

The Febrile Pregnant Woman

The following section is entitled “**The Febrile Pregnant Woman**”. This section deals with some of the basic concepts important in caring for infectious disease that are commonly seen in pregnant and postpartum women. The section begins with a *learner handout* with space for the learner to make their own notes. The *learner handout* is then followed by a *teaching script* for the educator, some cases for discussion and a brief bibliography for this topic.

THE FEBRILE PREGNANT WOMAN

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PREGNANT WOMAN**

For the most part, pregnant women get the same infections as nonpregnant individuals and can receive similar treatment.

However, some important pregnancy related issues must be considered in the assessment and treatment of the febrile pregnant woman.

Antibiotics

Most of the commonly used antibiotics have a good track record in pregnancy.

However, the tetracyclines and the fluoroquinolones (e.g. Ciprofloxacin) should be avoided when possible in pregnancy.

Use of penicillins, cephalosporins, and amnioglycosides is justifiable when indicated.

The Common Cold

Symptomatic relief of upper respiratory tract infections can be provided through the use of acetaminophen (Tylenol[®]), pseudoephedrine (Sudafed[®]), codeine containing cough syrups, and dephenhydramine (Benadryl[®]).

Do not overdiagnose sinusitis in pregnancy.

TORCH and Parvovirus

Parvovirus and the TORCH infections (Toxoplasmosis, Rubella, CMV, Herpes and Syphilis) can cause fetal mutation and disease and should be considered in every febrile pregnant woman.

Primary Varicella Infection

Primary varicella infection in pregnancy is associated with a high risk of pneumonitis. Non-immune pregnant women exposed to varicella should be treated prophylactically with VZIG.

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Viral Hepatitis

The most significant risk of hepatitis B and C in pregnancy is that of maternal-fetal transmission.

Hepatitis E however, can take a particularly fulminant course in pregnancy that often results in hepatic failure.

HIV

The course of HIV is not affected by pregnancy and the main risk HIV represents to the fetus is that of maternal-fetal transmission.

Maternal-fetal transmission without intervention is on the order of 30%.

Use of AZT decreases the maternal-fetal transmission from 30% to 8%.

Triple therapy probably decreases the risk of transmission even further.

HIV

AZT is well tolerated by the fetus.

In general, prophylaxis for opportunistic infections should be given in the same manner for pregnant women with HIV infection as for nonpregnant women.

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Urinary Tract Infections

Asymptomatic bacteriuria (ASB) should be screened for in all pregnant women and treated because of the strong relationship between ASB and pyelonephritis in pregnancy.

Pyelonephritis in pregnancy is associated with preterm labor and pulmonary edema and therefore, should generally be treated as an inpatient.

Urinary Tract Infections

Any woman who has had pyelonephritis in pregnancy warrants subsequent antibiotic prophylaxis during the pregnancy because of a high recurrence risk.

Listeria

Pregnant women, like the elderly and alcoholic, have a predisposition toward listeria septicemia.

This is a rapidly progressive and life threatening infection that often results in fetal loss.

Treatment must be with ampicillin as cephalosporins do not cover this organism.

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Chorioamnionitis

Chorioamnionitis presents with a maternal fever, fetal tachycardia and possibly uterine tenderness.

The diagnosis is made clinically and by amniocentesis.

Treatment is always delivery.

Endometritis

Prolonged rupture of membranes, instrumentation and cesarean section are all risk factors for endometritis.

Endometritis in the first few days postpartum is usually caused by ascending Group A/B streptococci, Enterobacteriaceae and Bacteroides.

Endometritis presenting more than 7 days postpartum may be caused by chlamydia or mycoplasma *hominis*.

Endometritis

Treatment regimens for endometritis occurring in the first 48 hours include: cefoxitin and doxycycline, gentamycin and clindamycin; or ampicillin/sulbactam and doxycycline.

Once a patient has been afebrile for 48 hours, the antibiotics may be discontinued and no oral antibiotic course is necessary.

However, endometritis presenting more than 7 days postpartum warrants a complete 14 day course of doxycycline.

