani et al., 2010).

Given the frequency of anaerobic organisms post-caesarean section, it may be prudent to add an antimicrobial with enhanced anaerobic activity such as metronidazole or clindamycin where delivery by CS is warranted (Newton, 1993). However, the only RCT to evaluate this regimen found no difference in rates of endometritis, though sample size may not have been sufficient to draw this conclusion (Maberry *et al.*, 1992).

It is important to note that if a woman already has suspected infection, prophylactic antibiotic regimes are not appropriate. If she develops evidence of infection despite prophylactic antibiotics then the same antibiotics should not be used therapeutically because it suggests that the organism responsible is not

sensitive to the antibiotic used prophylactically. If infective chorioamnionitis is diagnosed clinically, there is strong evidence that immediate broad-spectrum antibiotics reduce maternal and fetal complications (Tita and Andrews, 2010). The optimal antibiotic regime has not been established and current recommendations are based largely on consensus.

The key to the successful treatment of infective chorioamnionitis is the administration of appropriate intravenous antibiotics quickly in the correct dose. Once this has been implemented, depending on the clinical circumstances, consideration may have to be given to delivering the baby. The time-to-delivery interval after starting antibiotics has not been shown to affect morbidities (Tita and Andrews, 2010). The decision about the timing and mode of delivery should be individualised and taken by a senior obstetrician and, if appropriate, in consultation with the neonatal team.

The decision when to deliver depends, for example, on the woman's clinical condition, her response to antibiotics, the gestational age and her previous obstetric history. There is no international consensus about when and how the woman should be delivered. However, in cases of suspected clinical chorioamnionitis which has not responded to intravenous antibiotics it may be necessary to deliver the woman before fetal demise irrespective of gestation. After delivery in cases of suspected chorioamnionitis, the placenta should be cultured on the fetal and maternal surfaces for infection. The placenta and umbilical cord should be sent for histological examination.

6.2 Endometritis (with or without retained products of conception)

6.2.1 Background

Endometritis may be defined as infection of the decidua in the uterine cavity which occurs postpartum. It occurs when normal vaginal microflora cause ascending infection within the normally sterile uterine cavity. It may also be associated with adnexal or pelvic infection. It is more likely to occur if there are retained products of conception which acts as a nidus for infection. Thus, it is important always to inspect the placenta for completeness soon after delivery and to check that the uterine cavity is empty after delivery of the baby and placenta at CS. If retained products are suspected in the postpartum period then intravenous antibiotics should be administered in advance of any attempt to explore the uterine cavity surgically.

6.2.2 Diagnosis

Endometritis may present with "flu-like" symptoms, a purulent vaginal discharge, an associated secondary postpartum hemorrhage, abdominal pains and tenderness. It is a difficult diagnosis to confirm because organisms identified on vaginal swabs may not be those responsible for the intrauterine infection. Direct intrauterine sampling is technically challenging, and is not used in routine practice. The clinical manifestations may be non-specific and an exact diagnosis difficult to pin-point. A gentle vaginal examination should be performed to exclude a swab retained after a previous intervention.

6.2.3 Antibiotic Therapy

In a review of antibiotic regimes for endometritis a Cochrane Review included 39 trials with 4,221 participants (French and Smaill, 2004). A combination of gentamicin and clindamycin was found to be the most appropriate treatment. Regimens with activity against penicillin-resistant anaerobic bacteria were better than those without. There was no evidence that any one regime was associated with fewer side-effects. It also concluded that once endometritis has responded clinically to intravenous therapy, oral therapy was not needed. In four studies comparing one daily with thrice daily dosage of gentamicin there were fewer failures with once daily dosing (French and Smaill, 2004; Locksmith *et al.*, 2005).

6.3 Perineal infections postpartum

6.3.1 Background

Perineal trauma is common after vaginal childbirth and may occur spontaneously or following an episiotomy. Perineal infection postpartum is usually associated with trauma and the risk of infection is related to the location and the extent of the trauma. Anterior perineal trauma is associated with a low risk of morbidity or infection. Posterior perineal trauma may involve the posterior vaginal wall, perineal muscles or anal sphincter and is associated with the need for suturing, considerable morbidity postpartum and a higher risk of infection.

