006702

Review

Foodborne Infections during Pregnancy†

JAMES L. SMITH*

Microbial Food Safety Research Unit, U.S. Department of Agriculture, Eastern Regional Research Center, Agricultural Research Service, 600 East Mermaid Lane, Wyndmoor, Pennsylvania 19038, USA

MS 98-314: Received 1 December 1998/Accepted 22 March 1999

ABSTRACT

The consequences of foodborne illness can be particularly devastating during pregnancy because both the woman and her fetus are at risk. Escalated production of progesterone during pregnancy leads to down-regulation of cellular (cell-mediated) immune functions. Many foodborne pathogens (and other pathogens) are intracellular pathogens, and infections caused by these pathogens are controlled by cell-mediated immunity. The pregnancy-induced decrease in cell-mediated immune functions leads to increased susceptibility of the pregnant woman to certain infections. Hepatitis E virus, *Coxiella burnetii, Listeria monocytogenes,* and *Toxoplasma gondii* are intracellular pathogens that have a predilection for the maternal–fetal unit and may induce serious disease in the mother and/or fetus. In the United States, *T. gondii* and *L. monocytogenes* are the most important foodborne pathogens in pregnancy, and these organisms can induce death or grave disease in the fetus and newborn. The pregnant woman, in order to protect herself and her fetus from the consequences of foodborne illness, must practice a high standard of food hygiene and personal cleanliness.

Baird-Parker *(6)* has coined the acronym, YOPI (young, old, pregnant, and immunocompromised) to describe individuals who are at increased risk for foodborne and other infections. In addition to elevated susceptibility to infections, YOPIs generally suffer more serious illnesses. YOPIs make up approximately 20% of the population of the United States *(102)*.

Pregnant women are a particularly vulnerable segment of the YOPI population because their infections also may be transmitted to their fetuses. In 1992, 10.7% of women of child-bearing age (15 to 44 years of age) in the United States were pregnant. Thus, ~6.5 million pregnant women were at increased risk for infections *(118)*. The changes in hormonal and immunological parameters that take place during pregnancy *(24, 125, 126)* influence the susceptibility of pregnant women to a number of infections including those caused by foodborne pathogens. The present review is concerned with the effect of foodborne pathogens on both the pregnant woman and fetus and how to minimize foodborne infections during pregnancy.

IMMUNOLOGICAL AND HORMONAL CHANGES OCCURRING DURING PREGNANCY

Certain immunological and hormonal changes must take place in the woman's body in order to have a successful pregnancy. The most important of these changes are down-regulation of the cellular immune system and a substantial increase of progesterone production. The fetus can be considered as a semiallogenic graft, i.e., the fetus has genetic traits partially maternal and partially paternal and is therefore antigenically different from the mother. Nonetheless, the maternal immunological system is tolerant of the foreign tissue antigens present in the fetus *(94)*. The cellular immune system, i.e., cell-mediated immunity, plays a major role in foreign tissue graft rejection *(5)*. Therefore, in order to prevent rejection of the fetus by the maternal immune system, cell-mediated immunity must be down-regulated during pregnancy *(94, 109, 124, 125)*.

In the pregnant female, a number of steroid hormones such as estradiol, estriol, and progesterone are produced at levels severalfold higher than those levels produced by nonpregnant females *(24, 126)*. The most important hormone is progesterone, which is absolutely required for maintenance of pregnancy *(109)*. Down-regulation of cell-mediated immunity is favored by progesterone *(78, 86, 110)*. Thus, maternal down-regulation of cellular immunity is induced and maintained by increased production of progesterone with resultant development and survival of the fetus.

Intracellular pathogens invade host cells and spend most of their existence in the host cell intracellular environment. The intracellular location protects intracellular pathogens from the humoral immune system but not from cell-mediated immunity *(54)*. Thus, cell-mediated immunity is of primary importance in controlling intracellular pathogens. Examples of foodborne facultative intracellular pathogens include *Brucella, Listeria monocytogenes, Salmonella, Shigella,* and *Yersinia,* whereas hepatitis A and E (HEV) viruses, *Coxiella burnetii,* and *Toxoplasma gondii* are examples of obligate intracellular pathogens *(71, 77)*. Down-regulation of cell-mediated immunity during pregnancy would be expected to lead to increased susceptibility of the

* Author for correspondence. Tel: 215-233-6520; Fax: 215-233-6581; E-mail: jsmith@arserrc.gov.

† Mention of brand or firm names does not constitute an endorsement by the U.S. Department of Agriculture over others of a similar nature not mentioned.

woman and her fetus to infections by intracellular pathogens.

EFFECT OF FOODBORNE PATHOGENS ON MOTHER AND/OR FETUS

The effects that potential foodborne agents may have on the pregnant female and her fetus are detailed in Table 1. Pregnant women are no more susceptible to most foodborne pathogens than the general healthy public. However, there are a few foodborne pathogens to which the pregnant woman and/or her fetus are more susceptible or that produce a more severe disease (Table 1). There are indications that pregnant women are more susceptible to HEV *(69)*. There is decreased resistance to infections by *L. monocytogenes* in pregnant mice, and they have reduced ability to develop immunity to the pathogen *(64)*. Pregnant mice are also more susceptible to the lethal effects of listerial infections *(57)*. A majority of cases of human *L. monocytogenes* infections occur in individuals whose cellular immunity has been suppressed either by disease, drugs, or pregnancy *(37)*. Luft and Remington *(64)* demonstrated that pregnant mice were more susceptible to infection with the parasite *T. gondii* than virgin mice. It is not clear, however, that pregnant women are more susceptible to infection by the parasite.

A few foodborne pathogens appear to produce a more severe disease in pregnant women (Table 1). These include HEV *(47, 69)*, *Vibrio cholerae (8, 108)*, *Entamoeba histolytica (76)*, and *Giardia lamblia (58)*. There are no data concerning *Escherichia coli* O157:H7 infections in pregnant women but hemolytic uremic syndrome (HUS) during pregnancy can be quite severe for both mother and fetus *(27, 36, 66, 127)*. Treatment with plasma transfusion or plasmapheresis is effective in decreasing or preventing fetal and maternal symptoms of HUS. Thus, an infection by *E. coli* O157:H7 during pregnancy would be expected to have drastic effects on both fetus and mother if the disease progresses beyond the bloody diarrhea stage into HUS.

For the year 1997, 8,676 laboratory-confirmed diarrhea cases were identified for nine foodborne pathogens in an active bacterial surveillance system; 46.3% of those cases were due to *Campylobacter* infections. Interestingly, *Salmonella* species accounted for only 25.7% of the cases *(18)*. One of the sequelae of *C. jejuni* infection is Guillain-Barré syndrome (GBS). Buzby et al. *(16)* have estimated that 2,628 to 9,575 GBS cases occur each year in the United States. Approximately 30% of these GBS cases are believed to have their origin in a *C. jejuni* infection *(73)*. GBS is an autoimmune disorder of the peripheral nervous system characterized by weakness of limb muscles and/or respiratory muscles and loss of reflexes. Up to 20% of GBS patients require mechanical ventilation. Plasmapheresis or injection of intravenous human immunoglobulin is an effective treatment *(73)*. It has been estimated that there is one case of *C. jejuni*-induced enteritis per 100 persons per year in the United States *(112)*. Such a high frequency of infection indicates that a substantial number of women will be infected with *C. jejuni* during pregnancy. Nachamkin et al. *(73)* estimate that 1 out of every 1,058 *C. jejuni* infections in the United States will be followed by GBS. Thus, there is a good possibility that a certain percentage of pregnant women will have GBS if they become infected with *C. jejuni*. Bolik et al. *(10)* stated that the incidence rate of GBS during pregnancy is similar to the rate found for nonpregnant females. However, a Swedish study indicates that the risk for GBS is lower during pregnancy *(51)*. By 1995, 49 cases of GBS during pregnancy had been reported in the literature with four maternal deaths *(10)*; thus, the death rate for pregnant women with GBS was 8.2%. Five to 10% of patients with GBS die as a direct consequence of their disease *(2)*. GBS during pregnancy does not impair fetal or infant development. In addition, treatent (plasmapheresis or intravenous human globulin) of the mother for GBS has no effect on pregnancy or fetal development *(10)*. Rolfs and Bolik *(93)* stated that no case has been reported in which the neonate of a GBS mother developed symptoms of GBS. Recently, Luijckx et al. *(65)* described a case in which both the newborn and mother had GBS. Twelve days after birth, the neonate showed symptoms of GBS; treatment with intravenous immunoglobulin alleviated the GBS symptoms. Even though the pregnant woman may be severely affected with GBS, in the great majority of cases, a normal healthy child is delivered.

