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Sexually Transmitted Disease and Pregnancy

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Thirteen million Americans acquire sexually transmitted diseases (STD) annually (Martens, 1994). This RISK||NEWSLETTER will look at the intrauterine and intrapartum risks associated with pregnancy in women infected by four common STD's: herpes, chlamydia, gonorrhea and genital warts.

HERPES SIMPLEX 2

Herpes simplex 2 is a virus that presents in adults with itchy, painful blisters, swelling and redness in the genital region, and on occasion, flu-like symptoms. Once a person is infected, the virus remains with them, and periods of latency can be interrupted by symptomatic outbreaks. It is estimated that up to 56% of infected people experience recurrent lesions (Martens, 1994). Brunham et al. (1990) found that between 0.5 and 1% of all pregnant women are infected with herpes.

Most research indicates an increased risk of miscarriage in primary maternal herpes infection, ranging from 20-54% (Robb et al., 1986; Naeye, 1993; Whitley, 1990). A study by Harger et al. (1989) found that women with recurrent infection are not at an increased risk of having a miscarriage, while another study (Naeye, 1993) found a 25% miscarriage rate when recurrent infection occurred before 20 weeks gestation. One study indicated a 35% rate of premature birth when herpes was acquired after 20 weeks gestation (Naeye, 1993).

Intrauterine infection of herpes in humans is rare. There are only approximately 80 cases of such an infection reported in the literature (Teris, 1994). Three different studies that looked at a total of 302 infants born to mothers with herpes, found no instances of congenital herpes (Grossman et al., 1981; Harger et al., 1983; Brown et al., 1985). The risk of intrauterine infection appears to be greater in women who experience a primary rather than a recurrent infection during pregnancy (Brown et al., 1987).

Some of the adverse outcomes associated with intrauterine herpes infection are intrauterine growth retardation, microcephaly, hydranencephaly, hydrocephaly, chorioretinitis, porencephaly, intracranial calcification, microphthalmia and cutis aplasia (Hutto et al., 1987; Whitley, 1990). The findings associated with intrauterine infection were similar for women who contracted herpes in the first trimester and those who acquired the infection later in pregnancy. This indicates that the teratogenic effects of intrauterine infection represents disruption rather than malformation (Teris, 1994).

85 to 90% of neonatal herpes is acquired during delivery (Whitley, 1990). If the virus is present, the neonate is susceptible to infection. Women with primary infection are at an increased risk of passing on the infection than women with recurrent infection. A study done by Brown et al. (1991) found that 6 out of 18 (33%) women with primary infection passed the infection to their neonate, while only one out of

34 (3%) women with recurrent infection passed it on to their infant. Martens (1994), in her review of herpes literature, found that the risk of intrapartum transmission of herpes in women with primary infection to be between 40 and 60%, while the risk was only 5% in women with recurrent infection. This difference is thought to be due to the protective effect of maternal antibodies in women with an older infection (Prober et al., 1987) and the increased duration and amount of viral shedding in a primary infection (Corey et al., 1983).

Not all virus shedding presents in the pregnant woman with obvious herpetic skin lesions. One study found that 70% of mothers with newborn herpes infection had no herpes symptoms at the time of delivery (March of Dimes web site, 1992). Neonates born to women with symptomless primary infection were 10 times more likely to develop infection than those babies born to mothers experiencing symptomless recurrent infection (March of Dimes web site, 1992).

Asymptomatic viral shedding can last up to two days, and the amount of virus shed is less than viral shedding that results in an outbreak of symptoms. In contrast, symptomatic viral shedding lasts about 7-10 days and the amount of virus shed is much greater than during asymptomatic shedding. Maximum asymptomatic viral shedding occurs 6 months after the initial episode of symptomatic herpes. Shedding has been found to occur 10 to 18 days in the six months following the initial infection. After this point, asymptomatic shedding has been estimated to occur 3 to 10 days per year. The percentage of women with a history of herpes actually shedding the virus during pregnancy (regardless of whether lesions are present) has been estimated to be between 0.2 and 7.4% (Whitley, 1990). Another study found that 3 in 1000 women had asymptomatic herpes virus shedding at the time of labor regardless of whether they were experiencing primary or recurrent infection (March of Dimes web site, 1992).