6.3.2 Prevalence

In one unit, the incidence of perineal trauma after a spontaneous vaginal delivery was 85% in nulliparous and 60% in multiparas (Coombe Women and Infants University Hospital, 2013). The overall incidence of $3^{rd}/4^{th}$ degree tears was 3% in nulliparous and 0.6% in multiparas giving an overall rate of 1.6%.

In a study of 341 women who sustained perineal tears and were contacted by telephone three weeks postpartum, 11% (n=39) had developed a perineal wound infection based on any two of the following markers: perineal pain, wound dehiscence or purulent vaginal discharge (Johnson, Thakar and Sultan, 2012). In a study of operative vaginal delivery in two UK hospitals, episiotomy was associated with a 5.1% risk of perineal infection (Macleod *et al.*, 2008). The risk of infection calculated will vary depending on the population studied, but there may also be confounding variables including but not limited to prolonged rupture of the membranes, prolonged labour and smoking. The risk is also likely to be underreported by maternity units because the diagnosis may be made in a primary care setting following discharge home.

6.3.3 Antibiotic therapy

In a retrospective chart review of 909 women who had an obstetric anal sphincter injury (OASIS), wound complications including infection occurred in 7.3% (n=66) (Stock *et al.*, 2013). The women who received intrapartum antibiotics were protected against postpartum perineal infection (OR 0.29, 95% CI 0.14 - 0.59, p=0.001). Half the cases of infection were readmitted. The risk

of infection is also increased by the presence of foreign bodies in the vagina such as retained swabs following perineal suturing (Lamont *et al.*, 2010).

A systematic review to assess the effectiveness of antibiotic prophylaxis for reducing maternal morbidity and side-effects in the 3rd and 4th degree tears during vaginal birth identified only one small trial on antibiotic prophylaxis with 147 participants (Buppasiri *et al.*, 2010). The study compared a single dose of a second generation cephalosporin with a placebo (Duggal *et al.*, 2008). Perineal wound complications were 8.2% in the antibiotic group and 24.1% in the placebo group (RR 0.34 95% CI 0.12 – 0.96). Although this is a small study, it does support the use of antibiotic prophylaxis in the small number of women whose delivery is complicated by a 3rd / 4th degree tear (<u>RCPI Clinical Guideline</u> No. 7 Management of Obstetric Anal Sphincter Injury).

If a woman presents postpartum with symptoms and signs suggestive of a perineal infection, close vaginal inspection should be accompanied by microbiological culture. With the woman's consent, careful vaginal and rectal examination should be performed so that any abnormalities such as fistula formation are identified.

6.4 Wound infection

6.4.1 Background

A wound infection is a common complication of caesarean section (CS) and may lead to maternal sepsis. In a national surveillance study in the United States the mean wound infection rate was 3.2%, ranging from 2.7% for low-risk women to 7.5% for high-risk women (National Nosocomial Infections Surveillance System, 2004). In a UK study across 14 hospitals, 9.6% (n=394) developed surgical infection post CS and 0.6% (n=23) required readmission (Wloch *et al.*, 2012). High wound infection rates are also a concern in the light of escalating CS rates nationally and internationally (Brick and Layte, 2009). Wound infection rates reported vary greatly because definitions are not standardised, the quality of surveillance varies, there are differences in the populations studied, prophylactic antibiotic policies differ and there may be differences in aseptic and surgical techniques. Decreasing average length of postnatal stay may decrease the risk of hospital-acquired infection but may lead to under-reporting of wound infections because they are diagnosed in primary care (Wilson *et al.*, 2013).

Necrotising fasciitis is a rare post-operative infection which progresses rapidly and has a high mortality rate (Gallup *et al.*, 2002). Its early signs may be subtle, with severe pain the most striking feature. The degree of reported pain is often not in keeping with clinical examination (Gallup *et al.*, 2002). Therefore a high index of suspicion is required for diagnosis in the early phase of the condition. Signs include subcutaneous oedema, skin discolouration and gas seen in the soft tissue on radiological imaging (Gallup *et al.*, 2002). Early surgical debridement and broad spectrum antibiotics are the key to successful treatment (Gallup *et al.*, 2002).