Most of the pathogens listed in Table 1 are facultative or obligate intracellular pathogens, and therefore, cellular immunity is important in their control. Thus, these intracellular pathogens would be expected to be major disease agents during pregnancy because pregnancy leads to the down-regulation of cellular immunity. However, with the exception of *L. monocytogenes* and *T. gondii*, the intracellular pathogens listed in Table 1 are not common disease agents during pregnancy in the United States.

***Listeria monocytogenes* and pregnancy.** There is evidence that the incidence of listeriosis in the United States decreased by 44% from 1989 through 1993; listeriosis-related deaths decreased by 48% in the same time period *(111)*. Nonetheless, 1,795 to 1,860 cases of listeriosis and 474 listeriosis-induced deaths are estimated to occur each year in the United States with a total cost of 232.7 to 264.4 million dollars *(17)*. Most of the cases and costs are attributable to foodborne *Listeria*, because 85 to 95% of listeriosis is foodborne *(17)*. Consumption of foods containing *L. monocytogenes* can cause both outbreaks and sporadic illnesses. Outbreaks of foodborne listeriosis have been caused by ingestion of contaminated coleslaw, pasteurized milk, soft cheeses, paté, or jellied pork tongue *(32, 37, 111)*. However, human listeriosis occurs most often by sporadic foodborne transmission *(32, 37)*. Foods implicated in sporadic listeriosis include foods obtained from delicatessen counters, Mexican-style and feta cheeses, undercooked chicken, and nonreheated hot dogs *(32, 37, 111)*.

Buzby et al. *(17)* have estimated that 252 pregnant women are hospitalized each year with listeriosis, and there are 295 to 360 fetal/newborn cases. There are no deaths in the maternal cases, but 14 to 79 deaths are estimated to occur in fetal/newborn cases. Among the fetal/newborn survivors of listeriosis, 43 develop chronic complications in

TABLE 1. *Effect of foodborne pathogens on mother and fetus during pregnancy*

Foodborne pathogen	Susceptibility to pathogen during pregnancy	Effect on fetus or newborn	Reference
Hepatitis A virus	No increased susceptibility	Transplacental transmission not reported; no increased risk for spontaneous abortion, stillbirth, or congenital malformation; infection of woman during third trimester may increase preterm delivery; baby may contract disease from mother during neonatal period	*47, 75, 123, 130*
HEV	HEV appears to have a high predilection for pregnant women with a death rate of 15 to 25% (HEV is generally limited to underdeveloped nations)	Transplacental transmission may occur; increased abortion and intrauterine death; increased preterm delivery; baby can be infected during birth	*47, 55, 69, 75, 85, 117*
Brucella species (generally *B. melitensis*)	No increased susceptibility in humans (tropism occurs in ungulate placenta due to presence of erythritol); brucellosis is a rare disease in the United States	Transplacental transmission has been reported; abortion has been reported; presence of organism in mother's milk has been reported	*1, 3, 22, 62, 80, 103, 129*
Campylobacter jejuni	No increased susceptibility	Transplacental transmission has been reported; abortion may occur if woman is infected early in pregnancy; later infection may result in stillbirth or preterm delivery; newborn may be infected during delivery	*46, 100, 108*
Coxiella burnetii (Q fever)	*C. burnetti* appears to have a tropism for placental tissue	Transplacental infection may occur; abortion, preterm birth, intrauterine growth retardation, intrauterine death may occur; baby may be uninfected even when organisms are present in placental tissue	*39, 41, 63, 87, 89, 106, 113*
Escherichia coli O157:H7 (HUS)	Infections in pregnant women have not been reported. However, HUS in pregnancy is associated with high mortality or long term morbidity unless the woman is treated	HUS in pregnancy may lead to preterm delivery or intrauterine death of fetus	*27, 36, 66, 127*
Listeria monocytogenes	Organism has predilection for feto-placental unit	Transplacental infection of fetus occurs with the possibility of a live congenitally infected baby; infection early in pregnancy poses greatest risk to fetus and newborn; abortion, intrauterine death, stillbirth, premature labor may occur; babies may be infected during delivery	*11, 57, 64, 96, 97, 108*
Salmonella Typhi (typhoid)	No increased susceptibility; in absence of antibiotic treatment, there is significant fetal and maternal mortality	Transplacental infection of fetus may occur; abortion, stillbirth, premature labor may occur; baby may be infected during delivery	*30, 79, 108*
Salmonella species (nontyphoid)	No increased susceptibility	No transplacental transmission; bacteremia in mother may lead to stillbirth; infection of baby during delivery is uncommon	*79, 98, 108*
Shigella species	No increased susceptibility	No transplacental transmission; shigellosis not identified as a cause of abortion, stillbirth or premature labor; infection of baby during delivery is uncommon	*79, 108*
Vibrio cholerae	No increased susceptibility but cholera is more severe in pregnant women	No transplacental transmission; abortion, premature labor, and intrauterine fetal death may occur	*8, 108*
Yersinia enterocolitica	No increased susceptibility	No transplacental transmission; little evidence of abortion in humans; infection of baby during delivery does not appear to occur	*74, 108*
Cryptosporidium parvum	No increased susceptibility	No transplacental transmission; fetal distress may occur if mother's diarrhea is severe; baby may be infected during delivery	*20, 26, 59*

TABLE 1. *Continued*

Foodborne pathogen	Susceptibility to pathogen during pregnancy	Effect on fetus or newborn	Reference
Entamoeba histolytica	No increased susceptibility but pregnant women are at greater risk for fulminant disease	No transplacental transmission; infection of woman early in pregnancy may lead to abortion; dehydration and malnutrition induced by disease in mother may lead to intrauterine growth retardation; baby may be infected during delivery	*20, 76*
Giardia lamblia	No increased susceptibility; disease may be more severe in pregnancy	No transplacental transmission; severe maternal infection that compromises nutrition may affect fetal growth; baby may be infected during birth by fecal contamination	*4, 58*
Toxoplasma gondii	Parasite has predilection for fetoplacental unit	Transplacental transmission occurs with possibility of live congenitally infected baby; stillbirth and early perinatal death may occur; it is not certain that parasite induces abortion in humans	*20, 64, 88, 122*
Trichinella spiralis	Increased susceptibility?	Infection of placenta has been observed; transplacental transmission? (there are no reports of congenital trichinosis in live newborns); abortion, stillbirth, premature labor may occur; baby not infected during birth (the parasite has been found in infected mother's milk, which can result in infected baby)	*20*

which the children have some level of permanent neurological and/or physical disability *(17)*.

The costs (medical and productivity loss) of the maternal listeriosis cases are estimated to be 3.4 million dollars *(17)*. Medical costs and productivity losses for fetal/newborn cases are estimated at 20.4 to 52.1 million dollars. The life-time costs generated by the estimated 43 cases of chronically disabled babies that are born each year are estimated at 25.2 to 45.5 million dollars and reflect medical costs, special education costs, and loss of productivity *(17)*.

Listeriosis as a disease of pregnancy. Animal studies indicate that both the mother and fetus are at risk for serious illness if the mother is infected by *L. monocytogenes* during pregnancy. *L. monocytogenes*-infected pregnant mice did not clear the pathogen from their spleens and livers as efficiently as infected virgin mice, and the pregnant mice had a much higher mortality rate *(57, 64)*. Necropsy of dead pregnant mice revealed that most of the mice had aborted *(64)*. Schlech *(95, 96)* demonstrated that oral infection of pregnant rats with *L. monocytogenes* led to fetal resorption, still births, or heavily infected living pups. Midgestational infection had greater adverse effects on fetal outcome as compared to infection during the earlier or later part of pregnancy. Oral infection of pregnant mice led to abnormal reproductive outcomes similar to that seen in rats *(70)*. Menudier et al. *(70)* also noted that pregnant mice were susceptible to listeriae-induced encephalitis or death.

That female and pregnant mice or rats are more susceptible to listerial infection suggests that sex hormones play a role in the increased susceptibility. Female mice given high doses of estrogenic substances (diethylstilbestrol, 17-β-estradiol, α-dienestrol) showed increased morbidity when exposed to *L. monocytogenes (28, 83)*. Estrogen-induced decrease in immunity against *L. monocytogenes* is probably due to estrogen suppression of cellular immune functions. In humans, *L. monocytogenes* has a predilection for the fetoplacental unit *(11, 13)*. Listeriosis most commonly occurs during the third trimester *(13, 45)*. Infections are rare during the second trimester and even more rare during the first trimester *(13, 42)*. Early gestational listeriosis is associated with septic abortion, whereas late listeriosis may result in premature delivery of a stillborn or septic baby *(11)*. However, if the disease is promptly diagnosed and antibiotic treatment of the mother initiated, then the outcome is favorable for both mother and baby *(42, 52, 99, 132)*. An interesting observation by Mascola et al. *(68)* indicates that women pregnant with multiple gestations (two or more fetuses) are at greater risk for listeriosis than women pregnant with a single gestation.

