Letter to the Editor

Serological Tests for Chlamydia trachomatis Infections

In her review of the current methods of laboratory diagnosis of Chlamydia trachomatis infections, Black (1) reported that serologic tests were generally not useful in the diagnosis of genital tract infection caused by C. trachomatis and that the presence of immunoglobulin M (IgM) antibodies was an unreliable marker of acute infection in adolescents and adults.

Chlamydial infections during pregnancy cause a variety of perinatal complications. Inclusion conjunctivitis, pneumonia, and other complications develop in neonates born to mothers infected with C. trachomatis. Delivery of low-birth-weight infants and premature rupture of membranes occurred more frequently in women infected with C. trachomatis. It also has been suggested that C. trachomatis infection in pregnant women may be related to premature labor and to perinatal death.

Contrary to Black’s assertion, Gencay et al. (2) reported that the rates of IgM seropositivity for C. trachomatis during pregnancy were significantly higher in mothers who had given birth to infants with complications than in matched controls. The frequency of chorioamnionitis and meconium-stained amniotic fluid was also higher in the anti-C. trachomatis IgM antibody-positive pregnant women. However, in serological studies of C. trachomatis infections, the possibility of cross-reactivity with C. pneumoniae should be considered.

We also reported that some babies born to IgG and IgA antibody-positive pregnant women had fetal and neonatal distress (3). Although Black (1) reported that the enzyme immunoassay (EIA) should be used only for serosurveys of high-risk populations or for the detection of IgM in infants with chlamydial pneumonia, a commercially available EIA kit used in our study detected serum IgG, IgA, and IgM antibodies against C. trachomatis (3).

Several investigators have reported that 2 to 20% of pregnant women harbor C. trachomatis in the endocervix. Pregnant women who carry C. trachomatis in their genital tracts may suffer from a general disturbance of immunoregulation. Although transmission of the organism from mothers to their infants generally occurs at the time of delivery with passage of the infant through the infected cervix, the possibility of intrauterine infection has been reported (5). Chorioamnionitis is a frequent finding in cases of prematurity and respiratory insufficiency in premature babies and may be attributable to intrauterine infection.

Detection of C. trachomatis antigen from endocervical specimens has been used widely for the purpose of screening for chlamydial infections during pregnancy. These tests are easily performed and less costly than culture but have lower sensitivities and low positive predictive values in low-prevalence populations such as in Japan. However, we reported four infants who developed neonatal C. trachomatis infections and whose mothers had no detectable chlamydial antigens during pregnancy (4).

The fact that neonates having the symptoms of chronic lung disease also manifest elevated serum IgM levels to C. trachomatis suggests that these respiratory tract disorders arise from infections during pregnancy (5). Early diagnosis and appropriate treatment of chlamydial infections may reduce these complications. Detection of serum antibodies to C. trachomatis during pregnancy also permits more laboratories to diagnose perinatal chlamydial infections and is also useful for screening for infection.

REFERENCES

Author’s Reply

I appreciate the interest and comments of Dr. Numazaki with regard to my recent review of methods for diagnosis of C. trachomatis infection (1). In that review, I stated that serologic tests are generally not useful for diagnosis of acute C. trachomatis genital tract infections due to the fact that antibodies elicited during infection are long-lived, so that a positive antibody test will not distinguish a previous from a current infection. This is particularly true for populations with a high seroprevalence and a high prevalence of infection, e.g., those from a sexually transmitted disease clinic. In addition, I stated that IgM is an unreliable marker of acute infection since it is often not present, presumably because the patient had previous chlamydial infections and is manifesting an anamnestic immune response to subsequent infections.

Serum IgM antibodies against C. trachomatis have been associated with adverse outcomes of pregnancy in several studies (2, 3, 8). In contrast, the study by Numazaki that is cited in his letter did not find an association of adverse outcomes in mothers or babies with the presence of IgM in maternal serum (5). Instead, Numazaki reports an association of adverse outcomes with IgA. These results strongly suggest that chlamydial infections during pregnancy cause perinatal complications and indicate the need for early diagnosis and treatment of infections to prevent adverse outcomes of pregnancy. However, laboratory tests based on nucleic acid detection, nucleic acid amplification, and antigen detection technologies remain a better choice for diagnosis of chlamydial infections during pregnancy and in other settings than do serologic tests based on a single serum specimen, due to their higher positive and negative predictive values. Tests that detect chlamydial nucleic acid or antigen have the ability to accurately diagnose infection much earlier than serologic tests, and with treatment, inflammatory responses are limited sooner, thus reducing the potential for immunopathologic sequelae. Since antibodies can take up to 4
weeks or longer to develop, a false-negative serologic test can occur when patients are tested early during the course of infection. In the absence of paired specimens, which take a month or more to collect, a single IgG titer against *C. trachomatis* proves nothing except that the patient has been exposed sometime in the past. The length of time required for collection of paired specimens is not appropriate for therapy and management of infected patients, particularly during pregnancy. IgM titers are predictive of infection only in patients with first-exposure infections, which may not apply to many pregnant women. Furthermore, IgM antibodies to *C. trachomatis* may not develop in persons who have been previously exposed to *C. pneumoniae*. The commercial enzyme immunoassays (EIA) used by Numazaki (6) and by others as serologic tests for *C. trachomatis* infection are not species specific, and a positive result cannot distinguish a *C. trachomatis* infection from an infection caused by any other chlamydial species. The EIA serologic tests have also been reported to have low predictive values when single serum specimens are used and to be unreliable for detection of IgM antibodies (7).

Numazaki reported four infants who developed neonatal *C. trachomatis* infections and whose mothers had negative chlamydial antigen test results during pregnancy (6), but that report does not indicate whether the mothers were also tested for chlamydial antibodies. It is possible that the antigen detection tests were performed prior to the time that the mothers became infected. Since antigen detection tests have lower sensitivities than culture or nucleic acid amplification methods, it is possible that these were false-negative results, highlighting the need for use of highly sensitive diagnostic tests for chlamydial infection. Nucleic acid amplification tests are now becoming more widely available and have been shown to be cost-effective on the basis of preventing the morbidity associated with undiagnosed and untreated infections, including neonatal infections (4).

REFERENCES


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