Intrapartum contraction of herpes presents three different ways in the neonate. Infection can be localized to the skin, eye or mouth, cause encephalitis, or cause disseminated infection (Whitley, 1990). The infection confined to the skin, eye and mouth causes symptoms such as skin lesions, keratoconjunctivitis, chorioretinitis and retinal dysplasia. Long term problems of infection confined to the skin, eye and mouth involve: cataracts, spastic quadriplegia, microcephaly and blindness (Whitley, 1990).

Approximately one third of infants develop encephalitis. Symptoms include seizures, lethargy, irritability, tremors, poor feeding, temperature instability, bulging fontanel and pyramidal tract signs. Long term problems associated with encephalitis include psychomotor retardation, microcephaly, hydranencephaly, porencephalic cysts, spasticity, blindness, chorioretinitis and learning disabilities (Whitley, 1990). There is a 50% mortality rate for these infants (Whitley, 1990).

Disseminated infection poses the greatest risk to the infant, with a greater than 80% mortality rate. The most common causes of death in these infants are herpes simplex pneumonitis and disseminated intravascular coagulopathy (Martens, 1994). Symptoms of disseminated disease include irritability, seizures, respiratory distress, jaundice, bleeding diathesis, shock and vesicular exanthem (Whitley, 1990). When a mother has lesions at the time of delivery, the risk of having a baby with disseminated infection ranges from 5 to 25% (Monif & Hardt, 1984; Whittaker & Cho, 1991; McIntosh & Isaacs, 1992).

Since direct contact with the virus accounts for the majority of transmission, it is common obstetrical practice to perform a cesarean section at the time of delivery only if lesions are present (Gibbs et al., 1988). One study found that 1 in 16 babies born to mothers experiencing primary infection had herpes at birth after a cesarean section (March of Dimes web site, 1992) as compared to 1 in 2 babies infected after a vaginal delivery. However, it is still controversial as to whether or not cesarian section prevents transmission (Maslow & Bobitt, 1989).

The next most common mode of herpes transmission to neonates after delivery is through postnatal

exposure. Breast feeding poses a slight risk to the baby, especially if herpetic lesions are present on a woman's breast (Sealander et al., 1988; Dunkel et al., 1979). Contact with other children who have herpes is another common postnatal mode of transmission, since the virus is shed in their saliva.

Treatment of the infected neonate with antiviral drugs such as acyclovir has been shown to improve prognoses (Whitley, 1990).

CHLAMYDIA

Chlamydia, caused by the bacteria, *chlamydia trachomatis*, is the most widespread sexually transmitted disease, with 4 million new cases reported yearly. It is the most common cause of preventable infertility. Chlamydia is asymptomatic in up to 70% of women (Wendel, 1990). Cervical cultures have been found to be positive in 2 to 24% of pregnant women (Rettig, 1988).

There have been no studies found in the literature reporting a relationship between embryonic dysmorphism and maternal chlamydia infection. While many studies show an increase in pregnancy complications such as ectopic pregnancies, premature labor, premature rupture of membranes, low birth weight babies, stillbirths and neonatal deaths (Martin et al., 1982; Harrison et al., 1983; Sweet et al., 1987), other studies did not show such a relationship (Hardy et al., 1984; Quinn et al., 1985). Harrison (1985) found that women experiencing a new chlamydia infection to be at higher risk of having a low birth weight infant than women experiencing a recurrent infection. Both Ryan et al. (1990) and Cohen et al. (1990) showed a decrease in adverse pregnancy outcomes in women whose chlamydia was treated when compared to an untreated population of infected pregnant women.

The infant is at greatest risk of acquiring chlamydial infection at the time of delivery. It has been estimated that up to 70% of infants born to infected mothers tested positive for chlamydial infection by seroconversion (Bell et al., 1987; Schachter et al., 1986). The most common site of neonatal chlamydial infection is the nasopharynx (Martens, 1994). Chlamydia is considered to be the most common cause of neonatal conjunctivitis. 20 to 50% of infected infants present with conjunctivitis (Martens, 1994). Chlamydia is also one of the leading causes of neonatal pneumonia. Chlamydial pneumonitis occurs in 10 to 20% of infected infants (Wendel et al., 1990). Although the pneumonia is easily treated with antibiotics, studies have demonstrated a long term negative impact of chlamydia pneumonia on pulmonary function in childhood (Harrison et al., 1982; Weiss et al., 1986). Other sites of neonatal infection include the lower respiratory tract, vagina and rectum (Martens et al., 1994).

