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Pneumonia in the Pregnant Patient

Samar Khan and Michael S. Niederman

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Community acquired pneumonia is a common illness, and pneumonia and influenza serve as the seventh leading cause of death in the United States. In the pregnant patient, pneumonia is the most common cause of fatal non-obstetric infection *(1–3)*. Pneumonia can have adverse consequences for both the mother and her fetus, with certain infections (particularly viral and fungal) assuming greater virulence and mortality than in non-pregnant women of similar age *(2, 3)*. Pneumonia is a relatively common cause of respiratory failure in pregnant patients, but in contrast to older studies, newer data suggest that not all pneumonias are more common or more serious in pregnant women than in other populations. However, because pneumonia can impact both the mother and fetus, it may lead to an increased likelihood of complicated preterm delivery, compared to pregnancies in which infection is absent.

The pathogens responsible for community-acquired pneumonia (CAP) are similar in pregnant and non-pregnant patients, with *Streptococcus pneumoniae*, *Hemophilus influenzae, Mycoplasma pneumoniae, Legionella* spp., *Chlamydophila pneumoniae*, and influenza A accounting for the majority of cases *(2–4)*. However, reduction in cell-mediated immunity associated with pregnancy (especially during the third trimester) places women at an increased risk of more severe forms of pneumonia and disseminated diseases from pathogens normally contained by this type of immune response, including herpes virus, influenza, varicella, and coccidioidomycosis *(3, 5–7)*.

In this review, we discuss the epidemiology, risk factors, maternal and fetal impact of pneumonia, microbiology, clinical features, and management of pneumonia in pregnancy. Tuberculosis in pregnancy was discussed in Chapter 12.

Epidemiology

The incidence of pneumonia has varied widely in a number of published surveys, largely reflecting the types of populations that were evaluated and the era of the study. A very high incidence was reported in the series by Finland *(8)* and Hopwood *(9)* in the years before 1965 ranging from 6.3 per 1,000 deliveries to

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8.5 per 1,000 deliveries *(8, 9)*. Benedetti et al. examined 89,219 deliveries in a university and county hospital setting from 1972 to 1975 *(10)* and documented a lower incidence of pneumonia (0.4 per 1,000), with only 1 in every 2,288 deliveries being affected. Madinger et al. studied 32,179 deliveries at a community hospital from 1983 to 1988 and found pneumonia to complicate 1 out of every 1,287 deliveries (0.78 per 1,000) *(11)*. Berkowitz and LaSalsa examined 1,120 case records at a large city hospital from 1988 to 1989 and found that antepartum pneumonia occurred in 1 of every 367 deliveries *(12)*. This pattern of an apparent decrease, followed by an increasing incidence of pneumonia complicating pregnancy in recent years may reflect the fact that women with chronic illnesses are now able to become pregnant, and there is also a rising prevalence of immune deficiencies (such as HIV infection) and illicit drug use in pregnant women. However, Munn and colleagues *(13)* estimated the prevalence of antepartum pneumonia to potentially be much lower, ranging from 0.78 to 2.7 per 1,000 deliveries.

Two recent Canadian studies have compared the rates of CAP in pregnant and non-pregnant women. In the first, Jin et al. found the rate to be similar to the non-pregnant population, with reported rates of hospitalization for pneumonia of 1.51 per 1,000 deliveries versus 1.47 per 1,000 in non-pregnant controls *(14)*. In a similar study, comparing the incidence of CAP in pregnant women and non-pregnant age-matched controls presenting to a hospital, the incidence was 1.1 per 1,000 and 1.3 per 1,000, respectively *(15)*. Thus, compared to earlier studies, the incidence of pneumonia in pregnancy has declined, but the rates may be higher in large urban hospitals than in community settings, reflecting the different populations at risk. In addition, the available data generally come from those who are seen in a hospital, and may not reflect milder forms of illness seen in a physician's office.

There are very few formally collected data sets about nosocomial pneumonia in the pregnant or post-partum patient, but one form of pneumonia that falls into this category is aspiration pneumonia complicating labor and delivery. In fact, Mendelson's original description of gastric acid aspiration was made in obstetric patients undergoing labor and delivery *(16, 17)*. In the 1960s, as many as 2% of all maternal deaths were due to aspiration *(17)*. The pregnant woman is physiologically predisposed to aspiration because of elevation of the intragastric pressure due to the gravid uterus, a relaxed gastroesphageal sphincter due to the circulating progesterone, and delayed gastric emptying that accompanies pregnancy. These factors, coupled with sedation and analgesia that may be given during labor, increased abdominal pressure and vigorous abdominal palpation during examinations and extraction of the baby, all increase the threat of aspiration. The incidence of this complication has declined over time, with an increased awareness of the problem and with efforts directed towards prevention. In Mendelson's original series, the incidence was 1 in 667 deliveries, but in the 1970s, the rate was as low as 1 in 6,000 vaginal deliveries, but still 1 in 430 Caesarean sections. More recent studies of Caesarean section patients report a rate of 1 in 1,431 to 1 in 1,547 *(17)*. Mortality from this complication has been very low in recent years, with one death in 9,200 pregnancies *(17)*.

Risk Factors

The onset of pneumonia can be any time during gestation, with the mean gestational age at admission for pneumonia ranging from 24 to 31 weeks in the study by Yost et al. *(18)*. The same study also found that there was no significant difference

in maternal age or parity between the women who have pneumonia during pregnancy and those who do not *(18)*. In a case-control study of 59 women with pneumonia and 118 controls, using multivariate analysis, both anemia (measured as hematocrit of 30% or less) and a history of asthma were found to be independently associated with a fivefold increased risk for the development of pneumonia *(13)*. The study also reported the use of a tocolytic agent to delay labor as a risk factor for development of pneumonia. In another case-control study of 37 pneumonia patients and 74 controls, the use of antepartum corticosteroids was associated with a higher rate of infections (64.5% versus 17.5%) including four pneumonias in previously healthy women *(19)*. In one series of 71 women with CAP, 31 had underlying chronic diseases, although their presence did not lead to an adverse outcome *(20)*. In other series, women with CAP have had a high frequency of cigarette smoking and drug abuse.