L. monocytogenes infection during pregnancy may be asymptomatic or may present as a flu-like illness with fever, headache, and myalgia. Gastrointestinal symptoms are less common. The mild flu-like prodrome, occurring in approximately two-thirds of infected pregnant women, occurs during the period of bacteremia. Invasion of the uterus, placenta, and fetus may be the outcome of listerial bacteremia. Bacteremia during the third trimester usually results in premature delivery *(11, 45)*. Severe listeriosis in pregnant women is rare *(99)*, and listeriosis in the pregnant female is usually self-limiting (even without treatment) with the delivery of an infected baby.

Infection of the fetus may result from transplacental

transmission following listerial bacteremia of the mother, or it may occur by ascending spread if the vagina has been colonized by *L. monocytogenes (60, 61, 97).* Intrauterine infection may cause amnionitis, preterm labor, spontaneous abortion, stillbirth, or early onset infection of the neonate. Late-onset listeriosis may occur if the neonate is infected during passage through the birth canal, by contamination with feces if the mother is a carrier, by hospital caretakers, or from hospital or home environments *(60, 61, 97).* Thus, depending on how and when the neonate was infected, there may be early-onset or late-onset listeriosis.

Symptoms of early-onset listeriosis (which is due to infection in utero) are seen up to 7 days after birth. The child is generally preterm with low birth weight and with septicemia as the major symptom. The neonate may have respiratory distress, cyanosis, apnea, pneumonia, microabscesses in various organs, as well as other symptoms. Mortality of live-born neonates ranges from 15 to 50% with early-onset listeriosis *(11, 37).*

Cases of late-onset listeriosis are seen later (>5 to 7 days after birth) than early-onset disease. The neonate is infected at or after birth. Meningitis is the major presenting symptom in late-onset listeriosis. The neonate may show fever, poor feeding, irritability, and colitis with diarrhea. Mortality in late-onset listeriosis ranges from 10 to 20% *(11, 37).* Few studies have been done on the long-term consequences of early-onset and late-onset neonatal listeriosis, but it can be assumed that a number of children will have long-term physical, neurological, and/or physiological defects. Estimates of the number and severity of neonatal listeriosis cases have been given by Buzby et al. *(17).*

Early diagnosis and initiation of antibiotic therapy is necessary during pregnancy and after birth to ensure the survival of the infected neonate. However, data indicate that antibiotic resistance is increasing in *L. monocytogenes,* and susceptibility to antibiotics commonly used against gram-positive bacteria can no longer be assumed to be effective *(21).* Multiple-antibiotic-resistant *L. monocytogenes* have been isolated from listeriosis patients *(81, 84, 116).* Many antibiotic resistance genes are mediated by transferable plasmids in enterococci and streptococci, and these organisms are probably the source of antibiotic resistance in listeriae *(21, 81).* In vitro, conjugative transfer of *vanA* vancomycin resistance from *Enterococcus faecium* to *L. monocytogenes* (and to the nonpathogenic *L. ivanovii* and *L. welshimeri*) was demonstrated by Biavasco et al. *(9).* Interestingly, the nonpathogenic *Listeria* transconjugants were able to transfer vancomycin resistance to both *L. monocytogenes* and *E. faecium.* The facile transferal of vancomycin resistance to *L. monocytogenes* in vitro would suggest that vancomycin-resistant listeriae will soon appear in a clinical setting. Thus, with the emergence of multiple-antibiotic-resistant strains of *L. monocytogenes,* there may be decreased efficacy in treatment of listeriosis during pregnancy and an increase in fetal wastage as well as an increase in babies born with early-onset listeriosis.

***T. gondii* and pregnancy.** Approximately 30% of the adults in the United States and the United Kingdom show serological evidence of infection with *T. gondii*; however, in continental Europe, infection ranges from 50 to 80% of the population *(33).* Todd *(115)* has estimated that approximately 1.5 million *T. gondii* infections occur each year in the United States, and the huge majority of these infected individuals are asymptomatic and do not even know that they have been infected. Thus, *T. gondii* infection is common, but clinical toxoplasmosis is rare. Infected immunocompetent individuals have few or no symptoms, but infected immunocompromised or immunosuppressed individuals generally show clinical manifestations of toxoplasmosis *(40, 102).* Clinical disease in immunocompromised or immunosuppressed individuals may be due to reactivation of pre-existing infection or may represent a new infection.

Toxoplasmosis outbreak data indicate that *T. gondii* can be transmitted to humans by the ingestion of foods *(101),* water *(7, 12),* or dust and soil *(38, 105, 114).* Most of the foodborne outbreaks involving *T. gondii* were due to ingestion of raw or undercooked meats, and ingestion of unpasteurized goat milk has been implicated in a few outbreaks *(101).* It is unknown what percentage of the ~1.5 million infections that occur each year in the United States are caused by eating *T. gondii*-containing foods. Buffolano et al. *(14)* found that eating cured pork or raw meats was a major risk factor for *T. gondii* infection in pregnant women in Naples, Italy. Women who ate cured pork or raw meat during pregnancy were three times more likely to be infected by the parasite than pregnant women who avoided those foods. Similarly, Kapperud et al. *(53),* studying risk factors for *T. gondii* during pregnancy in Norway, determined that eating raw or undercooked meats (minced meats, mutton, pork), eating unwashed raw vegetables, and cleaning cat litter boxes were significant risk factors for infection by *T. gondii.*

Buzby and Roberts *(15)* have estimated that ~1,581 children are born each year with congenital toxoplasmosis. Severe acute toxoplasmosis is seen in 217 babies at birth; 40 of these cases die soon after birth. The 177 surviving cases of severe congenital toxoplasmosis either have or will develop serious complications (blindness or mental retardation) by age 17. There are 1,364 cases that do not show signs of toxoplasmosis at birth but will show symptoms of toxoplasmosis by age 17. Thus, congenital toxoplasmosis results in 1,541 infants each year who sooner or later will suffer toxoplasmosis complications of varying degrees of severity. Buzby and Roberts *(15)* estimate an annual cost of $7.7 billion (1995 dollars) for congenital toxoplasmosis. These costs include medical care, loss of productivity (death or disability), special education, and residential care *(92).*

Toxoplasmosis as a disease of pregnancy. Female mice have a lower survival rate when infected with *T. gondii* than male mice *(91).* In addition, the brain tissue cyst burden in surviving female mice was at least two times that of surviving male mice. Luft and Remington *(64)* indicated that pregnant mice were more susceptible to *T. gondii* infection than virgin mice and demonstrated earlier and great-

er mortality when infected. That female mice as well as pregnant mice have increased susceptibility to toxoplasmosis suggest that sex hormones may play a role. Kittas and Henry *(56)* found that gonadectomized male and female mice given estrogens had approximately threefold increased brain tissue cyst burden than that of control gonadectomized mice. When Pung and Luster *(82)* administered high levels of estrogenic compounds (to simulate those levels found in pregnancy) to female mice, they found at least a twofold increase in tissue cyst burden in the brain. The increased levels of estrogens led to decreased resistance of the mice to *T. gondii.*

Studies with animals infected by *T. gondii* during pregnancy indicate that the parasite can be isolated from fetuses and placentas *(88).* Infection of mice and rats by *T. gondii* after initiation of pregnancy leads to infected progeny; however, if infection occurs a few weeks before initiation of pregnancy, infected progeny are not found. Mice or rats that were infected during pregnancy and produced infected young did not give birth to parasitized progeny in subsequent pregnancies *(34, 35, 90, 131).* Seropositive pregnant animals, therefore, do not give birth to parasitized young. Thus, animal data indicate that the fetal–placental unit is a favored area for *T. gondii* infection. Similarly in humans, the isolation of *T. gondii* from placentas and fetuses of infected pregnant women suggests that the parasite has a tropism for placental and fetal tissue *(88).*

When a pregnant seronegative woman is infected by *T. gondii,* the infection is similar to that of any adult infected by the parasite and is not recognized in approximately 90% of cases. Symptoms and signs of acute infection are generally so minor, the woman does not recall the incident *(128).* The infected fetus always shows symptoms—at birth, during infancy, in childhood, in teenage, or in adult years. Sooner or later, the individual, congenitally infected with *T. gondii* will show symptoms of toxoplasmosis.

In humans, congenital toxoplasmosis (i.e., toxoplasmosis in infants who were infected by *T. gondii* in utero) usually does not occur when a seropositive woman becomes pregnant. However, if a *T. gondii*-seronegative woman is infected during pregnancy, the fetus is at risk for toxoplasmosis *(88).* While the fetus and neonate may show severe symptoms of toxoplasmosis, the mother is asymptomatic or shows only mild illness.