6.4.2 Prevalence

In an English study from 15 hospitals, the median length of stay post CS was 3 days (Wilson *et al.*, 2013). Out of the 4,107 CS included, 401 (9.8%) women developed a surgical site infection (SSI). Of these, only 21 (5.2%) were diagnosed during the admission and 24 (5.2%) were diagnosed during a readmission. The rate of SSI post CS varied from 5-18% due, in part, to variations in case ascertainment in primary care and due probably to differences in surgical practices. There are many confounding variables which determine the risk of wound infection. The risk is increased for emergency compared with elective CS and, an increased risk is associated with prolonged labour, prolonged rupture of the membranes and the number of vaginal examinations. An emergency CS may lead to inadequate aseptic preparations or a surgical field that is contaminated by ascending infection in to the uterine cavity.

A CS wound infection may be caused by multiple organisms but the common pathogens include *E. coli* and other gram negative rods, GBS, *Enterococcus faecalis*, *Staphylococcus aureus* and coagulase negative staphylococci, anaerobes (including bacteroides) and *Gardnerella vaginalis* (Smaill and Gyte, 2010). The risk of a CS wound infection is determined, on the one hand, by the decisions concerning the mode of delivery, and the other hand, by careful aseptic and surgical techniques (Mackeen, Berghella and Larsen, 2012; Corcoran *et al.*, 2013; Dahlke *et al.*, 2013). However, there is now a consensus that all women undergoing CS should receive a single intravenous dose of antibiotics before the start of surgery (Smaill and Gyte, 2010).

In a meta-analysis of 86 studies involving > 13,000 women, prophylactic antibiotics reduced the risk of wound infection (RR 0.39 95% CI 0.32 – 0.48). There was also a similar reduction in other serious maternal infectious complications. The findings were similar for both elective and emergency CS and whether the antibiotic was given before or after cord clamping. No conclusions could be drawn on the impact of prophylactic antibiotics on the infant or on bacterial drug resistance. Various antibiotic regimes have been used and there is emerging consensus that a single intravenous dose should be administered before the skin incision and that this does not affect the neonatal outcome adversely (Smaill and Gyte, 2010; Dahlke *et al.*, 2013).

A Canadian review of the evidence concluded that all women undergoing CS should receive a single dose of a first-generation cephalosporin 15-60 minutes before skin incision (van Schalkwyk, Van Eyk and Society of Obstetricians and Gynaecologists of Canada Infectious Diseases Committee, 2010). No additional doses were recommended. If the CS is prolonged or complicated, a second prophylactic dose is recommended and if the woman has a Body Mass Index (BMI) > 35.0 kg/m² consideration should be given to doubling the dose of antibiotic. While prophylactic antibiotics may prevent wound infections post CS and prevent wound infections progressing, alternative antibiotic regimes may be required therapeutically following culture of the wound site and, if appropriate, culture of other sites. Sample antibiotic regimens are included in Appendix Three.

6.5 Infective Mastitis

6.5.1 Background

Mastitis is an inflammatory condition of the breast, usually associated with lactation (WHO, 2000). The primary cause of lactational mastitis is milk stasis which may or may not be associated with infection. Infective mastitis usually presents within the first 6 weeks of breastfeeding although it can develop during weaning (Dixon and Khan, 2011). The most common organism responsible is staphylococcus aureus, including strains of methicillin resistant *Staphlococcus aureus* (MRSA), particularly if the infection is acquired in hospital (Dixon and Khan, 2011; Branch-Elliman *et al.*, 2012).

6.5.2. Diagnosis

The clinical symptoms of infective mastitis include unilateral breast pain, redness and swelling, which may be associated with a pyrexia and flu-like symptoms (Jahanfar, Ng and Teng, 2013). On examination there may be unilateral wedge-shaped erythema, oedema and tenderness of the affected breast. In about 5-10% of cases, a breast abscess may develop particularly if the initial management is suboptimal (Dixon and Khan, 2011). In cases of abscess formation, a fluctuating, tender and hard breast mass is found with overlying erythema (Jahanfar, Ng and Teng, 2013).

In contrast, breast engorgement is normally bilateral and uncomfortable rather than acutely painful. It may be difficult, however, to distinguish between infective and non-infective mastitis because both are associated with milk stasis. To help differentiate, the milk leucocyte count, bacteria colony count and microbiological culture may assist. Ideally, milk should be sent for culture as it may lead to modification of antibiotic therapy. A leucocyte count $> 10^6/\text{mL}$ and a bacteria count $> 10^3/\text{mL}$ of milk both support the diagnosis of infective mastitis (Thomsen, Espersen and Maigaard, 1984; Jahanfar, Ng and Teng, 2013).