A recent prospective study by Shariatzadeh et al. *(15)* compared 28 patients with pneumonia during pregnancy to 333 non-pregnant females in the same age group with pneumonia. Asthma requiring treatment was present in 46.5% of the pregnant pneumonia patients compared with 17.1% of the non-pregnant group, recognizing a large difference in sample size in the two groups. While other studies have found an association between asthma and pneumonia in pregnancy, none demonstrated an incidence as high as reported here. The accumulation of airway secretions and the presence of airway obstruction may account for the association of asthma with pneumonia, possibly accentuated by the reduction in functional residual capacity that occurs during pregnancy.

One other maternal problem associated with pneumonia is placental abruption *(21)*. Using a database of singleton births, the incidence of abruption was 0.96%, but was 2.05% (Odds ratio 2.2) in women with viral and bacterial pneumonia. The study commented only on the association but did not make clear a causative effect in either direction. It is possible that the association may be related to common risk factors (e.g., smoking, cocaine use) between pneumonia and abruption.

Pathogenesis of Pneumonia and its Complications in Pregnancy

Pneumonia can complicate pregnancy, in part because of altered host defenses in the parturient woman, and pneumonia can lead to potential adverse consequences for both the mother and the fetus adding morbidity and mortality when compared to the non-pregnant host. Particular types of pneumonia bear special significance for the pregnant woman, especially those of viral and fungal origin. In addition, pneumonia in the pregnant patient leads to an increased likelihood of complicated preterm delivery compared to pregnancies in which infection is absent.

Impact of Pregnancy on Pneumonia Risk (Table 13.1). Alterations in cellular immunity have been widely reported during pregnancy, especially in the second and third trimester, generally thought to protect the fetus from "rejection" by the mother. These include a decreased lymphocyte proliferative response, decreased natural killer cell activity, changes in T cell populations with a decrease in circulating helper T cells, reduced lymphocyte cytotoxic activity, and production of substances by the trophoblast that block maternal recognition of fetal major histocompatibility antigens *(2, 22)*. In addition, hormonal changes during pregnancy including elevation of progesterone, human chorionic gonadotropin, alpha fetoprotein, and cortisol may also inhibit cell mediated immune function *(22)*. These changes can predispose to infection with certain pathogens such as viruses, fungi, and tuberculosis.

Table 13.1 Alterations in pregnancy predisposing to an increased incidence and mortality from pneumonia.

Immunologic changes
Reduced lymphocyte proliferative response
Diminished cell-mediated cytotoxicity
Reduced number of helper T cells
Reduced lymphokine response to alloantigens
Physiologic changes
Increase in oxygen consumption
Increase in lung water
Elevation of diaphragm
Aspiration more likely in labor and delivery
Coexisting illnesses
Smoking
Anemia
Asthma
Cystic fibrosis
Illicit drug use
HIV infection
Immunosuppressive illness and therapy
Placental abruption
Labor and delivery
Increases risk for aspiration pneumonia

Catanzaro et al. *(23)* have shown that the hormonal changes lead to an increase in 17-estradiols, which can enhance the in vitro growth of *Coccidiodes immitis (17)*.

In addition to these changes, some of the physiologic changes of pregnancy can make the pregnant woman more prone to a severe pneumonia course. These include elevation of the diaphragm by up to 4 cm, decrease in functional residual capacity, an increase in oxygen consumption, and an increase in lung water *(2, 24)*. These alterations decrease the ability of the pregnant woman to clear respiratory secretions and aggravate airway obstruction associated with pulmonary infections. The elevation of the diaphragm and the associated decrease in functional residual capacity, coupled with the increase in oxygen consumption during pregnancy, make the pregnant woman less able to tolerate even brief periods of hypoxia, particularly in the third trimester.

Consequences of pneumonia on maternal outcomes. Pneumonia in pregnancy carries an increased risk of adverse outcomes when compared to pneumonia in non-pregnant women *(2, 3, 10–12, 24)*. In older data from the US Department of Health and Human Services *(1)*, 2,475 maternal deaths were examined from the years 1974–1978 and approximately 1% of these (24 deaths) were a result of pneumonia, which served as the most common non-obstetric infectious cause of mortality. Mortality data from the state of Massachusetts show that infection-related deaths in pregnancy have declined from 8.8 per 100,000 live births in the years of 1954–1957, to 0.6 per 100,000 births in 1982–1985 *(25)*. Although pneumonia is an uncommon cause of death among all pregnant women, the mortality rate can still be quite high among those who do develop pneumonia in pregnancy. In the preantibiotic era, the maternal death rate was observed to be as high as 32% of all such cases *(10)*, but in more recent series, the mortality attributable to pneumonia in pregnancy declined to 8.6% in one study *(9)*, while in another there was no maternal mortality *(10)*. Yost et al. found no deaths in 133 episodes, Jin observed no mortality in 333 pneumonia episodes in

pregnancy, and Shariatzadeh et al. observed no maternal deaths in 28 pneumonia episodes *(14, 15, 18)*. On the other hand, Richey and colleagues found 5 out of 71 pregnant women to have adverse outcomes including two maternal deaths, one early abortion, one preterm labor, and one fetal death *(20)*. These women tended to have more severe illness, with a lower initial mean oxygen tension, more diffuse radiographic pneumonia, and were more likely to be current smokers. In other more recent series, complications were also common, but mortality was not high, even when women with comorbid illnesses were evaluated. In one series, of the 25 patients studied, 40% suffered multiple complications including five requiring intubation, two developing empyema, one with pneumothorax, one with pericardial tamponade, and one with atrial fibrillation *(11)*, yet there was only one maternal death, occurring in a patient with cystic fibrosis.

While many series show low mortality rates overall from pneumonia in pregnancy *(12)*, viral lung infection and opportunistic lung infection still carry a substantial maternal mortality and morbidity *(3, 26–29)*. In one population study of eight influenza seasons, there were 297 respiratory disease hospitalizations, and seven women required ICU care, five during the third trimester. Ninety-two of these hospitalizations were for influenza or pneumonia and these women tended to have more cesarean deliveries than others, but mortality did not occur *(30)*.

Consequences of pneumonia on fetal outcomes. Although pneumonia can occur at any time during gestation, Hopwood's study found the mean time was 32 weeks *(9)*, but 17 of 23 patients developed pneumonia between weeks 25 and 36 of gestation and seven delivered during the course of their acute illness, with two mortalities among this group *(9)*. In the study by Benedetti et al., of 39 cases of pneumonia in pregnancy, 16 presented before 24 weeks gestation, 15 from weeks 25 and 36 of gestation and eight later than 37 weeks gestation *(10)*.