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Teaching Script

For the most part, pregnant women get the same infections as non-pregnant individuals and can receive similar treatments for them. However, some important pregnancy related issues must be considered in the assessment and treatment of the febrile pregnant woman. These pregnancy related issues include the facts that:

- 1) pregnant women are predisposed to certain infections,
- 2) the course of some infections is altered by pregnancy,
- 3) in dealing with infections in pregnancy, the issue of maternal-fetal transmission must always be considered, and
- 4) the use of some antimicrobial agents can have an impact upon the fetus.

Rather than focus on all infections in pregnancy, this lecture focuses on important and unique aspects of infections in pregnancy.

Antimicrobials

Most of the commonly used antibiotics have a good track record in pregnancy. The two antibiotic types which should be avoided during pregnancy are the tetracyclines and the fluoroquinolones (ie, ciprofloxacin, norfloxacin, et al). Tetracyclines will stain fetal teeth and bone when used after the first trimester. Fluoroquinolones impair cartilage formation in dogs. The penicillins, cephalosporins, and aminoglycosides do not appear to have significant fetal effects. The macrolides erythromycin and azithromycin (Zithromax[®]) appear to be safe in pregnancy but clarithromycin (Biaxin[®]) has some concerning animal data suggesting it should be used only in special circumstances in pregnancy. There is not a large experience with systemic antifungals in pregnancy, but it is known that ketoconazole can cause significant fetal

abnormalities when used in the first trimester and therefore should be avoided. However, topical antifungals for vaginal candidiasis may be used in pregnancy.

The Common Cold

Symptomatic relief of viral upper respiratory tract infections during pregnancy can be provided through the use of acetaminophen, pseudoephedrine, codeine containing cough syrups, and diphenhydramine. Most women in the third trimester of pregnancy will experience some nasal congestion due to increased blood flow through the nasal mucosa and the diagnosis of sinusitis in pregnancy should not be made simply on the basis of this complaint alone.

TORCHeS and Parvovirus

The ToRCHeS infections are Toxoplasmosis, Rubella, Cytomegalovirus, Herpes Simplex Virus, and Syphilis. All of these are infections that can cause fetal mutation and disease if a woman has a primary systemic infection with these pathogens during her pregnancy. Parvovirus, the pathogen responsible for Fifth's disease, is now also known to cause fetal hydrops if the mother is infected with this virus during pregnancy. Although there is no specific treatment for the majority of these infections, their profound impact upon the fetus makes them important considerations in the differential diagnosis of any febrile illness during pregnancy. The specific presentations and diagnostic features of these infections is beyond the scope of these lectures.

Varicella

Primary infection with varicella zoster (Chicken Pox) in pregnancy is associated with a high incidence of varicella pneumonia, as well as a potential for fetal infection. All women without immunity to varicella who are exposed to varicella should receive VZIG (varicella zoster immune globulin). If evidence of varicella infection develops, systemic Acyclovir (Zovirax[®]) should be initiated promptly.

Viral Hepatitis

The course of hepatitis B and C infections is unchanged by pregnancy. The most significant risk of viral hepatitis B and C during pregnancy is that of maternal-fetal transmission. Infants of mothers who are infectious for hepatitis B should also receive hepatitis B immune globulin at birth. Hepatitis B has a vertical transmission rate (without interventions) of 10-20%. This rate increases to 90% in the presence of the Hepatitis B_eAg. Hepatitis C virus has a lower rate of transmission estimated at 5% but varies considerably with maternal viral load. All infants in the US receive hepatitis B vaccine at birth. Infants born to mothers who are infectious for Hepatitis B should also receive Hepatitis B immune globulin at birth. Although the course of Hepatitis B and C is not affected by pregnancy acute Hepatitis E infection in pregnancy can have a particularly fulminant course that results in death from hepatic failure in 17% of patients.