Difficulty in collection of a "sterile" milk sample that has not been contaminated by skin bacteria during collection hinders correct identification of pathogens. Despite careful collection techniques half of milk cultures may be sterile while others show "normal" colony counts from 0 to 2,500 colonies per ml (WHO, 2000). Thus the presence of bacteria in milk does not necessarily indicate infection, even if they are not skin contaminants (WHO, 2000).

6.5.3. Antibiotic Therapy

Infective mastitis should be treated with appropriate oral antibiotics and by promoting milk flow from the engorged segment by continuation of breastfeeding or use of a breast pump. Delays in instituting the appropriate treatment may lead to the discontinuation of breastfeeding, ongoing pain, breast tissue damage, breast abscess formation, recurrence or, in a small number of cases, sepsis. Treating any postpartum infection promptly and effectively can have a positive effect on the continuation of breastfeeding. A Danish study found that a larger proportion (21%) of women with a postpartum infection stopped breastfeeding within four weeks after delivery compared to women without infection (Ahnfeldt-Mollerup *et al.*, 2012). This points to the need for specific

support for lactating women when infectious complications are suspected (http://www.hse.ie/portal/eng/health/az/M/Mastitis-breastfeeding-/).

A 2013 Cochrane Review on antibiotics for mastitis in breastfeeding women found little consensus on antibiotic prescribing (Jahanfar, Ng and Teng, 2013). Only two small studies were eligible for inclusion and they were not suitable for a meta-analysis. The evidence was insufficient to draw any firm conclusions. The evidence that is available does suggest that antibiotics achieve the fastest symptom clearance and prevent the development of an abscess.

In choosing an antibiotic for infective mastitis a number of issues need to be taken into account such as the likely organism and the probable sensitivity, the need to avoid the development of resistance to broad-spectrum antibiotics, the impact on the neonate, the side-effects and the cost, as well as the clinical impact of antibiotics on symptoms, the risk of abscess formation and the risk of recurrence. The antibiotic regime should be reviewed when the results of the microbiological milk cultures become available.

Postpartum, women and infants are at increased risk of community-acquired (CA) MRSA. In recent years MRSA has been isolated from the milk of women with mastitis and from aspirates of breast abscesses (Amir, 2014). Clinicians should be aware of the likelihood of CA-MRSA in their area and increase microbiological testing of milk if the risk of MRSA is high (Amir, 2014).

If the woman is unwell systemically, if a breast abscess is suspected or if the symptoms do not settle on antibiotics, the woman should be referred to a specialist with an interest in infective mastitis. When a breast abscess is suspected clinically, an ultrasound examination may be useful because it may identify collections of pus that might otherwise be missed (Dixon and Khan, 2011). Specialist practices have developed guidelines for the management of breast abscesses depending on whether the skin overlying the abscess is normal or thinned or necrotic (Dixon and Khan, 2011). In women with an inflammatory lesion that persists despite appropriate management, the possibility of a breast tumor should be considered and the woman referred urgently to a specialist breast clinic.

This guideline is not intended to address the management of non-infective mastitis and further information from the Health Services Executive is available at http://www.hse.ie/portal/eng/health/az/M/Mastitis-breastfeeding-/.

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8. Implementation Strategy

- Dissemination by the HSE Acute Hospitals Directorate to all acute hospitals and all maternity units, and to the community services.
- Distribution of guideline to all Members of the Institute of Obstetricians and Gynaecologists.
- Implementation through HSE Obstetrics and Gynaecology Programme Implementation Boards.
- Distribution to other interested parties and professional bodies

9. Key Metrics

- 1. Incidence of maternal bacteraemia.
- 2. Incidence of neonatal bacteraemia.
- 3. Incidence of severe maternal sepsis.
- 4. Number of cases of breast abscess requiring surgical drainage.
- 5. Number of cases of wound abscess requiring surgical drainage.
- 6. Number of cases required postpartum exploration of the genital tract for retained products.
- 7. Number of cases of vaginal swabs retained after perineal repair.

10. Qualifying Statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advising women of their choices and ensure informed consent is obtained.
- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.