Significant fetal complications have been observed in all of the large studies of pneumonia in pregnancy. The majority of poor fetal outcomes occurred in mothers with underlying comorbid illnesses such as chronic respiratory disease, or other maternal disease *(11)*. A number of studies have shown that women with pneumonia in pregnancy are more likely to deliver prematurely and have babies that are small for gestational age (SGA). Berkowitz et al. noted a 12% rate of SGA babies and women had infants who weighed 400 g less than randomly selected patients without pneumonia *(12)*. In this series of 25 patients, most pneumonias were in the second and third trimesters, full-term delivery occurred in 14, one had preterm delivery, three underwent voluntary termination of pregnancy, three had term SGA babies, and four were lost to follow-up. Munn et al. found that pneumonia patients delivered babies at a significantly earlier gestational age than women without pneumonia, were more likely to deliver before 34 weeks, and their infants weighed significantly less *(13)*. Yost and colleagues reported that the women with pneumonia had babies that were 150 g smaller than seen in the overall population, and the frequency of low birth-weight infants was 16% in the pneumonia population versus 8% in the general population. In addition, they observed a trend to more preterm labor in the women with pneumonia *(18)*. In another recent series, women hospitalized with CAP had a relative risk of SGA babies of 1.86 *(14)*.

Fetal death has been reported as a complication of CAP in earlier series, but seems less common in more recent studies *(15, 18, 20)*. In one series, no maternal or fetal deaths were noted, however, an abortion at 10 weeks gestation and two preterm deliveries were observed in the pneumonia group *(15)*. Benedetti et al. reported a 2.6% rate for intrauterine fetal death and Madinger et al. noted a 12%

neonatal death rate *(10, 11)*. On the other hand, no excess fetal death was observed in recent series, including the comparison study by Yost and colleagues and in the study by Jin et al. *(14, 15, 18)*. One study found an association between drug and alcohol abuse with preterm delivery, but not with low birth-weight *(14)*. Thus, although most pregnant patients with pneumonia do well, it is important to identify patients with additional risk factors for poor perinatal outcome such as comorbid illness, smoking, and drug and alcohol abuse to intensify monitoring in an effort to avoid fetal complications.

While no congenital syndrome has been attributed to antepartum pneumonia, fever, tachypnea, and hypoxemia may be harmful to the developing fetus. Preterm labor as a complication of infection may be the result of the uterine response to certain mediators of infection and inflammation *(11, 13)*. McGregor has hypothesized that certain bacteria induce the production of phospholipases, proteases, and prostaglandins that can induce labor, although these speculations evolved with cervicovaginal infection in mind *(31)*. Lung infection is known to induce a similar compartmentalized inflammatory response, which has now been well documented in the non-pregnant patient with pneumonia *(32)*. It is quite possible that the cascade of mediators released by the active host inflammatory response to infection could exert distant effects on the uterus, leading to a high rate of labor during the course of pneumonia

Bacteriology

Any infectious agent that causes lung infection in the non-pregnant patient has been observed to complicate the course of pregnancy. The relative incidence of infection with any given agent is difficult to estimate without the use of comprehensive methodology to diagnose the etiologic pathogen for pneumonia. The available data are derived mainly from observational, and often retrospective, studies where only routine microbiological investigations have been used. Sputum and blood cultures were the main methods of diagnosis (Table 13.2) *(2)*. Hopwood *(9)* identified a responsible pathogen in only 9 of 23 cases, with a mixture of gram-positive bacteria,

Table 13.2 Bacteriology of Pneumonia in Pregnancy (in decreasing order of frequency).

Streptococcus pneumoniae (including DRSP)
Hemophilus Influenzae
No pathogens identified
"Atypical" pneumonia agents:
Legionella species (more common in severe pneumonia)
Mycoplasma pneumoniae
Chlamydophila pneumoniae
Viral agents
Influenza A
Varicella
Pseudomonas aeruginosa (with bronchiectasis, cystic fibrosis)
Aspiration
Fungi
Coccidioidomycosis
Pneumocystis jiroveci (with HIV infection)

gram-negative bacteria, and Influenza A virus being implicated. Benedetti et al. *(10)* found a bacterial pathogen in 21 of 39 patients, with pneumococcus serving as the predominant pathogen, accounting for 13 cases, and *Hemophilus influenzae* being the second most common organism isolated. Madinger et al. *(11)* also found *Streptococcus pneumoniae* (pneumococcus) to be the most common, followed by *Hemophilus influenzae* as the second most common pathogen isolated. In these studies, serologic testing was rarely performed to search for atypical pathogens such as *Mycoplasma* or *Chlamydophila*. Berdowitz's series *(12)* also found pneumococcus and *Hemophilus influenzae* as the most common pathogens.

The methodologic limitations in these studies are multiple, primarily due to incomplete and non-prospective diagnostic testing, and the absence of routine testing for atypical pathogens, which are ordinarily common in women of childbearing age. Even the recent pneumonia series are subject to the same problems, with very little etiologic data presented, and no routine diagnostic testing, with most patients doing well with empiric therapy that assumes the same bacteriology of CAP as in non-pregnant patients. Numerous case reports and selected limited series have shown a role for other etiologic agents including mumps, infectious mononucleosis, swine influenza, influenza A, *Legionella, Varicella, Chlamydophila pneumoniae*, *Coccidioidomycosis*, and other fungal pneumonias *(3, 23, 28, 33–41)*. Whether infection with any of these agents is more common in pregnancy than in the non-pregnant state is unknown, but certain pathogens, such as influenza and varicella may represent a greater hazard to the pregnant woman because of her physiologic defects in cell-mediated immunity.

The overall incidence of varicella in pregnancy has been reported as 1–5 per 10,000 births and both fetal and maternal complications present several management problems for clinicians. Varicella pneumonia usually complicates primary infection in 0.3–1.8% of all cases, but as many as 9% of primary cases during pregnancy can be complicated by pneumonia *(27)*. Influenza A is a common infection in pregnant women during epidemics and carries a higher mortality than in the non-pregnant patient *(37)*, with the maternal mortality rates being as high as 30–50% in the 1918 epidemic *(2, 3, 42)*. In the Asian flu epidemic of 1957–1958, 10% of all deaths occurred in pregnant women and almost 50% of women of childbearing age who died were pregnant *(37, 41)*. This increased mortality was especially noted in the third trimester.

