All cases of intrauterine fetal death should be evaluated for parvovirus B19 viral deoxyribonucleic acid

To the Editors: We read with interest the article "Stillbirth Evaluation: What Tests Are Needed?" (Incerti MH, Miller DA, Samadi R, Selittage RH, Goodwin TM. Stillbirth evaluation: What tests are needed? Am J Obstet Gynecol 1998;178:1121-5). Although economic aspects are of great importance today the essential point, as the authors have shown, is to know your own results before deciding to omit certain laboratory tests.

Recently a report of parvovirus B19 as a significant cause of middle trimester fetal loss has been published. However, nonhydropic fetal loss in the third trimester associated with parvovirus B19 has hitherto not been a dominant issue. In a prospective study of the incidence of parvovirus B19 antibodies in a population of pregnant women, one woman with no B19 immunoglobulin (Ig) G or IgM antibodies was delivered of a nonhydropic, stillborn baby at 37 weeks gestation in December 1991. Parvovirus B19-specific deoxyribonucleic acid (DNA) was found in the placental tissue as well as in maternal blood samples collected 3 weeks before the death of the fetus and at delivery. The mother did not acquire antibodies against parvovirus B19 until 6 months after delivery. Because no other cause of the intrauterine fetal death was found, we proposed that the parvovirus infection caused the fetal loss, possibly because of a slow immunologic response to the infection by the mother. This case was the incentive for studying parvovirus B19 in all cases of intrauterine fetal death in our department.

Since 1992 all women admitted to Danderyd Hospital with intrauterine fetal death after 28 weeks' gestation have been examined for IgG and IgM antibodies against parvovirus B19 in serum and for parvovirus B19 DNA by nested polymerase chain reaction in maternal serum and in placental tissue. During the 1992 to 1997 study period 77 cases of intrauterine fetal death occurred. The total number of deliveries during that time was 28,548. Parvovirus B19 DNA was found in placental tissue as well as in maternal serum in a total of 6 cases of third-trimester fetal loss (n = 6/77, 8%). No patient had shown any obvious clinical signs of infection by parvovirus B19.

Parvovirus B19 is known mainly to affect erythropoiesis, causing fetal anemia and hydrops. The virus can affect other systems as well and has a particular affinity for the liver and myocardial cells. In the stillborn baby, however, the autolysis usually makes it impossible to investigate signs of myocarditis, for example.

Viral infections in pregnancy can be menacing to the fetus. In 2 of our 6 cases the period before the woman acquired antibodies against parvovirus B19 was considerably prolonged. The question arises whether these fetuses were especially vulnerable because of lack of maternal antibody protection. Estimation of the parvovirus B19 IgG and IgM antibody serum levels was obviously not sufficient to confirm the diagnosis in these cases, because the viral infection was not identified until the maternal serum and placenta were examined for parvovirus B19 DNA. We propose that examination of the placenta and maternal serum for parvovirus B19 DNA should be carried out in all cases of intrauterine fetal death.

At Danderyd Hospital women who have had an intrauterine fetal death are examined according to a standardized protocol after giving consent. The protocol includes examination of maternal blood samples for the Kleihauer-Beck test; antibodies against Toxoplasma gondii, rubella, cytomegalovirus, herpes simplex virus, parvovirus B19, and Listeria monocytogenes; thyroid hormone concentrations and thyroid hormone antibody concentrations. It also includes bacterial culture from the cervix. Chromosomal investigation is performed, and both bacterial and viral cultures from amniotic fluid are examined in most cases. After birth the fetal heart blood is sampled for bacterial culture. A microscopic examination of the placenta is performed, as is an analysis for parvovirus DNA in the placenta and in maternal serum. Autopsy of the fetus is recommended.

When an intrauterine fetal death occurs it certainly helps the parents if a rational explanation can be given. Unfortunately, no explanation has been found by means of our protocol in 30% to 40% of the cases of intrauterine fetal death in our hospital. We believe that the search...
for parvovirus B19 antibodies and parvovirus B19 DNA has contributed to our knowledge, however, because 6 of 77 intrauterine fetal deaths were caused by this infection.

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REFERENCES


Reply

To the Editors: We thank Skjöldebrand-Sparre et al for their interest in intrauterine fetal death and for their insightful comments as they relate to parvovirus B19 as a potential cause. They provide new information that has not been previously published and that may warrant further study. It is apparent that Skjöldebrand-Sparre et al share in our frustration in the inability to determine a cause in roughly a third of cases of intrauterine fetal death, even when a thorough, comprehensive assessment is undertaken. These investigators have adopted an extensive protocol in the evaluation of intrauterine fetal death at their institution in which numerous laboratory tests are performed. The purpose of our study was to try to determine which laboratory tests were most likely to be helpful and which tests could potentially be eliminated in determining the cause of intrauterine fetal death after 20 weeks' gestation. As a result of our study we have since eliminated several laboratory tests.

Skjöldebrand-Sparre et al appropriately point out that several reports in the literature1, 2 as well as their own experience demonstrate that maternal serologic studies for antibodies to parvovirus B19 can be unreliable. Given this fact it is not clear why Skjöldebrand-Sparre et al continue to include examination of maternal blood samples for antibodies against parvovirus B19 in their own protocol.

Although we did not specifically perform maternal serologic studies for parvovirus B19 in our study, we found that there was no benefit to routinely performing maternal serologic studies for antibodies to other viral infections. At Los Angeles County/University of Southern California Medical Center, we attempt to perform placental pathologic studies and autopsy in every case of intrauterine fetal death after 20 weeks' gestation. If there is a suspicion of parvovirus B19, a method of in situ hybridization similar to that described by Walters et al3 is carried out. Given the cost of such an analysis and the apparently low prevalence of infection with parvovirus B19 in our patient population, we have not chosen to do this in every case of intrauterine fetal death.

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REFERENCES


Appropriate model testing

To the Editors: Simchen et al (Simchen MJ, Dulitzky M, Mashiach S, Friedman SA, Schiff E. Adjustment of magnesium sulfate infusion rate in patients with preterm labor. Am J Obstet Gynecol 1998;179:994-9) have an interesting idea: that the magnesium infusion rate needed to achieve a desired serum magnesium concentration can be calculated on the basis of renal function, body mass, and serum albumin concentration. Unfortunately their article provides the possibly misleading suggestion that Simchen et al have discovered the correct means of calculating magnesium infusion rate.

To accomplish the goal of Simchen et al, they must obtain data from patients not used to develop their model to test it and then provide us with information about the distribution of error that would be incurred by applying that model to these patients. Finally, it should be emphasized that Simchen et al are only attempting to develop an equation for steady-state conditions, although similar methods might be used to develop parameters for differential equations that would describe dynamic changes in magnesium concentrations on the basis of renal function and magnesium infusion rate time history.

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