11. Glossary of Terms and Abbreviations

Irish Maternity Early Warning System (IMEWS) is a nationally agreed scoring system developed for early detection of life threatening illness in hospital in-patient care in obstetric and gynaecological services of a woman with a confirmed clinical pregnancy and up to 42 days in the postnatal period.

Systemic Inflammatory Response Syndrome (SIRS) is the presence of 2 or more SIRS criteria

Infection is a pathological process caused by invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic micro-organisms. It is important to point out that, frequently, infection is strongly suspected without being microbiologically confirmed.

Sepsis is the clinical syndrome defined by the presence of both infection and a systemic inflammatory response syndrome (SIRS). However, since infection cannot be always microbiologically confirmed, the diagnostic criteria are infection, suspected or confirmed and the presence of 2 or more SIRS criteria.

BMI Body Mass Index
CA Community-Acquired
CRP C Reactive Protein
CS Caesarean Section
GBS Group B Streptococcus
EWS Early Warning Score

IMEWS Irish Maternity Early Warning System

IV Intravenous

MRSA Methicillin Resistant Staphlococcus aureus

NEWS National Early Warning System
OASIS Obstetric and Sphincter Injury
PO per os (oral administration)

PPROM Preterm Premature Rupture of Membranes

SROM Spontaneous Rupture of Membranes

SSC Surviving Sepsis Campaign SSI Surgical Site Infection

TDM Therapeutic Drug Monitoring WHO World Health Organisation

12. Appendices

Appendix One: Clinical Guidelines and Reports

National Clinical Effectiveness Committee (NCEC) Guidelines

- i. National Clinical Guideline No. 1 National Early Warning Score
- ii. National Clinical Guideline No. 2 Prevention and Control MRSA
- iii. National Clinical Guideline No. 3 Clostridium difficile
- iv. <u>National Clinical Guideline No. 4 Irish Maternity Early Warning System</u>
 (IMEWS)
- v. National Clinical Guideline No. 5 Clinical Handover in Maternity Services
- vi. National Clinical Guideline No. 6 Sepsis Management

Obstetrics and Gynaecology Clinical Programme Guidelines

- i. Preterm Prelabour Rupture of membranes (PPROM), Guideline No. 24
- ii. Guidelines for the Critically Ill Woman in Obstetrics, Guideline No. 30
- iii. Management of Obstetric Anal Sphincter Injury, Guideline No. 8
- iv. Management of Second Trimester Miscarriage, Guideline No. 29

Other resources

- i. HIV and pregnancy
- ii. Mastitis and breastfeeding information

HSE Health Prevention Surveillance Centre

- i. Guidance on the Management of Pregnant Women with Suspected Influenza
- ii. Advice of the influenza subgroup of the scientific advisory committee, HPSC on the use of antivirals in pregnancy, for patients with influenza
- iii. Influenza in each Trimester of Pregnancy
- iv. Toxoplasmosis and Pregnancy

Irish College of General Practitioners (ICGP)

i. www.antibioticprescribing.ie/

HIQA

National Standards for the Prevention and Control of Healthcare Associated
 Infections

Appendix Two: IMEWS Version 1.2

Please see the following link for the latest version; http://bit.do/IMEWS_Chart

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE Hospital Name: Ward: Irish Mater		
Imple Com	ALL IMEWS TRIGGE sider context and complete full clinic ement measures to reduce triggers if plete a full set of observations on IM m the Midwife in charge.	al assessment. f appropriate.
	•	
1 YELLOW Repeat full set of observations on IMEWS after 30 and before 60 minutes.	2 YELLOWS OR 1 PINK Call the obstetrician to review. Repeat a full set of observations after 30 minutes.	≥2 YELLOWS OR ≥2 PINKS Call the obstetrician and request immediate review. Repeat a full set of observations within 15 minutes or monitor continuously.
	ALL IMEWS TRIGGE Liaise with the Midwife in cl Document all communication in Redefined plan of care Ongoing frequency of observa	harge ncluding:
2. If action is not carrie senior obstetrician o		vife in charge must contact the
Are 2 or more of the follow SIRS criteria present? • Temperature ≥38°C or <36°C • Respiratory rate ≥20 breaths • Heart rate ≥100 beats per mir • White cell count >16.9 or <4.0 • Bedside glucose >7.7 mmol/L (in the absence of diabetes) • Acutely altered mental status	per min is suspected after medical review	Intervention: within one hour COMPLETE SEPSIS SIX 1. Appropriate cultures* 2. FBC +/- lactate 3. Start urine output chart 4. Maintain O ₂ (94-98%) 5. Consider IV fluid bolus** 6. IV antibiotics *e.g. blood, wound, vaginal swab, urine etc *exercise caution in presence of pre-eclampsia