However, the fetus may present with congenital toxoplasmosis in a *T. gondii*-seropositive immunocompromised pregnant woman. The *T. gondii*-seropositive pregnant woman with acquired immune deficiency syndrome or other immunocompromising conditions may show reactivated toxoplasmosis with the possibility of transmission of the parasite to the fetus *(29, 67, 72, 88, 128).* It is rare for the *T. gondii*-positive presumedly immunocompetent pregnant woman to have an infected fetus, but it does happen. If pregnancy occurs shortly after infection (≤2 months), infection of the fetus is possible, although rare *(88, 121).* Cases have been reported in which babies born to immunocompetent *T. gondii*-seropositive women show signs of congenital toxoplasmosis *(31, 43, 44).* The authors suggest that reinfection of the women occurred during pregnancy with resultant infection to their fetuses.

TABLE 2. *The four cardinal rules of microbial food safety*

Rule 1.	Wash hands thoroughly with soap and hot water.
Rule 2.	Kill all of the microorganisms that you can. Keep microorganisms out of food. Keep microorganisms from growing (the 3K rule).
Rule 3.	Foods should be kept at temperatures ≤40°F (≤4.4°C) or ≥140°F (≥60°C) (the 40–140 rule).
Rule 4.	When in doubt, throw it out.

When a seronegative woman is infected by *T. gondii* during pregnancy, there is 30 to 40% chance that the fetus will be infected. An investigation of 500 women who were infected by *T. gondii* during pregnancy demonstrated that 66.8% of the fetuses escape infection, whereas the remainder (n = 166) were infected. There were 11 deaths (2.2%) from stillbirths or death in perinatal period. Of the live infected babies (n = 155), 77.4% had subclinical toxoplasmosis (seropositive but no clinical symptoms) at birth, whereas 22.6% (n = 35) showed signs of clinical disease. Of the children with clinical toxoplasmosis, 22 of 35 had mild symptoms and 13 of 35 were severely affected *(88).*

The incidence and severity of fetal infection depends on the stage of gestation when the woman is infected by the parasite. If the woman is infected late in pregnancy, i.e., third trimester, the incidence of transmission of the parasite is high (~60%), but the disease in the neonate will be relatively mild or subclinical; 85% of these babies will appear normal at birth *(23, 128).* However, if the woman is infected during the first trimester, there is less chance of fetal infection (~10 to 15%), but the risk of miscarriage, stillbirth, perinatal death, or severe clinical disease is high. The chance of fetal infection during the second trimester is approximately 30%; about 70% of these infections will be subclinical *(23, 128).*

Congenital toxoplasmosis may involve the ocular, auditory, and/or central nervous system. Infants with subclinical toxoplasmosis who appear normal at birth may show neurological and/or ocular abnormalities months or years later *(88, 128).* The minority of congenitally infected babies will show severe manifestations including hydrocephalus, intracranial calcifications, and/or retinochoroiditis; thus, the child may be mentally retarded and blind or have other neurological deficits. Other organs such as kidneys, liver, heart, and lungs may be severely affected also *(49, 88).* Congenital toxoplasmosis must always be treated. Treatment of the mother with spiromycin, as soon as *Toxoplasma* infection is diagnosed, has been shown to reduce the transmission of the parasite from mother to fetus; however, spiromycin does not change the disease course once the fetus has been infected. If the fetus becomes infected, treatment of the mother should be initiated with a pyrimethamine/sulfadiazine/folinic acid regimen until delivery, and the treatment of the baby should continue for the first year of life *(88, 104, 107).* Treatment in utero and during the first

TABLE 3. *General recommendations for safe food handling for the prevention of foodborne disease*[a]

1. Buying food
   a. Examine the condition of the food. Refrigerated foods should feel cold and frozen foods should be thoroughly frozen. Cans (for canned foods) should not be dented, cracked, or bulging. Meats should be fresh without excessive drip or odor, and vegetables and fruits should be fresh and not bruised or wilted. Do not buy cracked or dirty eggs.
   b. Check sell-by or use-by dates. Do not buy more product than can be used by the final date.
   c. Do not buy raw milk or dairy products made from raw milk. If the dairy product has been pasteurized, the product label will indicate it.
   d. When shopping, buy groceries last. Do not leave groceries in a hot car but drive straight home and promptly place food items at their proper storage temperature.
2. Storing food
   a. Check temperature of refrigerator and freezer. The refrigerator should be at ≤40°F (≤4.4°C). A good rule to follow is to keep the refrigerator as cold as possible without freezing milk or produce. The freezer should be at 0°F (−17.8°C).
   b. Raw red meats, poultry, or seafood should be placed on separate plates during refrigeration to prevent juices from dripping onto cooked foods or raw vegetables and fruit. Juices from flesh foods contain bacteria that can contaminate other foods.
   c. Refrigerate dairy foods such as milk, cheese, cottage cheese, yogurt, etc.
   d. Eggs should be refrigerated.
3. Preparing food
   a. Wash hands with soap and hot water before preparing foods.
   b. Prevent cross-contamination of foods by keeping raw meats, poultry, and seafoods (and their juices) away from other foods. When switching from preparing a particular food to another, wash hands, knives, cutting boards, countertop (including sink and faucets), and any utensils with soap and hot water to prevent cross-contamination. Cutting boards should be plastic and should be washed thoroughly when necessary during use.
   c. Pregant women as well as other immunocompromised individuals should dry their hands with disposable paper towels. Washed food preparation equipment should be dried with disposable paper towels, also. Use disposable paper towels to clean up meat or poultry juices. Cloth towels and sponges are excellent breeding grounds for bacterial growth and should be avoided. However, if cloth towels or sponges are used in the kitchen, they should be changed frequently and thoroughly cleaned before reusing.
   d. Frozen foods should not be thawed at room temperature on the kitchen countertop. Frozen foods should be allowed to thaw in the refrigerator or they may be thawed by microwaving. Meats should be marinated in the refrigerator.
   c. Vegetables (lettuce, carrots, etc.) or fruits that are eaten raw should be washed thoroughly. Vegetables should be washed before cooking.
   f. Pets should not be permitted in the kitchen area during preparation and cooking foods.
4. Cooking food
   a. Cook red meats (in particular, hamburger) to an internal temperature of 160°F (71.1°C) and poultry to an internal temperature of 180°F (82.2°C). Use a meat thermometer. Visual tests for doneness: red meat is gray or brown inside; poultry juices run clear; and fish flakes with a fork. For pregnant women and immunocompromised individuals, raw, rare, or undercooked hamburger, steaks, or roasts pose a potential microbial hazard and should be avoided. Stuffing for turkey or chicken should be cooked separately.
   b. Do not interrupt cooking. Cook foods, especially poultry and meats, completely at one time. Partial cooking may permit bacterial growth during the period before cooking is resumed.
   c. If cooking food, especially meat or poultry, from the frozen state, more cooking time is necessary. The cooking time should be approximately 1½ times longer than for thawed food.
   d. Ready-to-eat meat products (hot dogs, luncheon meats, cold cuts) may be eaten unheated unless the freshness of the product is in question or if the product has been temperature abused. Immunucompromised individuals should heat ready-to-eat meat products thoroughly to a steaming temperature before eating.
   e. Cook eggs thoroughly. The yolk and white should be firm, not runny. Scrambled eggs should have a firm texture. Use a pasteurized egg product for recipes that require uncooked or partially cooked eggs.
5. Serving food
   a. Dishes and utensils used in the preparation of food should not be used for serving foods, e.g., grilled meats should be served on a clean plate, not on the plate that held the raw meats.
   b. Hot foods should be served promptly, and cold foods should be removed from refrigerator just prior to serving.
   c. Picnic foods should be in a cooler with a cold pack. The cooler should not be placed in direct sun. Brown bag lunches should be packed in an insulated lunch bag with a cold pack.
   d. Perishable foods should not be left out of refrigerator for >2 h.
6. Handling leftovers
   a. Leftovers should be divided into several small shallow containers so that quick cooling is achieved in the refrigerator.
   b. The stuffing from stuffed fowl should be removed and the bird and stuffing refrigerated separately. However, stuffed fowl is not recommended for pregnant women or immunocompromised individuals unless fowl and stuffing have been cooked separately.
   c. Leftovers should be reheated thoroughly until steaming hot. Sauces, gravies, and soups should be brought to a boil.
   d. Either freeze leftover foods (thaw properly and cook properly when they are to be eaten) or use within 2 to 3 days after refrigerating.

[a] Adapted from U.S. Department of Agriculture *(119, 120)*.