HIV

The course of HIV infection is not affected by pregnancy. The main risk HIV represents to the fetus is that of maternal-fetal transmission. Maternal-fetal transmission without intervention appears to be on the order of 30%. Use of AZT (orally) by the mother during the course of the pregnancy, during labor (intravenously), and given for six weeks postpartum to the newborn decreases the transmission rate of HIV infection from 30% to 8%. AZT appears to be very well tolerated by the fetus. The remarkable efficacy of AZT in decreasing maternal-fetal transmission of HIV has been a major step forward in prevention of pediatric HIV. The safety of other anti-retroviral agents during pregnancy remains to be established but many individuals believe aggressive 'triple therapy' that includes AZT is justified because of the relationship between maternal viral load and vertical transmission.

In general, prophylaxis for opportunistic infection (OI) should be given in the same manner for pregnant women with HIV infection as they are for non-pregnant women with HIV infection. Discussion of the details of antiretroviral drug therapy and OI prophylaxis during

pregnancy is beyond the scope of this lecture, but it is worth mentioning here that despite theoretical concerns about use of trimethoprim sulfamethoxazole (Bactrim[®]) in pregnancy, the use of TMP/SMX for prevention of pneumocystis carinii infection is well tolerated by the fetus.

Urinary Tract Infections

All women should be screened for asymptomatic bacteriuria at the beginning of their pregnancy with a urine culture. Any pregnant woman with greater than 10^4 colony forming units per cc in her urine should be treated with antibiotics even in the absence of symptoms.

Treatment of asymptomatic bacteriuria in pregnancy is done because there is a strong association between asymptomatic bacteriuria and the development of pyelonephritis during pregnancy. Pyelonephritis during pregnancy can be associated with preterm labor and pulmonary edema, and our group sees no role for outpatient therapy of pyelonephritis during pregnancy.

In addition, any woman who has developed pyelonephritis during pregnancy should be placed on daily prophylactic antibiotics to prevent further urinary infections during pregnancy. This prophylaxis is necessary because of a very high recurrence risk of pyelonephritis during gestation. Acceptable antibiotic prophylactic regimens include once daily nitrofurantoin (macrochantin[®]), amoxicillin (Amoxil[®]) or cephalexin (Keflex[®]).

Listeria

Pregnant women, like the elderly and the alcoholic, have a predisposition towards Listeria septicemia. The reason that this infection occurs more frequently in pregnant women is not known, but it is believed to be related to some alterations in cell mediated immunity that occur during pregnancy to accommodate the growing fetus. Listeria monocytogenes in pregnant women can present initially as a mild flu-like illness but it is a very virulent organism that can lead to septic shock. Infection with Listeria has a significant mortality and is very often associated with fetal loss. Awareness of the possibility of Listeria sepsis in pregnant women is important because Listeria is not susceptible to the cephalosporins. The drug of choice to treat Listeria sepsis is ampicillin. Therefore, whenever treating high fevers in hemodynamically

unstable pregnant women *Listeria* infection needs to be in the differential diagnosis and ampicillin strongly considered as part of the antibiotic regimen.

Chorioamnionitis, Endometritis and Septic Pelvic Thrombophlebitis (SPT)

Chorioamnionitis is an infection of the amniotic sac and fluid. Diagnosis of this condition is usually the domain of the obstetrician. It tends to present with mild uterine tenderness and maternal fever. Fetal heart tracings done on patients with chorioamnionitis may show fetal tachycardia. The diagnosis is usually made clinically but can be confirmed by amniocentesis. In the setting of chorioamnionitis, gram stain of the amniotic fluid will usually reveal a pathogen and amniotic fluid glucose will usually be < 15 mg/dL. The presence of white blood cells in the amniotic fluid alone is not enough to make the diagnosis. Treatment of chorioamnionitis is always delivery as antibiotics alone will not eradicate chorioamnionitis.