												I	MEWS	T	riggers	Key			
Woman	ı's Name:						September 1		IN	1EWS T	rigger	N	Vormal Valu	es	Yello	w Zone		Pink	Zone
Date of Birth:						Respiratory rate (bpm)			1)	11-19		20-24			≤10 or ≥25				
							_		SpO ₂	S-41/1-1300			96-100			-			95
Healthcare Record No:		1	Temperature (°C)				36.0-37.4		35.1-35.9 or 37.5-37.9			≤35 or ≥38							
Docum	ent Number	(eg. 1	, 2):						Maternal HR (BPM)			+	60-99	_	50-59 o			<50 or ≥120	
Bookin	g BP:	_/_						A	Systolic BP (mmHg) Diastolic BP (mmHg)			_	100-139 50-89	-	90-99 c	or 90-9		<90 or≥160	
	on at Booki								-	60	(IIIIIIrig	+	909	-			9	<40 or ≥100 Voice, Pain or	
									AVPU				Alert			-		Unres	ponsive
C	ontact app	ropria	te doc	tor fo	early	interv	entior	if the	wom a	n trigg	ers on	e P	INK or tv	NO	YELLOW	zones	at ar	y one	time
Year:	Date :				_												_		
	Time : ≥25							Į.		//							1/1		≥25
esp per	20-24																		20-24
Resp. Rate per min	11-19																		11-19
	≤10 96-100%																		≤10 96-100%
SpO ₂ only if Resp.Rate	96-100% ≤95%							0											≤95%
	≥38.0																		≥38.0
Temp	37.5-37.9 36.0-37.4																		37.5-37.9 36.0-37.4
e G	35.1-35.9																		35.1-35.9
	≤35.0																		≤35.0
_	— 120 —																		120
Mate	— 110 — — 100 —																		110 100
Maternal Heart Rate	90																		90
Hea	— 80 —				-												+	+	80
콨	— 70 — — 60 —																		70 60
8	— 50 —									8 4								i i	50
	470											_		_					470
	— 170 — — 160 —																		170 160
Sy	— 150 —									-							-		150
stoll	— 140 — — 130 —																		140 130
C BIO	— 120 —				-											-	1		120
Systolic Blood Pressure	— 110 —																_		110
ress	— 100 — — 90 —																		90
ure	— 80 —																		80
	— 70 —																		70
Dia	— 110 —																		110
stoli	— 100 —																		100
Diastolic Blood Pressure	— 90 — — 80 —																		90
00 00	— 70 —				-												1		70
Pres	— 60 — — 50 —																		60 50
sure	— 40 —																		40
	Protein																		Protein
Urine	Glucose							1											Glucose
6	Other																		Other
Pain	Score 0-10				Ī	Ì												İ	Pain Score
	Alert (A)																		A
VPU Neuro Response	Voice (V)																		V P
	Pain (P) Unresponsive (U)																		U
52000 0000	llow Zones																		Total yellow zones
	ink Zones																		Total pink zones
				_	+	+	+	-								_	-		

Appendix Three: Sample antibiotic regimens

NOTE: These sample antibiotic regimes were developed following review of the regimes in all 19 maternity units. They may be customised locally depending on other factors such as antibiotic sensitivities and clinical practice.