Another viral infection documented in pregnancy was Severe Acute Respiratory Syndrome (SARS) infection, which is due to a coronavirus. One case series *(43)* described 12 patients with SARS during pregnancy, with seven in the first trimester and five in the second and third trimesters. Overall mortality was 25%, with half being admitted to the ICU and one-third requiring mechanical ventilation. Fetal complications were common with four of the seven first trimester infections leading to spontaneous abortion and most of the others leading to preterm labor and babies that were small for gestational age.

Several other new microbiologic concerns have now emerged for patients with CAP. Up to 40% of *S. pneumoniae* may be antibiotic resistant (DRSP), although it has been difficult to document an impact of relatively low level in vitro resistance on outcomes when usual therapies are used *(44)*. It is important to note that if any antibiotic has been used in the three months preceding CAP due to pneumococcus, the organism is more likely to be resistant to an agent that was recently used *(45)*. In addition to recent antibiotic therapy, another risk for DRSP is exposure to a child in daycare, a potentially common risk for women who are pregnant, so that this organism should be considered in all pregnant women *(44)*. Community-

acquired strains of methicillin-resistant *S. aureus* (CA-MRSA) are not being reported commonly, but may cause serious forms of CAP following influenza infection *(46)*. The organism can lead to a severe, bilateral necrotizing infection due to the production of a variety of toxins, including the Panton-Valentine Leukocidin (PVL). While this organism most commonly leads to skin and soft tissue infection, there is one case report of a severe necrotizing pneumonia due to CA-MRSA which seeded the lung, 9 days post-partum, from septic pelvic thrombophlebitis as a consequence of an infected episiotomy site *(47)*.

Aspiration is a form of pneumonia that can be a post-partum or an obstetrical complication, causing either a chemical pneumonitis, or a bacterial infection involving the pathogens found in the oropharynx and gastric contents, primarily anaerobes and gram-negative enteric organisms.

Clinical Features and Management of Specific Respiratory Infections

Bacterial Pneumonia

Clinical Features. Overall, the clinical presentation of pneumonia during pregnancy has not been found to differ substantially from the findings in non-pregnant adults, and include fever, cough, pleuritic chest pain, rigors, chills, and dyspnea *(8, 15)*. A report by Ramsey et al. *(48)* showed that during pregnancy 59.3% of patients with pneumonia reported a productive cough, 32.2% shortness of breath, and 27.1% pleuritic chest pain. Hopwood *(9)* reported that among 23 patients with pneumonia in pregnancy, all had preceding upper respiratory infection and 20 had cough. Fever above 101°F was present in 18 patients; only three reported dyspnea and five had chills.

Munn et al. demonstrated that 98% of patients with antepartum pneumonia had positive chest radiographs, either at admission or on repeat examination, with findings including infiltrates, atelectasis, pleural effusion, pneumonitis, or pulmonary edema *(13)*. Benedetti et al. *(10)* examined the radiographic features of pneumonia in pregnancy and found that 28 out of 39 patients had an infiltrate confined to a single lobe, while the remainder had multilobar pneumonia, and only one had a pleural effusion.

Most women with pneumonia do not have multilobar illness, but when present it correlates with a greater risk for a complicated course of illness *(18)*. There are many different methods used to define severity of illness in patients with CAP, but the Pneumonia Severity Index (PSI) is most widely used in the United States to help define the need for inpatient care and the need for ICU care *(49)*. The PSI uses an assessment of patient age, comorbidity, and laboratory and clinical data to define a patient's risk of death, with scores leading to categorization into one of five groups, each with increasing mortality risk. In its original derivation, pregnant patients were omitted, but Shariatzadeh and Marrie have observed that all pregnant patients that they evaluated fell into the low risk classes I and II, similar to age-matched controls *(15)*. However, twice as many pregnant patients were hospitalized as age-matched controls with similar PSI scores, yet they had a shorter length of stay. Thus, the PSI may either underestimate the need for inpatient care in pregnancy, or else physicians were being more cautious with admitting pregnant women, even if there was a relatively low mortality risk from pneumonia. The limits of the PSI were suggested in the study by Yost et al., with the finding that the use of the PSI would have recommended that two thirds of admitted pregnant CAP patients could have been sent home, but if this had been done, 10/79 would

likely have required later readmission because of a complicated course *(18)*. The limitations of scoring systems such as the pneumonia severity index and the APACHE score in pregnancy include the fact that some of the physiologic changes occurring in pregnancy may alter the scoring system. For instance, physiologic anemia with hematocrit as low as 30 are normally seen in pregnancy. The white cell count may be physiologically elevated in pregnancy as well and numbers as high as 14,000–15,000 may be seen. Other changes include a lower creatinine in pregnancy with a normal range being 0.5–0.7. Therefore, while a creatinine of 1.0 may be normal in the non-pregnant population, it is clearly an abnormal value in pregnancy and may contribute to inaccurate scoring.

Certain presenting signs suggest the need for ICU admission in the CAP patient and these criteria should probably be liberalized for the pregnant patient, because of a reduced physiologic reserve to tolerate hypoxemia. In addition, if certain infections are present, such as varicella-zoster, the potential for rapid progression in pregnancy is high enough that expectant ICU observation may be justified. Criteria for severe CAP, used in the new ATS/IDSA guidelines, but not specific to pregnant women, include the presence of at least one major criterion such as the need for mechanical ventilation or septic shock requiring vasopressors, or the presence of three minor criteria *(44)*. The minor criteria include the following: respiratory rate of at least 30 breaths /minute, PaO2/FiO2 ratio $\leq$ 250 mmHg, multilobar infiltrates, confusion or disorientation, BUN $\geq$ 20 mg/dL, WBC $<$ 4,000/ mm^3, platelet count $<$ 100,000/ mm^3, hypotension requiring aggressive fluid resuscitation, and hypothermia. The guidelines also suggested that criteria such as hypoglycemia, hyponatremia, asplenia (as in sickle cell disease), and unexplained acidosis be considered in deciding the need for ICU admission *(44)*.

Diagnostic Testing. When complications of pneumonia develop in the pregnant patient, they may be a consequence of a delay in recognition, leading Hopwood et al. to recommend that all women with persistent upper respiratory distress have a chest radiograph *(9)*. Madinger and colleagues reported that although all 25 patients who had pneumonia did have signs and symptoms of lung infection, the diagnosis was initially overlooked in five patients *(11)*. This may explain why respiratory failure, empyema, and other serious complications, adding to morbidity, complicated half of those diagnosed with pneumonia.