Endometritis is an infection that occurs postpartum only. It is an infection of the endometrium. Risk factors for this infection include prolonged rupture of membranes, delivery requiring the use of forceps, and cesarean section. It is an ascending polymicrobial infection. In early postpartum endometritis (the first 48 hours) the associated pathogens are typically genitourinary organisms, such as Group A and B Streptococci, Enterobacteriaceae (*E. coli*, *Klebsiella*, et al.) and *Bacteroides fragilis*. If the infection presents 'later', (that is to say greater than one week postpartum), alternative pathogens such as chlamydia or *Mycoplasma hominis* need to be considered. Treatment regimens for early postpartum endometritis (the first forty-eight hours) include all of the following: 1) cefoxitin (Mefoxin[®]) and doxycycline (Vibramycin[®]), 2) ampicillin, gentamycin and clindamycin 3) ampicillin-sulbactam (Unasyn[®]) and doxycycline. Endometritis presenting greater than one week postpartum can often be treated with a 14-day course of doxycycline alone or with metronidazole. Interestingly, in the treatment of early postpartum endometritis, once a patient has been afebrile for 48 hours, antibiotics may be discontinued altogether and no oral antibiotic treatment is necessary.

Persistent fevers in the setting of what otherwise appears to be appropriately treated postpartum endometritis can be a sign of an entity known as septic pelvic thrombophlebitis (SPT). Classically this entity presents as persistent postpartum fevers during which a patient does not appear to be ill. The traditional treatment for SPT has been an empiric seven to ten day course of intravenous heparin. The heparin is used without any confirmatory diagnostic testing. It has been the practice of our group however to try to confirm the diagnosis of septic pelvic thrombophlebitis through the use of CT scans or MRVs of the pelvis prior to embarking upon heparin therapy. We believe that a short course of heparin is unlikely to have any important therapeutic benefits and if investigations do confirm the presence of pelvic clot, we anticoagulate the patient for a three month period as we would do for any other deep venous thrombosis. If pelvic thrombosis is not seen, other sources of fever are to be considered, such as abscess, hematomas, drug fever and necrotizing fasciitis.

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Case Discussion

Case #1

The patient is a 35-year old woman you have been seeing for a number of years for general medical care. She is now in the 6th week of her first pregnancy. She calls you stating that her obstetrician's nurse just called her stating that a routine urine test showed infection. The nurse said this was nothing to worry about, and that the obstetrician would take care of it when he returned in two weeks. The patient now calls you for advice because she is worried. She denies urinary symptoms. You phone the obstetrician's nurse who states that the urinalysis was unremarkable with only 1-2 white blood cells/hpf, however, culture revealed 10^5 E. coli, sensitive to all antibiotics except ampicillin. Your records show that the patient has been treated twice over the past 10 years for cystitis.

What is the most likely diagnosis?

What is the appropriate management of this patient?

Six months later, now in her 30th gestational week, the patient comes to your office with complaints of two days of nausea but no vomiting, dysuria, urinary frequency and hematuria. She notes increasing mid-back and flank discomfort on the right. On exam her temperature is 38.5E C, pulse is 105/min, BP is 110/70 supine without significant change when she stands. She appears only mildly ill. There is marked right costovertebral angle tenderness. Urinalysis reveals cloudy, red urine, >50 white blood cells/hpf and many bacteria.

What is the appropriate management of this patient?

What might have been done at the time asymptomatic bacteriuria was identified in an attempt to prevent the current problem?

What complications of pyelonephritis in pregnancy is this woman at risk for?

After successfully treating this woman's pyelonephritis are there any additional concerns to be addressed?

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Case Discussion

Case #2

The Common Cold

While on call for the weekend, a 21-year-old patient in your practice calls with a complaint of two days of nasal congestion, sore throat and malaise. She is 12 weeks into her first pregnancy and wants to know what she can take for this cold. She tried to call her obstetrician but she cannot get through to their answering service.