TABLE 4. *Specific recommendations to prevent listeriosis and toxoplasmosis during pregnancy*[a]

1. Listeriosis[b]
   a. Do not drink raw milk and do not eat dairy products made from raw milks. Avoid soft cheeses such as Feta, Brie, Camembert, blue-veined cheeses, and any soft, ethnic-type cheeses such as Mexican-style white cheeses. Processed cheese slices, hard cheeses such as cheddar, and refrigerated dairy products such as cottage cheese, yogurt, or cream cheese are acceptable.
   b. Leftover foods or ready-to-eat foods such as hot dogs should be heated thoroughly until steaming before eating.
   c. Foods from delicatessen counters are not recommended. Prepackaged salads and pâté should not be eaten. Delistyle cold cuts should be heated thoroughly until steaming.
   d. Precooked meals that have subsequently been stored at refrigerated temperatures (cook–chill meals) should be thoroughly recooked until the product is steaming.
2. Toxoplasmosis[c]
   a. Meat: When preparing raw meats, avoid touching face, mouth, or eyes. Avoid eating raw or undercooked meat. Cook meat to an internal temperature of 160°F (71.1°C). Freezing meat to at least 9.2°F (−12.5°C) will inactivate *T. gondii.*
   b. Vegetables: Wash fruits, berries, and vegetables thoroughly. Do not touch mouth, face, or eyes when handling raw fruits, berries, and vegetables (cat feces containing the parasite may have contaminated the products).
   c. Cats: Because cats are the definitive host for *T. gondii,* the pregnant woman must take especial care concerning cats. Do not let house cats forage outside and do not send cats to a kennel because the cats may be infected with the parasite by eating infected rodents or birds or by coming in contact with feces from infected cats. Cats should be fed only well-cooked, dried, or canned foods. The pregnant woman should never clean the cat litter box.
   d. Gardening: Gardening during pregnancy should be discouraged. *T. gondii* may be present in garden soil contaminated by cat feces. Handling garden soil or breathing dust from garden soil may lead to infection.

[a] These recommendations are to be used in conjunction with the recommendations given in Tables 2 and 3.
[b] Adapted from Buchdahl et al. *(13)* and the Centers for Disease Control and Prevention *(19).*
[c] Adapted from Grant *(48).*

year of life has been shown to alleviate the severity of congenital toxoplasmosis *(25, 50).*

Prevention of foodborne disease during pregnancy. The pregnant woman can protect herself and her unborn child from foodborne illness by using a commonsense approach to food hygiene. The most important rules of microbial food safety are given in Table 2. Rule 1: A high standard of personal hygiene is the prime factor in the prevention of the transmission of foodborne disease. Hand washing with hot water and soap must be done (i) before food preparation; (ii) as often as necessary during food preparation (i.e., after handling raw meat or chicken, etc.); and (iii) before serving foods. Of course, handwashing is imperative after using toilet facilities, changing diapers, or handling pets. Rule 2: The 3K rule emphasizes that raw foods should be bought from a reliable and clean source to ensure that the foods have low numbers of microorganisms. The customer should store the foods at proper temperatures in a clean environment to minimize introduction of microorganisms as well as prevention of microbial growth. Finally, proper processing (pasteurization, cooking, or other processes that destroy microorganisms) will lead to the destruction of a large portion of the microbial population present in foods. Rule 3: The 40-140 rule is important because most bacteria can multiply at temperatures between 40 and 140°F—the danger zone. However, some microorganisms, e.g., *L. monocytogenes* or *Y. enterocolitica,* can grow slowly at ≤40°F. Therefore, pregnant women and other immunocompromised individuals should not allow foods to remain refrigerated for long periods. Freezing is proper for long-term storage. Keep cold foods cold and hot foods hot. If foods have been in the danger zone for >2 h, they should be discarded. Rule 4: If the microbial safety of a particular food is in doubt, it is wise to discard the food. Thus, if the freshness of the food is suspect (i.e., it is believed that bacterial growth has taken place), then the food should be disposed of. If the packaging of the food item is torn or punctured, or if temperature abuse has taken place, then the item should be discarded. Adherence to the four cardinal rules of microbial food safety will do much to minimize foodborne disease.

Some general recommendations that should be helpful to all individuals including the pregnant woman when buying, storing, preparing, cooking, and serving food are given in Table 3. In addition, Table 3 provides advice on handling leftover food. A number of specific recommendations for the prevention of listeriosis and toxoplasmosis during pregnancy are listed in Table 4.

Eating out may pose problems during pregnancy. A good basic rule to follow: what would not be eaten in one's own home should not be eaten in a restaurant or at someone's home. If the restaurant environment and restaurant personnel do not present a clean appearance or if the food has not been cooked or served properly, then the pregnant woman should eat elsewhere. The recommendations for pregnant women given in Tables 2, 3, and 4 apply to restaurants as well as to home kitchens. Similarly, those recommendations apply when the pregnant woman is eating as a guest at a friend's or neighbor's home.

Traveling during pregnancy requires vigilance on the part of the woman. If at all possible, the pregnant woman should not travel to underdeveloped countries. If she does travel to an underdeveloped country, the guidelines given in Tables 2, 3, and 4 must be followed religiously. In addition, tap water should be boiled (3 min) or disinfected by chemical treatment (iodine tablets); ice cubes should not be

used unless they have been prepared from properly treated water. Regardless of the country visited, the recommendations given in Tables 2, 3, and 4 for safe foods apply.

A FINAL RECOMMENDATION

Pregnancy is a time of particular vulnerability when a woman and her fetus are susceptible to foodborne infections. Foodborne infections can be controlled to a large extent if the woman follows the recommendations given in Tables 2, 3, and 4. In the long term, however, education is the real key to prevention of foodborne illnesses. The practice of safe food handling is not an innate ability and it must be learned. The younger an individual begins learning proper food safety techniques, the more likely he or she will practice them. Education in microbial food safety should start early in the child's life beginning in nursery school and continue through kindergarten, grade school, and high school. The education program should be developed so that the child can grasp concepts of microbial food safety suitable for his or her age and understanding. As the child's education continues, the concepts can be expanded so that by the time the individual graduates from high school, she or he will have a firm grasp on how to prevent foodborne disease. An individual trained in this manner will, as an adult, practice microbial food safety in the home and in the workplace. Thus, a female trained in concepts of microbial food safety from nursery school through high school would be able to protect herself and her baby from foodborne illness.