According to the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines for the management of adults with CAP, all patients with suspected CAP should have a chest radiograph *(44)*. All admitted patients should also have an assessment of gas exchange (oximetry or arterial blood gas), routine blood chemistry, and blood counts. Blood cultures can give false positive results and are only recommended in patients with severe illness, especially if there has been no prior therapy with antibiotics. Two sets of blood cultures are recommended. Sputum culture and gram stain should be obtained if a drug-resistant pathogen, or an organism not covered by usual empiric antibiotic therapy is suspected. Routine serologic testing is not recommended for any population with CAP. However, for patients with severe CAP, Legionella urinary antigen and pneumococcal urinary antigen should be measured and aggressive efforts at establishing an etiologic diagnosis should be made, including consideration of bronchoscopy.

Therapy. Based on the expected organisms in pregnant women with CAP, therapy should be directed at *Streptococcus pneumoniae* (including DRSP in patients with recent antibiotic therapy, underlying chronic heart or lung disease, and those with exposure to a child in daycare), *H. influenzae* (especially in cigarette smokers), and the "atypical" pathogens such as *Chlamydophila pneumoniae, Mycoplasma pneumoniae*,

and *Legionella pneumophila* (the latter in the setting of severe CAP). In choosing an antibiotic for bacterial pneumonia, the safety of the agent in pregnancy must be considered, along with its efficacy. Pencillins, cephalosporins, and erythromycin are all safe and potentially effective antimicrobials for CAP *(50)*. Clindamycin is probably also safe, but there is limited clinical experience with this agent *(51)*. The fluoroquinolones are commonly used to treat CAP in non-pregnant patients, but should not be used during pregnancy. They pose a theoretic risk of arthropathy, malformations, and can be both mutagens and carcinogens, although sporadic reports of safe use in pregnancy have appeared, suggesting that they can be used if absolutely necessary *(52)*. Other drugs to be avoided in pregnancy include tetracyclines (the mother is at risk for fulminant hepatitis and these agents can stain and deform fetal teeth and cause bony deformities), chloramphenicol (can cause bone marrow suppression in fetus, and if given near term can cause "gray baby syndrome" with gray facies, flaccidity, and cardiovascular collapse), and sulfa compounds (can cause fetal kernicterus) *(53)*. Aminoglycosides should be used only if there is a strong clinical indication of serious gram-negative infection, as there is potential risk of ototoxicity to the fetus. Vancomycin poses a risk to the fetus of fetal nephrotoxicity and ototoxicity and similarly should only be used if absolutely necessary. Linezolid is categorized as pregnancy Category C, and there is limited experience in pregnancy, but it is a protein synthesis inhibitor, so it should also be avoided unless no other alternative therapy is available.

Current guidelines for CAP recommend that all patients be treated for pneumococcus and atypical pathogens, which can often be present as co-pathogens *(44)*. Thus, no patient should receive empiric therapy with a beta-lactam (penicillin or cephalosporin) alone (Table 13.3). For an outpatient with mild CAP, and no risks for DRSP, therapy should be with an oral macrolide such as azithromycin,

Table 13.3 Recommended empiric therapy of community-acquired pneumonia in pregnancy.

Outpatients
No comorbid illness, no recent antibiotics, no DRSP risks (including exposure to a child in daycare)
Azithromycin (or erythromycin)
Co-existing cardiopulmonary disease, recent antibiotic therapy, or DRSP risk factors
Beta-lactam (high dose amoxicillin, cefuroxime, or cefpodoxime) plus azithromycin (or erythromycin)
Inpatient, not in ICU
No comorbid illness or DRSP risks
Intravenous azithromycin or erythromycin
Co-existing cardiopulmonary disease or DRSP risk factors
Intravenous beta-lactam (cefotaxime, ceftriaxone) PLUS intravenous azithromycin (or erythromycin)
Inpatient in ICU
No Pseudomonal risks
Intravenous beta – lactam (cefotaxime, ceftriaxone) PLUS intravenous azithromcyin (or erthromycin)
Pseudomonal risks present
Intravenous anti-Pseudomonal beta-lactam (cefepime, imipenem, meropenem, piperacillin/tazobactam) PLUS an aminoglycoside (amikacin, gentamycin, tobramycin) PLUS intravenous azithromycin (or erythromycin)

Clarithromycin is not recommended for use in pregnancy. Fluoroquinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin) are not recommended in pregnancy, but anecdotal experience suggests possible safety if alternative therapy is not available.

which is better tolerated than erythromycin. Clarithromycin is not recommended for use in pregnancy because of adverse embryonic and fetal outcomes in animal studies. If an outpatient with mild illness is at risk for DRSP, then therapy should be given with a macrolide combined with either high dose amoxicillin (3 g per day), cefpodoxime, or cefuroxime (500 mg twice daily).

If the patient is admitted to a hospital, therapy should be initially given intravenously, with azithromycin or erythromycin if the patient has no risks for DRSP. Yost and colleagues studied 119 women with CAP who were hospitalized and 83% of them received erythromycin monotherapy, with only one having a poor clinical response, but with five requiring discontinuation because of intestinal symptoms *(18)*. Azithromycin may be better tolerated as an intravenous macrolide than erythromycin. Although tetracyclines are not recommended in pregnancy, one case report discussed that they may be necessary in certain select patients, such as those with *Chlamydophila psittac*i pneumonia and a failure to respond to macrolide therapy *(36)*. If DRSP risks are present, therapy can be with ceftriaxone or cefotaxime, with the addition of an intravenous macrolide (azithromycin or erythromycin). Intravenous cefuroxime is not recommended because some studies have reported a worse outcome if this drug is used in patients with pneumococcal bacteremia and in vitro resistance is present, while the same findings have not occurred with the cephalosporins that are recommended.

In the ICU-admitted patient with severe CAP, no patient should get monotherapy, and combination therapy should be with cefotaxime or ceftriaxone plus a macrolide (azithromycin or erythromycin) if Pseudomonal risks are not present. Pseudomonal risks include bronchiectasis, prolonged corticosteroid therapy, and cystic fibrosis. If Pseudomonal risks are present, therapy should be with an anti-Pseudomonal beta-lactam (imipenem, meropenem, cefepime, or piperacillin-tazobactam), with an aminoglycoside (amikacin, gentamycin, tobramycin), and a macrolide. Imipenem is classified as pregnancy Category C, while piperacillin with tazobactam is pregnancy Category B. Community-acquired MRSA should be considered in patients with severe CAP after influenza, but as mentioned above, the safety of vancomycin and linezolid in pregnancy is not known.