Chlamydia is conventionally treated in pregnant women with erythromycin (Martens, 1994). All infants receive ophthalmia prophylaxis with silver nitrate or antibiotic ointment, which usually cures chlamydial conjunctivitis; however Heggie et al. (1981) found that some infants developed conjunctivitis even after prophylactic treatment. Cesarean section is not indicated in cases of maternal chlamydial infection (Reprotox, 1996).

GONORRHEA

Gonorrhea infection is caused by the bacteria, *Neisseria gonorrhoeae*. Although symptomless in as many as 75% of infected women (Charles, 1993), it presents with urethritis, cervicitis, salpingitis, proctitis and pharyngitis, and in rare instances can lead to arthritis and disseminated disease (Reprotox, 1996). Infected pregnant women appear to be at a greater risk of developing disseminated disease than non-pregnant women (Holmes et al., 1971). The pelvic inflammatory disease caused by gonorrhea are more likely to undergo an ectopic pregnancy (Ankum et al., 1996).

The estimated prevalence of gonorrhea in pregnant women ranges from 0.2 to 15% (Nguyen, 1984). Studies done to determine the adverse effects of maternal gonorrhea infection on pregnancy show an increased incidence of chorioamnionitis, premature rupture of membranes, spontaneous abortion, premature birth and low birth weight infants (Edwards et al., 1978; Elliott et al., 1990; Mercer et al.,

1991).

The greatest risk to the neonate occurs during delivery. 30 to 35% of all infants passing through the infected birth canal of a mother with gonorrhea contract the infection (Charles, 1993). The most common manifestation of gonorrheal infection in neonates is ophthalmia neonatorum (Martens, 1994). Untreated ophthalmic N. gonorrhoeae can lead to permanent corneal damage. The anal canal and pharynx are other places that are commonly infected (Gutman & Holmes, 1990). In rare instances, infection has been seen in the vagina, urethra and deep tissue (Fletcher & Gordon, 1990; Oppenheimer & Winn, 1982). Besides septic arthritis, systemic gonococcal infection is extremely rare in the neonate. Symptoms of disseminated infection are sepsis and meningitis (Gutman & Holmes, 1990).

The prognosis for these infants is excellent if they receive the proper antibiotic treatment (CDC, 1993). It is current practice to give all neonates (regardless of their risk of being infected) prophylactic eye treatment consisting of silver nitrate or erythromycin. This treatment is effective in treating conjunctivitis caused by gonorrhea infection. For infants with disseminated infection and infants born to mothers with disseminated infection, the CDC (1993) recommends treatment of the neonate with ceftriaxone.

GENITAL WARTS

Genital warts (condyloma) are caused by the human papilloma virus (HPV). It is estimated that between 2 and 10% of women of childbearing age are infected with genital warts (Robert, 1992). Besides the presence of warts, HPV is associated with cervical intraepithelial neoplasia (Wendel & Wendel, 1993).

Developmental abnormalities with maternal HPV infection has not reported, although Dias et al. (1995) did a pathological study on five stillborns with vulvar congenital papillomas and papillomatoses and found hyperkeratosis, acanthosis, papillomatosis, perinuclear halos and nuclear abnormalities.

Perinatal transmission of HPV has been documented (Pakarian et al., 1994; Dimpleby et al., 1996; Cason et al., 1995). It had been found that neonates appear to be at greater risk of oral-pharyngeal infection by HPV rather than genital infection (Smith et al., 1991). Puranen et al. (1994) did a follow-up study of 98 children ages 3 to 11.6 years of age whose mothers were followed for HPV infection. 31.6% of these children tested positive for the HPV virus. While vertical transmission of HPV has been established, the effects of the virus on these children, especially whether or not female children are predisposed to cervical neoplasia, remains to be seen.

Genital warts tend to increase in size and number during pregnancy (Wendel & Wendel, 1993), which can interfere in vaginal delivery. The preferred modes of removal of these warts during pregnancy is cryotherapy and laser ablation (Bergman et al., 1984; Ferenczy, 1985).

SUMMARY

STDs have been associated with adverse outcomes in pregnancy, although the severity of the risk differs depending upon the disease and the degree of infection. In all instance, the greatest risk to the neonate is with primary maternal infection at the time of delivery. With the bacterial infections, antibiotic treatment can clear up an infection before delivery and eliminate the risk to the neonate. In most cases, antibiotics can cure the neonate of infection acquired during delivery. Viral infections must be monitored at the time of delivery, and if herpes lesions are present, or if genital warts are too profuse, a C-section maybe indicated.