REFERENCES

1. Al-Eissa, Y. A., and S. M. Al-Mofada. 1992. Congenital brucellosis. Pediatr. Infect. Dis. J. 11:667–671.
2. Allos, B. M. 1998. *Campylobacter jejuni* infection as a cause of the Guillain-Barré syndrome. Infect. Dis. Clin. N. Am. 12:173–184.
3. Al-Mofada, S. M., Y. A. Al-Eissa, E. S. Saeed, and A. M. Kambal. 1993. Isolation of *Brucella melitensis* from human milk. J. Infect. 26:346–348.
4. Arvin, A. M., and Y. A. Maldonado. 1995. Protozoan and helminth infections (including *Pneumocystis carinii*), p. 757–804. *In* J. S. Remington and J. O. Klein (eds.), Infectious diseases of the fetus and newborn infant. W. B. Saunders Co., Philadelphia.
5. Auchincloss, H., and D. H. Sachs. 1993. Transplantation and graft rejection, p. 1099–1141. *In* W. E. Paul (ed.), Fundamental immunology, 3rd ed. Raven Press, New York.
6. Baird-Parker, A. C. 1994. Foods and microbiological risks. Microbiology 140:687–695.
7. Benenson, M. W., E. T. Takafuji, S. M. Lemon, and A. J. Sulzer. 1982. Oocyst-transmitted toxoplasmosis associated with ingestion of contaminated water. N. Engl. J. Med. 307:666–669.
8. Bennish, M. L. 1994. Cholera: pathophysiology, clinical features, and treatment, p. 229–255. *In* I. K. Wachsmuth, P. A. Blake, and O. Olsvik (eds.), *Vibrio cholerae* and cholera: molecular to global perspectives. American Society for Microbiology Press, Washington, D.C.
9. Biavasco, F., E. Giovanetti, A. Miele, C. Vignaroli, B. Facinelli, and P. E. Varaldo. 1996. In vitro conjugative transfer of vanA vancomycin resistance between *Enterococci* and *Listeriae* of different species. Eur. J. Clin. Microbiol. Infect. Dis. 15:50–59.
10. Bolik, A., J. Wissel, and A. Rolfs. 1995. Guillain-Barré syndrome in pregnancy—two case reports and a discussion of management. Arch. Gynecol. Obstet. 256:199–203.
11. Bortolussi, R., and W. F. Schlech. 1995. Listeriosis, p. 1055–1073. *In* J. S. Remington and J. O. Klein (eds.), Infectious diseases of the fetus and newborn infant. W. B. Saunders Co., Philadelphia.
12. Bowie, W. R., A. S. King, D. H. Werker, J. L. Issac-Renton, A. Bell, S. B. Eng, and S. A. Marion. 1997. Outbreaks of toxoplasmosis associated with municipal drinking water. Lancet 350:173–177.
13. Buchdahl, R., M. Hird, H. Gamsu, A. Tapp, D. Gibb, and C. Tzannatos. 1990. Listeriosis revised: the role of the obstetrician. Br. J. Obstet. Gynaecol. 97:186–189.
14. Buffolano, W., R. E. Gilbert, F. J. Holland, D. Fratta, F. Palumbo, and A. E. Ades. 1996. Risk factors for recent toxoplasma infection in pregnant women in Naples. Epidemiol. Infect. 116:347–351.
15. Buzby, J. C., and T. Roberts. 1996. ERS updates U.S. foodborne disease costs for seven pathogens. FoodReview (USDA, Economic Research Service) 19:20–25.
16. Buzby, J. C., T. Roberts, and B. M. Allos. 1997. Estimated annual costs of *Campylobacter*-associated Guillain-Barré syndrome. Agricultural Economic Report 756. Food and Consumer Economics Division, Economic Research Service, U.S. Department of Agriculture, Washington, D.C.
17. Buzby, J. C., T. Roberts, C.-T. J. Lin, and J. M. MacDonald. 1996. Bacterial foodborne disease. Medical costs and productivity losses. Agricultural Economic Report 741. Food and Consumer Economics Division, Economic Research Service, U.S. Department of Agriculture, Washington, D.C.
18. CDCP (Centers for Disease Control and Prevention). 1998. Incidence of foodborne illness—FoodNet 1997. Morbid. Mortal. Weekly Rep. 47:782–786.
19. CDCP (Centers for Disease Control and Prevention). 1992. Update: foodborne listeriosis—United States, 1988–1990. Morbid. Mortal. Weekly Rep. 41:251, 257–258.
20. Chan, M. C. K., and A. Y. Sweet. 1991. Parasitic diseases, p. 183–213. *In* A. Y. Sweet and E. G. Brown (eds.), Fetal and neonatal effects of maternal disease. Mosby Year Book, St. Louis.
21. Charpentier, E., G. Gerbaud, C. Jacquet, J. Rocourt, and P. Courvalin. 1995. Incidence of antibiotic resistance in *Listeria* species. J. Infect. Dis. 172:277–281.
22. Chheda, S., S. M. Lopez, and E. P. Sanderson. 1997. Congenital brucellosis in a premature infant. Pediatr. Infect. Dis. J. 16:81–83.
23. Cook, G. C. 1990. *Toxoplasma gondii* infection: a potential danger to the unborn fetus and AIDS sufferer. Q. J. Med. New Ser. 74 273:3–19.
24. Cunningham, F. G., P. C. MacDonald, N. F. Gant, K. J. Leveno, L. C. Gilstrap, G. D. V. Hankin, and S. L. Clark. 1997. Williams obstetrics, 20th ed. Appleton and Lange, Stamford, Conn.
25. Daffos, F. J., F. Forestier, M. Capellal-Pavlovsky, P. Thulliez, C. Aufrant, D. Vanlenti, and W. L. Cox. 1988. Prenatal management of 746 pregnancies at risk for congenital toxoplasmosis. N. Engl. J. Med. 318:271–275.
26. Dale, B. A. S., G. Gordon, R. Thomson, and R. Urquhart. 1987. Perinatal infection with cryptosporidium. Lancet i:1042–1043.
27. Dashe, J. S., S. M. Ramin, and F. G. Cunningham. 1998. The long-term consequences of thrombotic microangiopathy (thrombotic thrombocytopenic purpura and hemolytic uremic syndrome) in pregnancy. Obstet. Gynecol. 91:662–668.
28. Dean, J. H., M. I. Luster, G. A. Boorman, R. W. Luebke, and L. D. Lauer. 1980. The effect of adult exposure to diethylstilbestrol in the mouse: alterations in tumor susceptibility and host resistance parameters. J. Reticulendothel. Soc. 28:571–583.
29. D'Ercole, C., L. Doubli, J. Franck, M. Casta, J.-R. Harle, C. Chagnon, L. Cravello, M. Leclaire, and B. Blanc. 1995. Recurrent congenital toxoplasmosis in a woman with lupus erythematosus. Prenatal Diagn. 15:1171–1175.
30. Dildy, G. A., M. G. Martens, S. Faro, and W. Lee. 1990. Typhoid fever in pregnancy. A case report. J. Reprod. Med. 35:273–276.
31. Dollfus, H., P. Dureau, C. Hennequin, Y. Uteza, A. Bron, and J. L. Dufier. 1998. Congenital toxoplasma chorioretinitis transmitted by preconceptionally immune woman. Br. J. Ophthalmol. 82:1444–1448.
32. Donnelly, C. W. 1994. *Listeria monocytogenes,* p. 215–252. *In* Y. H. Hui, J. R. Gorham, K. D. Murrell, and D. O. Cliver (eds.),