Supportive therapy of the pregnant patient with pneumonia is no different than in the non-gravid state; hydration, antipyretic therapy, and supplemental oxygen remain the key therapies. The goal of oxygen therapy is to maintain the arterial oxygen tension well above 70 mmHg, as hypoxemia is less well tolerated in the pregnant female. Importantly, respiratory alkalosis leads to reduction in uterine blood flow and thus work of breathing should be decreased whenever possible in the pregnant pneumonia patient: adequate oxygenation is mandatory for that matter. Respiratory failure mandating mechanical ventilation has occurred in pregnancy and requires close monitoring of both the mother and the fetus. Preterm labor is a well described complication of pneumonia and may also need to be treated using tocolytics if the patient can tolerate them, although tocolytics have been reported to cause maternal pulmonary edema.

Viral Pneumonias

Influenza Virus

The influenza viruses are myxoviruses of three antigenically different types, A, B, C, that can cause disease in humans, but most epidemics in humans are due to type A. First identified in 1933, influenza remains a significant cause of morbidity and

mortality from febrile respiratory illness worldwide *(42, 54)*. Pregnant women are at increased risk for both acquiring influenza, and for developing complications of infection. In one study by Neuzil et al., pregnant women were affected more often than non-pregnant women *(42)*. Influenza also led to hospitalization for acute cardiopulmonary illness more often in women during the third trimester, in those with advanced age, and in those with underlying medical conditions such as asthma *(30, 42)*. Historically, influenza in pregnancy has been associated with higher rate of morbidity and mortality *(5)*. The course of influenza was first reported during the epidemic of 1918 when 1,350 cases in pregnant women who had an influenza-like illness were evaluated, and pneumonia was a complication in 585 (43%) of these cases. In 52% of these patients, pregnancy was interrupted, and there were 308 (23%) maternal deaths. The mortality was highest in the last three months of pregnancy, and increased if influenza was complicated by pneumonia *(54)*. Overall, in the 1918 epidemic, influenza during pregnancy had a 30% maternal mortality, increasing to 50% in the presence of pneumonia *(55)*. Mortality rose in tandem with the duration of pregnancy to a maximum of 61% when influenza was contracted in the ninth month of pregnancy. In the 1957 epidemic, 50% of women of childbearing age who died were pregnant and 10% of all the influenza deaths were among pregnant women *(37)*. However since 1958, pregnancy studies have shown a variable association with an enhanced morbidity and mortality from influenza *(55)*.

The clinical presentation of influenza does not appear to be altered by pregnancy. The incubation period is one to four days, and symptoms include cough, fever, malaise, coryza, headache, and myalgias *(56)*. In an uncomplicated case, influenza may resolve in 3 days or less. If symptoms persist for more than 5 days, especially in a pregnant patient, complications such as pneumonia should be suspected. Pneumonia, due to a viral or a secondary bacterial infection, is a well-recognized complication of influenza. Influenza pneumonia occurred in 12% of 102 pregnant patients with influenza in the 2003–2004 season, and led to complications such as respiratory failure, meningitis, and myocarditis *(3)*.

When pneumonia complicates influenza in pregnancy, antibiotics should be started and should be directed at the likely pathogens that can cause secondary infection including pneumococcus, *H. influenzae*, and *S. aureus*, including MRSA. Therapy for these organisms has been discussed above, but antiviral agents should be considered if a viral pneumonia is likely, especially early in the course of illness *(2)*. Anti-viral agents such as amantadine and rimantadine can prevent illness in exposed patients and reduce the duration of symptoms if given within 48 h of the onset of illness. Amantadine is effective against Influenza A and acts by blocking the release of viral nucleic acids and can be used for prophylaxis in high-risk pregnant women or for therapy in complicated cases *(3)*. It has been found to be non-embryotoxic in mice at 25 times the dose used in humans. When used in post partum women, Amantadine is excreted in breast milk and therefore should only be used in the highest risk patient. There is little experience in pregnancy with the newer neuraminidase inhibitors, zanamivir and oseltamivir, which can also be effective for treatment and prophylaxis, if started within 48 h of the onset of symptoms.

While anti-virals can be prophylactic after exposure, the primary method of influenza prevention is vaccination. The recommendation of the Advisory Committee on Immunization Practices is that all women who will be pregnant during influenza season receive the vaccine. Vaccination can also be performed safely in any trimester of pregnancy and so should be recommended to all pregnant women who have not yet been vaccinated *(57–58)*. The inactivated form of the

vaccine is used for pregnant women as well as other high-risk groups. Breast-feeding is not a contraindication to vaccination *(58)*.

Varicella Pneumonia

Varicella has a higher incidence and severity in pregnant than in non-pregnant patients, and so has the potential to complicate the course of pregnancy and lead to congenital defects. Pneumonia is the most serious complication of varicella, but when varicella pneumonia is present in the non-pregnant individual, it leads to a mortality of 11–17%, in contrast to a rate of 35–40% in pregnant patients *(3, 27)*. Haake et al. reviewed 34 cases of varicella pneumonia in pregnancy and found a 35% mortality *(27)*. Although only 5–10% of cases occur in adults, this population accounts for 25–55% of fatal cases *(3)*.

Varicella-Zoster (VZ) is a DNA virus that usually causes a benign, self-limited illness in children, but up to 10% of the adult population is susceptible to primary infection *(3)*. Studies show that the infection rate in pregnant women is as high as 4–6.8%, but after a close exposure, the risk of infection may be as high as 70% *(59)*. Pregnancy may also increase the rate of pneumonia as a complication of primary infection, and smoking may also be a risk factor, with infected smokers having a higher rate of pneumonia than infected non-smokers *(60)*. An increased intensity of skin eruption is also cited as a risk factor for developing subsequent pneumonia, especially if there are more than 100 skin lesions *(61)*.

Pregnancy also enhances the virulence of the VZ virus, as a consequence of functional T cell abnormalities, as well as higher levels of circulating corticosteroids, increased blood volume and altered respiratory reserve. Most reports have shown that when varicella pneumonia complicates pregnancy, it is usually in the third trimester and that infection occurring at this time is more severe and complicated than if it occurs earlier *(28, 62)*. The incidence of pulmonary involvement in primary varicella infection is approximately 16% *(3)*.