Key Points to Review

- 1. It should be emphasized to every patient seeking medical treatment for upper respiratory tract infections that treatment for these conditions provides only symptomatic relief and does not shorten the course of the illness.*
- 2. Medications that have excellent pregnancy data that are commonly used for the common cold include Acetaminophen (Tylenol[®]), Pseudoephedrine (Sudafed[®]), Dextromethaphen (DM), Guanefasine (the active ingredient in Robitussin[®]) and Afrin[®] nasal spray. Diphenhydramine (Benadryl[®]) has some concerning data that suggests an association with cleft palate if used during the first trimester but its use during the rest of pregnancy appears to be reasonable. Use of the newer antihistamines such as Cetirizine (Zyrtec[®]), Fexofenadine (Allegra[®]) and Loratidine (Claritin[®]) should occur only when strongly indicated because although animal data looks very good for these medications there is a paucity of human pregnancy data at this time. Use of Atropine nasal spray (Atrovent[®] nasal spray) and the inhaled nasal steroids appears to be supported by presently available data.*
- 3. Many women have some symptoms of sinus congestion especially in the third trimester and this, in itself, may not require treatment depending upon the severity of symptoms.*

- Calhoun BC, Brost B: Emergency management of sudden puerperal fever. *Obstetrics and Gynecology Clinics of North America* 1995; 22(2): 357-67.
- Casey BM, Cox SM: Chorioamnionitis and endometritis. *Infectious Disease Clinics of North America* 1997; 11(1):203-222.
- Cherubin CE, Appleman MD, Heseltire PNR, et al. Epidemiological spectrum and current treatment of listeriosis. *Rev Infect Dis* 1991; 13:1108.
- Craig S, Permezel M, Doyle L, et al: Perinatal infection with *Listeria Monocytogenes*. *Aust. NZ J Obstet Gynaecol* 1996; 36(3): 286-90.
- Duff P: Pathophysiology and management of postcesarean endomyometritis. *Obstet Gynecol* 1986; 67:269-76.
- Eschenbach D. Amniotic fluid infection is a fetal infection. *Prenat Neonat Med* 1998; 3:76-81.
- Floreani A, Paternoster D, Zappala F: Hepatitis C virus infection in pregnancy. *British Journal of Obstetrics and Gynaecology* 1996; 103:325-9.
- *Garland SM, O'Reilly MA: The risks and benefits of antimicrobial therapy in pregnancy. (Review) *Drug Safety* 1995; 13(3):188-205.**
- Gellin BG, Broome CV: Listeriosis. *JAMA* 1989; 261(9): 1313-20.
- Gilbert GL: Infectious diseases. *Bailliere's Clinical Obstetrics and Gynaecology* 1995; 9(3):529-43.
- Lynch CM, Pinelli DM, Cruse CW, Spellacy WN, Sinnott JT, Shashy RG. Maternal death from postpartum necrotizing fasciitis arising in an episiotomy: a case report. *Infectious Diseases in Obstetrics and Gynecology*. 1997; 5:341-44.
- Peiris JSM, Madeley CR: Viral infections. IN: Barron, Lindheimer, Davison, eds. Medical Disorders During Pregnancy, 2nd ed. St. Louis: Mosby; 1995; 14:389-430.
- Reilly K. Clemenson N. Infections complicating pregnancy.. *Primary Care: Clinics in Office Practice*. 1993;20(3):665-84.
- Rodis JF: Parvovirus infection in pregnancy. In: Lee RV, Garner PR, Barron WM, Coustan DR, eds. Current Obstetric Medicine. St. Louis: Mosby, 1995; 3:159-81.
- Rudoff JM, Astaukas LJ, Rudoff JC, Spier RE, Schabel SI, Darling CA. Ultrasonographic diagnosis of septic pelvis thrombophlebitis. *J Ultrasound Med* 1988; 7:287-91.
- Simons GR, Piwnica-Worms DR, Goldhaber SZ. Ovarian vein thrombosis. *American Heart Journal* 1993; 126:641-47.
- Struthers BJ. Metronidazole appears not to be a human teratogen: review of literature. *Infectious Diseases in Obstetrics and Gynecology*. 1997; 5:326-35.
- Obstetric Medicine Curriculum Bibliography

Sweet RL: Antibiotic use during pregnancy. In: Lee RV, Garner PR, Barron WM, Coustan DR, eds. Current Obstetric Medicine. St. Louis: Mosby, 1996; 4:59-61.