Foodborne disease handbook, vol. 1. Marcel Dekker, Inc., New York.
33. Dubey, J. P., and C. P. Beattie. 1988. Toxoplasmosis of animals and man. CRC Press, Inc., Boca Raton, Fla.
34. Dubey, J. P., and S. K. Shen. 1991. Rat model of congenital toxoplasmosis. Infect. Immun. 59:3301–3302.
35. Dubey, J. P., S. K. Shen, O. C. H. Kwok, and P. Thulliez. 1997. Toxoplasmosis in rats *(Rattus norvegicus)*: congenital transmission to first and second generation offspring and isolation of *Toxoplasma gondii* from seronegative rats. Parasitology 115:9–14.
36. Egerman, R. S., A. G. Witlin, S. A. Friedman, and B. M. Sibai. 1996. Thrombotic thrombocytopenic purpura and hemolytic uremic syndrome in pregnancy: review of 11 cases. Am. J. Obstet. Gynecol. 175:950–956.
37. Farber, J. M., and P. I. Peterkin. 1991. *Listeria monocytogenes,* a food-borne pathogen. Microbiol. Rev. 55:476–511.
38. Fleck, D. G., B. S. Chessum, and M. Perkins. 1972. Coccidian-like nature of *Toxoplasma gondii.* Br. Med. J. 3:111–112.
39. Fournier, P.-E., T. J. Marrie, and D. Raoult. 1998. Diagnosis of Q fever. J. Clin. Microbiol. 36:1823–1834.
40. Frenkel, J. K. 1990. Toxoplasmosis in human beings. J. Am. Vet. Med. Assoc. 196:240–248.
41. Friedland, J. S., I. Jeffrey, G. E. Griffin, M. Booker, and R. Courtenay-Evans. 1994. Q fever and intrauterine death. Lancet 343:288.
42. Fuchs, S., D. Hochner-Celnikier, and O. Shalev. 1994. First trimester listeriosis with normal fetal outcome. Eur. J. Clin. Microbiol. Infect. Dis. 13:656–658.
43. Garcia, A. C. P. 1968. Congenital toxoplasmosis in two successive sibs. Arch. Dis. Child. 43:705–709.
44. Gavinet, M. F., F. Robert, G. Firtion, E. Delouvrier, C. Hennequin, J. R. Maurin, C. Tourte-Schaefer, and J. Dupouy-Camet. 1997. Congenital toxoplasmosis due to maternal reinfection during pregnancy. J. Clin. Microbiol. 35:1276–1277.
45. Gellin, B. G., and C. V. Broome. 1989. Listeriosis. J. Am. Med. Assoc. 261:1313–1320.
46. Goh, J., and M. Flynn. 1992. *Campylobacter jejuni* in pregnancy. Aust. N.Z. J. Obstet. Gynaecol. 32:246–248.
47. Gold, E., M. L. Kumar, G. Nankervis, and A. Y. Sweet. 1991. Viral infections, p. 1–83. *In* A. Y. Sweet and E. G. Brown (eds.), Fetal and neonatal effects of maternal disease. Mosby Year Book, St. Louis.
48. Grant, A. 1996. Varicella infection and toxoplasmosis in pregnancy. J. Perinat. Neonat. Nurs. 10:17–29.
49. Hall, S. M. 1992. Congenital toxoplasmosis. Br. Med. J. 305:291–297.
50. Hohlfeld, P., F. Daffos, P. Thulliez, C. Aufrant, J. Couvreur, J. MacAleese, D. Descombey, and F. Forestier. 1989. Fetal toxoplasmosis: outcome of pregnancy and infant follow-up after in utero treatment. J. Pediatr. 115:765–769.
51. Jiang, G.-X., J. de Pedro-Cuesta, K. Strigård, T. Olsson, and H. Link. 1996. Pregnancy and Guillain-Barré syndrome: a nationwide register cohort study. Neuroepidemiology 15:192–200.
52. Kalstone, C. 1991. Successful antepartum treatment of listeriosis. Am. J. Obstet. Gynecol. 164:57–58.
53. Kapperud, G., P. A. Jenum, B. Stray-Pedersen, K. K. Melbey, A. Eskild, and J. Eng. 1996. Risk factors for *Toxoplasma gondii* infection in pregnancy. Results of a prospective case-control study in Norway. Am. J. Epidemiol. 144:405–412.
54. Kaufmann, S. H. E. 1993. Immunity to intracellular bacteria, p. 1251–1286. *In* W. E. Paul (ed.), Fundamental immunology, 3rd ed. Raven Press, New York.
55. Khuroo, M. S., S. Karmili, and S. Jameel. 1995. Vertical transmission of hepatitis E virus. Lancet 345:1025–1026.
56. Kittas, C., and L. Henry. 1980. Effect of sex hormones on the response of mice to infection with *Toxoplasma gondii.* Br. J. Exp. Pathol. 61:590–600.
57. Klink, M., and W. Rudnicka. 1995. *Listeria monocytogenes* infection in pregnant mice: abnormalities in the function of non-adherent accessory light density dendritic cells. FEMS Immunol. Microbiol. 12:143–152.
58. Kreutner, A. K., V. E. Del Bene, and M. S. Amstey. 1981. Giardiasis in pregnancy. Am. J. Obstet. Gynecol. 140:895–901.
59. Lähdevirta, J., A. M. M. Jokipii, K. Sammalkorpi, and L. Jokipii. 1987. Perinatal infection with cryptosporidium and failure to thrive. Lancet i:48–49.
60. Lamont, R. J., R. Postlethwaite, and A. P. MacGowan. 1988. *Listeria monocytogenes* and its role in human infection. J. Infect. 17: 7–28.
61. Lorber, B. 1990. Clinical listeriosis—implications for pathogenesis, p. 41–49. *In* A. J. Miller, J. L. Smith, and G. A. Somkuti (eds.), Foodborne listeriosis. Elsevier, New York.
62. Lubani, M. M., K. I. Dudin, D. C. Sharda N. M. A. Sinna, T. Al-Shab, A. A. Al-Refe'ai, S. M. Labani, and A. Nasrallah. 1988. Neonatal brucellosis. Eur. J. Pediatr. 147:520–522.
63. Ludlam, H., T. G. Wreghitt, S. Thornton, B. J. Thomson, N. J. Bishop, S. Coombe, and J. Cunniffe. 1997. Q fever in pregnancy. J. Infect. 34:75–78.
64. Luft, B. J., and J. S. Remington. 1982. Effect of pregnancy on resistance to *Listeria monocytogenes* and *Toxoplasma gondii* infections in mice. Infect. Immun. 38:1164–1171.
65. Luijckx, G. J., J. Vies, M. de Baets, R. Buchwald, and J. Troost. 1997. Guillain-Barré syndrome and mother and newborn child. Lancet 349:27.
66. Martínez-Román, E. Gratacós, A. Torné, R. Torra, F. Carmona, and V. Cararach. 1996. Successful pregnancy in a patient with hemolytic-uremic syndrome during the second trimester of pregnancy. A case report. J. Reprod. Med. 41:211–214.
67. Marty, P., A. Bongain, A. Rahal, P. Thulliez, D. Wasfi, J. C. Lambert, Y. Le Fichoux, and J. Y. Guillet. 1994. Prenatal diagnosis of severe fetal toxoplasmosis as a result of toxoplasmic reactivation in an HIV-1 seropositive woman. Prenatal Diagn. 14:414–415.
68. Mascola, L., D. P. Ewert, and A. Eller. 1994. Listeriosis: a previously unreported medical complication in women with multiple gestations. Am. J. Obstet. Gynecol. 170:1328–1332.
69. Mast, E. E., and K. Krawczynski. 1996. Hepatitis E: an overview. Annu. Rev. Med. 47:257–266.
70. Menudier, A., C. Bosgiraud, and J. A. Nicolas. 1994. Virulence de *Listeria monocytogenes* sur des souris gestantes. Pathol. Biol. 42: 510–520.
71. Mims, C., N. Dimmock, A. Nash, and J. Stephen. 1995. Mims' pathogenesis of infectious disease, 4th ed. Academic Press, New York.
72. Minkoff, H., J. S. Remington, S. Holman, R. Ramirez, S. Goodwin, and S. Landesman. 1997. Vertical transmission by human immunodeficiency virus-infected women. Am. J. Obstet. Gynecol. 176: 555–559.
73. Nachamkin, I., B. M. Allos, and T. Ho. 1998. *Campylobacter* species and Guillain-Barré syndrome. Clin. Microbiol. Rev. 11:555–567.
74. Paisley, J. W., and B. A. Lauer. 1992. Neonatal *Yersinia enterocolitica* enteritis. Pediatr. Infect. Dis. J. 11:331–332.
75. Pastorek, J. G. 1993. The ABCs of hepatitis in pregnancy. Clin. Obstet. Gynecol. 36:843–854.
76. Pastorek, J. G. 1990. Protozoan diseases in pregnancy, p. 221–245. *In* L. G. Gilstrap and S. Faro (eds.), Infections in pregnancy. Wiley-Liss, New York.
77. Peterson, J. W. 1996. Bacterial pathogenesis, p. 121–135. *In* S. Baron (ed.), Medical microbiology, 4th ed. University of Texas Medical Branch, Galveston, Tex.
78. Piccinni, M. P., M.-G. Giudizi, R. Biagiotti, L. Beloni, L. Giannarini, S. Sampognaro, P. Parronchi, R. Manetti, F. Annunziato, C. Livi, S. Romagnani, and E. Maggi. 1995. Progesterone favors the development of human T helper cells producing Th2-type cytokines and promotes both IL-4 production and membrane CD30 expression in established Th1 cell clones. J. Immunol. 155:128–133.
79. Pickering, L. K., R. L. Guerrant, and T. G. Cleary. 1995. Microorganisms responsible for neonatal diarrhea, p. 1142–1222. *In* J. S. Remington and J. O. Klein (eds.), Infectious diseases of the fetus and newborn infant. W. B. Saunders Co., Philadelphia.
80. Poole, P. M., D. B. Whitehouse, and M. M. Gilchrist. 1972. A case

of abortion consequent upon infection with *Brucella abortus* biotype 2. J. Clin. Pathol. 25:882–884.