The incubation period of varicella is between 14–18 days *(3, 61, 63)* but can vary from 10 days to 3 weeks. In the mother the virus is in the blood for 24–48 h before the exanthem, and during this period 24% of fetuses develop transplacental infection *(64)*, which can lead to congenital malformations in 1.2% of the exposed fetuses. Clinically, varicella pneumonia presents 2–5 days after the onset of fever, vesicular rash (chickenpox), and malaise and is heralded by the onset of pulmonary symptoms *(2, 28)* including cough, dyspnea, pleuritic chest pain, and even hemoptysis. In one series all patients with VZ pneumonia had oral mucosal ulcerations *(28)*. Severity of illness may range from asymptomatic radiographic infiltrates to fulminant respiratory failure and acute lung injury *(27, 28)*. Typically chest radiographs reveal interstitial, diffuse miliary or nodular infiltrates that resolve by 14 days unless complicated by acute lung injury and respiratory failure *(65)*. The severity of infiltrates has been described to peak with the height of the skin eruption *(66)*. One late sequela of varicella pneumonia is diffuse pulmonary calcification *(62)*.

All patients with VZ pneumonia require aggressive therapy with antiviral agents (acyclovir) and early hospitalization. Mechanical ventilation may be needed in up to half of all pregnant women with varicella pneumonia, and this group has a mortality rate of at least 25%. Multiple investigators have used acyclovir, a DNA polymerase inhibitor in the pregnant patient, demonstrating its safety in pregnancy *(3, 27, 65, 66)* and its lack of teratogenicity *(67)*. In a study of 312 pregnancies in which acyclovir was used, no increase in the number or pattern of birth defects was seen *(67)*. Haake et al. reviewed the early initiation of therapy within 36 h of

admission, and found that those receiving early therapy had an improved hospital course after the fifth hospital day, lower mean temperature, less tachypnea, and improved oxygenation, compared to those who were not treated *(27)*. The recommended dose is 7.5 mg/kg every 8 h intravenously, although doses of 3–18 mg/kg have been used. Treatment is recommended for 7 days. Some small series have suggested a benefit from adjunctive corticosteroid therapy at modest doses *(3)*.

Fetal and Neonatal Effects

The effects of varicella on the fetus are of concern, and include intrauterine infection in 10–20% *(68)*. Traditionally fetal involvement has been in three areas: "varicella embryopathy" stemming from maternal disease developing before 20 weeks gestation; congenital varicella from 20 weeks gestation until term, but more commonly close to term; and neonatal disease occurring when the pregnant patient has active lesions at the time of delivery *(69)*. Varicella embryopathy was first described in 1947 by Laforet and Lynch and has since been redefined by a number of authors *(69–72)*, but includes limb hypoplasia, skin scarring, central nervous system involvement, and other skeletal lesions. This embryopathy has been reported with infection occurring as late as 26 weeks *(69)*.

The largest series of congenital varicella reported 1,373 pregnancies complicated by VZ from 1980–1993. Fetal abnormalities occurred most commonly in the children of women infected between 13 and 20 weeks of gestation than at any other time in pregnancy *(73)*. Fetal anomalies varied from skin lesions to lethal multi-organ system involvement. Because of concern about fetal effects, the use of prophylactic immune globulin is recommended within 96 h of exposure to prevent maternal illness, in women without prior varicella infection (negative IgG titers) or immunization. Importantly the use of VZ immune globulin in a pregnant woman may not eliminate the incidence of embryopathy, but if given before maternal infection develops, it may decrease or attenuate fetal disease *(73)*. Immunoprophylaxis with zoster immune globulin should be given early after close exposure of a seronegative pregnant woman, with the aim of preventing disease in the mother, but not in the fetus. Although expensive, one analysis suggested that the use of this approach is likely to be cost-effective *(34)*. The varicella vaccine, however, is contraindicated in pregnancy because it is a live-attenuated vaccine.

Other Viruses

Pneumonia may complicate up to 50% of adult measles cases, and bacterial super-infection is common. In one report of three cases of rubeola during pregnancy, all patients had bacterial super-infection and two had preterm labor *(38)*.

Severe acute respiratory syndrome is caused by a coronavirus, which can affect pregnant women, leading to symptoms that are the same as in non-pregnant women, and include fever, chills, rigors, malaise, and myalgias *(74)*. Patients are most infectious in the second week of illness. Laboratory findings are remarkable for marked lymphopenia and thrombocytopenia. Chest radiograph findings are patchy to generalized interstitial infiltrates *(74)*. The case fatality was 25% in 12 cases that were reported in pregnancy *(43)*, and other complications included first trimester spontaneous abortions, preterm births, and intrauterine growth restriction. Treatment includes broad-spectrum antibiotics to cover super-imposed bacterial infections, high dose corticosteroids, and possibly ribavirin, which has shown teratogenic effects in animals *(43)*.

Fungal Pneumonia

Fungal pathogens that have caused pneumonia include *Cryptococcus neoformans, Histoplasma capsulatum, Sporothrix Schenkii, Blastomyces dermititidis, and Coccidioides immitis (48)*. Fungal pneumonia in pregnancy is rare and when it does occur, it usually resolves without treatment in healthy women. In contrast, disseminated disease carries a more serious prognosis and can complicate pregnancy, particularly with infection in the third trimester *(22, 33)*.

Coccidioidomycosis generally occurs in the Southwestern United States and symptoms include fever, cough, headache, malaise, weight loss, and erythema nodosum. While most patients have pulmonary involvement (including an infiltrate, pleural effusion, miliary infiltrates, or cavitation), disseminated disease includes central nervous system involvement, skin, and bony lesions. Those with erythema nodosum have a lower rate of disseminated disease and a higher rate of recovery *(33)*.

Cantanzaro examined the published experience with Coccidioidomycosis in pregnancy and looked at both maternal and fetal complications as a function of when the infection was acquired *(23)*. In one 1951 series, among five patients who had infection before pregnancy, the disease remained stable and did not disseminate. There were 12 patients who acquired infection in the first trimester leading to one fatal disseminated disease with associated fetal loss. The other 11 had pulmonary infection only and recovered without dissemination, and 10 of the pregnancies were completed successfully. Among five women who were infected in the second trimester, one developed meningitis and one died of disseminated infection. The course was much different for the 11 women who acquired infection in the final trimester. Disseminated infection developed in seven, all of whom died. Other investigators also reported high rates of dissemination and maternal mortality, especially for infection acquired in the third trimester. Stevens *(75)* reported that 20% of patients with Coccidioidomycosis pneumonia in the third trimester of pregnancy developed disseminated disease, likely as a consequence of the alteration in maternal cell-mediated immunity during late pregnancy *(2)*.