A. Antibiotics for chorioamnionitis

- If a diagnosis of chorioamnionitis is suspected, treatment with antibiotics should be started as a matter of urgency after microbiological samples have been taken. Co-amoxiclav 1.2 g IV every 8 hours combined with gentamicin 5mg/kg IV per day is a suitable empirical choice. Normal gentamicin precautions including Therapeutic Drug Monitoring (TDM) should be carried out.
- If the woman is allergic to penicillin, the co-amoxiclav can be substituted with clindamycin 900 mg IV every 8 hours. When the microbiological culture results become available, the antibiotic regimen should be reviewed by the clinical team in light of the pathogens cultured and local antibiotic sensitivities.
- Depending on the laboratory results and the clinical course over the first 48
 hours it may be necessary to add additional antibiotics. For example, IV
 vancomycin 1g IV every twelve hours may be considered if GBS is suspected
 and resistance is a concern. Consider vancomycin TDM.
- If the woman is improving, the clinician may decide that oral antibiotic therapy is now appropriate. The woman can be started on a course of coamoxiclav 625 mg every 8 hours (if this covers local sensitivity data). Duration of treatment depends on the clinical picture but should be minimised to avoid potential complications e.g. *C. difficile* and neonatal necrotising enterocolitis. If available, contact the consultant microbiologist or antimicrobial pharmacist for suitable PO switch for penicillin-allergic women.
- Clinicians should exercise their discretion with respect to length of treatment.

B. Antibiotics for endometritis

- For women presenting with mild endometritis a five to seven day course of co-amoxiclav 625 mg every 8 hours may be prescribed. For women who are allergic to penicillin, clindamycin 300 mg PO every 6 hours may be prescribed. The woman should be advised to return for review if symptoms do not improve.
- For severe endometritis, the woman should be commenced on clindamycin 600-900 mg IV every 8 hours and Gentamicin 5 mg/Kg/day IV. This regimen suits both penicillin allergic and non-allergic women. Normal gentamicin precautions including TDM should be carried out. In severe disease or if symptoms do not improve, the treatment may be stepped up to include amoxicillin IV 1 g every 8 hours (where allergy status allows) and/or vancomycin 1 g every 12 hours IV. The latter should be given slowly over at least 120 minutes. Consider vancomycin TDM.
- When clinically appropriate, the antibiotics may be switched to oral therapy.

C. Antibiotics for perineal infection

- Mild episiotomy or perineal wound infections can be treated with oral antibiotics with good anaerobic cover e.g. co-amoxiclav 625 mg three times daily;
- Women allergic to penicillin may be treated with oral clindamycin 300 mg every 6 hours.
- If the infection is more severe, the woman may be admitted for IV antibiotic treatment after samples are taken for culture. Treatment options include co-amoxiclav 1.2g three times IV or, the combination of amoxicillin 1g every 8 hours IV plus metronidazole 500mg every 8 hours IV plus gentamicin 5mg/Kg/day IV for more severe infections or perineal repairs where there is already infection. Normal gentamicin precautions including TDM should be carried out.
- For penicillin allergies, the amoxicillin may be replaced by clindamycin 900 mg IV every 8 hours. The duration of treatment and route of administration depend on severity of the disease.

D. Antibiotics for wound infection

- Where treatment is required, flucloxacillin 500 mg-1g PO every 6 hours, or clindamycin 300 mg PO every 6 hours (penicillin allergy) for 5-7 days may be sufficient. Oral treatment may be stepped up to include metronidazole 400 mg every 8 hours or co-amoxiclav 375-625 mg every 8 hours if deemed appropriate. Cellulitis, if present, should be marked and examined for extension regularly and pus should be drained.
- If the woman is systemically unwell, treatment may be initiated IV with coamoxiclav 1.2g every 8 hours and gentamicin 5 mg/Kg per day. Clindamycin 900 mg IV every 8 hours should replace the co-amoxiclav in women allergic to penicillin. Normal gentamicin precautions including TDM should be carried out. IV treatment should be switched to PO as soon as the woman is apvrexial and the cellulitis has resolved.
- IV treatment may be required for longer if symptoms are severe.

E. Antibiotics for infective mastitis

- For mild infections, course of flucloxacillin 500 mg-1g PO every 6 hours for 7-14 days should be prescribed.
- Clindamycin 300 mg every 6 hours may be prescribed if the woman is allergic to penicillin. The woman should be advised to continue breastfeeding.
- For severe infections and where there is an abscess present, the woman should be commenced on IV treatment.
- Flucloxacillin IV 1-2 g or clindamycin 600 mg (penicillin allergy) every 6 hours should be commenced.
- Amoxicillin 1 g every 8 hours IV and or gentamicin 5 mg/Kg per day may be added if deemed appropriate. Normal gentamicin precautions including TDM should be carried out. IV treatment should be continued for 48-72 hours and reviewed when microbiological results become available.
- IV to PO switch should occur as soon as clinically possible