81. Poyart-Salmeron, C., C. Carlier, P. Trieu-Cuot, A.-L. Courtieu, and P. Courvalin. 1990. Transferable plasmid-mediated antibiotic resistance in *Listeria monocytogenes.* Lancet 335:1422–1426.
82. Pung, O. J., and M. I. Luster. 1986. *Toxoplasma gondii*: decreased resistance to infection in mice due to estrogen. Exp. Parasitol. 61: 48–56.
83. Pung, O. J., M. I. Luster, H. T. Hayes, and J. Rader. 1984. Influence of steroidal and nonsteroidal sex hormones on host resistance in mice: increased susceptibility to *Listeria monocytogenes* after exposure to estrogenic hormones. Infect. Immun. 46:301–307.
84. Quentin, C., M. C. Tribaut, J. Horovitz, and C. Bebear. 1990. Multiresistant strain of *Listeria monocytogenes* in septic abortion. Lancet 330:375.
85. Rab, M. A., M. K. Bile, M. M. Mubarik, H. Asghar, Z. Sami, S. Siddiqi, A. S. Dil, M. A. Barzgar, M. A. Chaudhry, and M. I. Burney. 1997. Water-borne hepatitis E virus epidemic in Islamabad, Pakistan—a common source outbreak traced to the malfunction of a modern water treatment plant. Am. J. Trop. Med. Hyg. 57:151–157.
86. Raghupathy, R. 1997. Maternal anti-placental cell-mediated reactivity and spontaneous abortions. Am. J. Reprod. Immunol. 37:478–484.
87. Raoult, D., and A. Stein. 1994. Q fever during pregnancy—a risk for women, fetuses, and obstetricians. N. Engl. J. Med. 330:371.
88. Remington, J. S., R. McLeod, and G. Desmonts. 1995. Toxoplasmosis, p. 140–267. *In* J. S. Remington and J. O. Klein (eds.), Infectious diseases of the fetus and newborn infant. W. B. Saunders Co., Philadelphia.
89. Riechman, N., R. Raz, A. Keysary, R. Goldwasser, and E. Flatau. 1988. Chronic Q fever and severe thrombocytopenia in a pregnant woman. Am. J. Med. 85:253–254.
90. Roberts, C. W., and J. Alexander. 1992. Studies on a murine model of congenital toxoplasmosis: vertical disease transmission only occurs in BALB/c mice infected for the first time during pregnancy. Parasitology 104:19–23.
91. Roberts, C. W., S. M. Cruickshank, and J. Alexander. 1995. Sex-determined resistance to *Toxoplasma gondii* is associated with temporal differences in cytokine production. Infect. Immun. 63:2549–2555.
92. Roberts, T., K. D. Murrell, and S. Marks. 1994. Economic losses caused by foodborne parasitic diseases. Parasitol. Today 10:419–423.
93. Rolfs, A., and A. Bolik. 1994. Guillain-Barré syndrome in pregnancy: reflections on immunopathogens. Acta Neurol. Scand. 89: 400–402.
94. Sabahi, F., M. Rola-Plesczcynski, S. O'Connell, and L. D. Frenkel. 1995. Qualitative and quantitative analysis of T lymphocytes during normal human pregnancy. Am. J. Reprod. Immunol. 33:381–392.
95. Schlech, W. F. 1990. *Listeria,* animals and man: aspects of virulence, p. 51–54. *In* A. J. Miller, J. L. Smith, and G. A. Somkuti (eds.), Foodborne listeriosis. Elsevier, Amsterdam, The Netherlands.
96. Schlech, W. F. 1993. An animal model of foodborne *Listeria monocytogenes* virulence: effect of alterations in local and systemic immunity on invasive infection. Clin. Invest. Med. 16:219–225.
97. Schuchat, A., B. Swaminathan, and C. V. Broome. 1991. Epidemiology of human listeriosis. Clin. Microbiol. Rev. 4:169–183.
98. Scialli, A. R., and T. L. Rarick. 1992. Salmonella sepsis and second-trimester pregnancy loss. Obstet. Gynecol. 79:820–821.
99. Sirry, H. W., R. H. George, and M. J. Whittle. 1994. Meningoencephalitis due to listeria monocytogenes in pregnancy. Br. J. Obstet. Gynaecol. 101:1083–1084.
100. Skirrow, M. B., and M. J. Blaser. 1995. *Campylobacter jejuni,* p. 825–848. *In* M. J. Blaser, P. D. Smith, J. I. Ravdin, H. B. Greenberg, and R. L. Guerrant (eds.), Infections of the gastrointestinal tract. Raven Press, New York.
101. Smith, J. L. 1993. Documented outbreaks of toxoplasmosis: transmission of *Toxoplasma gondii* to humans. J. Food Prot. 56:630–639.
102. Smith, J. L. 1997. Long term consequences of foodborne toxoplasmosis: effects on the unborn, the immunocompromised, the elderly and the immunocompetent. J. Food Prot. 60:1595–1611.
103. Smith, L. D., and T. A. Ficht. 1982. Pathogenesis of *Brucella.* Crit. Rev. Microbiol. 17:209–230.
104. St. Georgiev, V. 1994. Management of toxoplasmosis. Drugs 48: 179–188.
105. Stagno, S., A. C. Dykes, C. S. Amos, R. A. Head, D. D. Juranek, and K. Walls. 1980. An outbreak of toxoplasmosis linked to cats. Pediatrics 65:706–712.
106. Stein, A., and D. Raoult. 1998. Q fever during pregnancy: a public health problem in southern France. Clin. Infect. Dis. 27:592–596.
107. Stray-Pedersen, B. 1992. Treatment of toxoplasmosis in the pregnant mother and newborn child. Scand J. Infect. Dis. (Suppl. 84): 23–31.
108. Sweet, A. V. 1991. Bacterial infections, p. 84–167. *In* A. Y. Sweet and E. G. Brown (eds.), Fetal and neonatal effects of maternal disease. Mosby Year Book, St. Louis.
109. Szekeres-Bartho, J. 1993. Endocrine regulation of the immune system during pregnancy, p. 151–172. *In* G. Chaouat (ed.), Immunology of pregnancy. CRC Press, Boca Raton, Fla.
110. Szekeres-Bartho, J., and T. G. Wegmann. 1996. A progesterone-dependent immunomodulatory protein alters the Th1/Th2 balance. J. Reprod. Immunol. 31:81–95.
111. Tappero, J. W., A. Schuchat, K. A. Deaver, L. Mascola, and J. D. Wenger. 1995. Reduction in the incidence of human listeriosis in the United States. J. Am. Med. Assoc. 273:1118–1122.
112. Tauxe, R. V. 1992. Epidemiology of *Campylobacter jejuni* infections in the United States and other industrialized nations, p. 9–19. *In* I. Nachamkin, M. J. Blaser, and L. S. Tompkins (eds.), *Campylobacter jejuni*: current status and future trends. American Society of Microbiology, Washington, D.C.
113. Téllez, J., S. Moreno, D. Valkova, C. Domingo, P. Andra, F. de Ory, F. Albarrán, and D. Raoult. 1998. Q fever in pregnancy: case report after a 2-year follow-up. J. Infect. 37:79–81.
114. Teutsch, S. M., D. D. Juranek, A. Sulzer, J. P. Dubey, and R. K. Sikes. 1979. Epidemic toxoplasmosis associated with infected cats. N. Engl. J. Med. 300:695–699.
115. Todd, E. C. D. 1989. Preliminary estimates of costs of foodborne disease in the United States. J. Food Prot. 52:595–601.
116. Tsakris, A., A. Papa, J. Douboyas, and A. Antoniadis. 1997. Neonatal meningitis due to multi-resistant *Listeria monocytogenes.* J. Antimicrob. Chemother. 39:553–554.
117. Tsega, E., B.-G. Hansson, K. Krawczynski, and E. Nordenfeldt. 1992. Acute sporadic viral hepatitis in Ethiopia: causes, risk factors, and effects on pregnancy. Clin. Infect. Dis. 14:961–965.
118. U.S. Bureau of the Census. 1996. Statistical abstracts of the United States: 1996, 116th ed. Washington, D.C. (Tables 13, 14, 109).
119. U.S. Department of Agriculture (FSIS). 1995. A quick consumer guide to safe food handling. Home and Garden Bulletin 248.
120. U.S. Department of Agriculture (FSIS). 1984. The safe food book. Your kitchen guide. Home and Garden Bulletin 241.
121. Vogel, N., M. Kirisits, E. Michael, H. Bach, M. Hostetter, K. Boyer, R. Simpson, E. Holfels, J. Hopkins, D. Mack, M. B. Mets, C. N. Swisher, D. Patel, N. Roizen, L. Stein, M. Stein, S. Withers, E. Mui, C. Egwuagu, J. Remington, R. Dorfman, and R. McLeod. 1996. Congenital toxoplasmosis transmitted from an immunologically competent mother infected before conception. Clin. Infect. Dis. 23:1055–1060.
122. Walker, W., C. W. Roberts, D. J. P. Ferguson, H. Jebbari, and J. Alexander. 1997. Innate immunity to *Toxoplasma gondii* is influenced by gender and is associated with differences in interleukin-12 and gamma interferon production. Infect. Immun. 65:1119–1121.
123. Watson, J. C., D. W. Fleming, A. J. Borella, E. S. Olcott, R. E. Conrad, and R. C. Baron. 1993. Vertical transmission of hepatitis A resulting in an outbreak in a neonatal intensive care unit. J. Infect. Dis. 167:567–571.

124. Wegmann, T. G., H. Lin, L. Guilbert, and T. R. Mosmann. 1993. Bidirectional cytokine interactions in the maternal–fetal relationship: is successful pregnancy a T_H2 phenomenon? Immunol. Today 14:353–356.
125. Weinberg, E. D. 1984. Pregnancy-associated depression of cell-mediated immunity. Rev. Infect. Dis. 6:814–831.
126. Weinberg, E. D. 1987. Pregnancy-associated immune suppression: risks and mechanisms. Microbiol. Pathogen. 3:393–397.
127. Weiner, C. P. 1987. Thrombotic microangiopathy in pregnancy and the postpartum period. Semin. Hematol. 24:119–129.
128. Wong, S.-Y., and J. S. Remington. 1994. Toxoplasmosis in pregnancy. Clin. Infect. Dis. 18:851–862.
129. Young, E. J. 1983. Human brucellosis. Rev. Infect. Dis. 5:821–841.
130. Zeldis, J. B., and C. S. Crumpacker. 1995. Hepatitis, p. 805–834. *In* J. S. Remington and J. O. Klein (eds.), Infectious diseases of the fetus and newborn infant. W. B. Saunders Co., Philadelphia.
131. Zenner, L., F. Darcy, M.-F. Cesbron-Delauw, and A. Capron. 1993. Rat model of congenital toxoplasmosis: rate of transmission of three *Toxoplasma gondii* strains to fetuses and protective effect of a chronic infection. Infect. Immun. 61:360–363.
132. Zervoudakis, J., and L. L. Cederqvist. 1977. Effect of *Listeria monocytogenes* septicemia during pregnancy on the offspring. Am. J. Obstet. Gynecol. 129:465–467.