For disseminated disease or severe pneumonia treatment with intravenous amphotericin B (pregnancy category B) is recommended followed by oral fluconazole post-partum *(33, 76, 78)*. Earlier series used ketoconazole and itraconazole, but fluconazole is preferred as a more effective, more bioavailable agent, with less potential for teratogenicity *(33)*. If possible, fluconazole should not be used in the first trimester when it may be teratogenic, and it may predispose to premature birth if used in the second trimester. Thus, amphotericin B is the preferred therapy in early pregnancy, with fluconazole in the third trimester, if needed.

Other fungal infections have been reported in pregnancy such as cryptococcosis, blastomyosis, and sporotrichosis. These are rare events and the impact of pregnancy on these infections or how these infections alter the outcome of pregnancy is not clear *(2)*.

Aspiration Pneumonia

As discussed earlier, pregnancy can increase the risk of aspiration, particularly in the peri-partum period *(16)*. Aspiration may involve bacteria from the oropharynx (enteric gram-negatives or anaerobes), solid particulate matter from the stomach, or liquid stomach contents including gastric acid. The aspiration of bacteria leads to a pneumonic infection that usually begins at least 24 h after the event. When

particulate matter is aspirated, it can lead to immediate bronchospasm, cough, and possibly cyanosis. Aspiration of gastric contents leads to symptoms that begin 6–8 h after the event, at which time the patient usually is symptomatic including tachypnea, bronchospasm, pulmonary edema, and hypotension *(16)*. The risk for pneumonitis is substantially increased if the aspirated fluid has a pH of less than 2.4 *(77)*.

The major thrust of management is prevention. Regional anesthesia is preferred over general anesthesia, and if the latter is used, the patient should have nothing by mouth for 24 h, if possible. Airway protection is paramount even with regional anesthesia and cricoid pressure and rapid sequence induction at the time endotracheal intubation can reduce the risk of aspiration *(17)*. Raising gastric acid pH pharmacologically may also help avoid some of the complications of aspiration, but there are no data to document a clear benefit nor a preference for antacids over histamine-type 2 blockers and proton pump inhibitors.

Prevention of Pneumonia

Several strategies are effective in preventing pneumonia in high-risk populations and can be applied to women of childbearing ages or during pregnancy *(3)*. Vaccinations are available for Influenza, pneumococcus, and varicella. The risk of influenza related respiratory illness in pregnancy is similar to high-risk non-pregnant populations. Therefore, the influenza vaccine is recommended for all women who will be pregnant during influenza season, regardless of gestational age *(57)*. Varicella vaccination is recommended for susceptible women considering pregnancy at 1–3 months before pregnancy or post-partum. Vaccination may reduce the risk of congenital varicella syndrome and decrease morbidity from adult complications of varicella. The varicella vaccine is not recommended for use during pregnancy because it is a live-attenuated vaccine *(78)*. The current pneumococcal vaccine contains the purified capsular polysaccharide from the 23 serotypes that cause 85–90% of the infections. The vaccine is effective in decreasing the prevalence of pneumococcal pneumonia and is recommended to women with underlying medical illnesses, including immunocompromised states, asplenia, sickle cell disease, diabetes, or chronic cardiopulmonary disease *(44)*. It may be given during pregnancy in women with the listed risk factors *(79)*. For women with children at home at the time of pregnancy, it may be useful to be sure that the children have received the new pneumococcal conjugate vaccine, since it can prevent disease in the children, which in turn may reduce the risk of maternal disease and of maternal infection with DRSP.

Pneumonia Complicating Human Immunodeficiency Virus (HIV) Infection

Although a thorough discussion of this topic is beyond the scope of this review, many women with HIV infection are of childbearing age, and pregnancy can interact in a potent fashion with HIV infection *(29)*. Pregnancy can theoretically accelerate the progression of underlying HIV infection-related immune suppression, and respiratory infection can be the AIDS defining illness for some pregnant patients, leading to an increased risk of both maternal and fetal mortality *(80)*. In addition, vertical transmission of HIV infection to the newborn is a serious concern. Antiretroviral therapy may improve CD4+ count, and reduce the risk of respiratory infection, so therapy should be continued during pregnancy.

Bacterial respiratory infections are the most common respiratory complication of HIV infection, but a low CD4+ count (<200 cells/μL) predisposes not only to bacterial pneumonia, but also to pneumonia with *Pneumocystis jeroveci* (PCP), which can be a serious infection risk for both mother and fetus. In one review of 22 patients with PCP in pregnancy, 59% had respiratory failure necessitating mechanical ventilation and mortality was 50% for the mothers, and there were five intrauterine deaths and four neonatal deaths *(81)*. Women with PCP infection should receive therapy with trimethoprim-sulfa (TMP-SMX), along with corticosteroids if hypoxemia is present. These patients should be monitored for preterm labor and at the time of delivery, any woman receiving TMP-SMX or dapsone should have their baby monitored closely for hyperbilirubinemia and kernicterus. For HIV infected women, without active PCP, prophylaxis is best done when the CD4+ cell count falls below 200 cells/μL, using TMP-SMX. Because of the potential teratogenic risk of TMP in the first trimester, consideration should be given to the use of aerosolized pentamidine because of its lack of systemic absorption.

Summary

Although pregnancy is infrequently complicated by pneumonia, lung infection in the antepartum period, by bacteria, viruses, and fungi can be associated with significant maternal and neonatal morbidity. Beyond the influence of pregnancy induced changes on cell immunity, there are certain physiological changes in pregnancy that both predispose to infection and also make it more difficult for the pregnant women to sustain any type of respiratory infectious insult. Thus pregnant patients require a higher level of surveillance and early intervention, and the prognostic scoring systems used in non-pregnant patients may not apply in pregnancy. Certain types of pneumonias, particularly influenza and aspiration, can be avoided if patients at risk are identified and existing strategies for prevention are applied. The safety of antimicrobial must also be considered when a pregnant patient is being treated for pneumonia.

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