dations of Freda[3] and Queenan[4] (>1:16). As a consequence of this stricter critical titer, more patients require invasive testing or require it earlier in pregnancy.

My questions: (1) In their current series, in a first sensitized pregnancy what was the lowest fetal hematocrit observed when the indirect Coombs' titer within 1 to 2 weeks of sampling was ≤1:16? (2) Do the observations in the current series justify invasive sampling in the first sensitized pregnancy when a recent indirect Coombs' titer is 1:8 or 1:16? (3) Can their historic observation of severe fetal hemolytic disease with a titer of 1:8 be explained by (a) its occurrence in an other-than-first sensitized pregnancy, (b) delivery remote from the 1:8 titer with possible intervening unobserved increases in titer, or (c) an unobserved increase in titer caused by invasive sampling after the titer? MacGregor et al.[5] reported a rise from 1:8 to 1:4096 within weeks of cordocentesis.

If the answers to these questions do not support invasive testing in first sensitized pregnancies with 1:8 or 1:16 titers, the authors should acknowledge this and adjust their critical titer. This adjustment would allow the selection of invasive testing only when the fetal risk truly warrants it.

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Reply

To the Editors: We thank Spinnato for his inquiry. We expect may questions will arise regarding the proposed management scheme because it is difficult to give adequate detail in an initial publication.

Spinnato asked about the antibody titer at which an invasive evaluation should be undertaken during the first sensitized pregnancy. His specific concern was that we selected 1:8 although the American College of Obstetricians and Gynecologists Technical Bulletin states that a titer of <1:16 indicates that the fetus is not in serious jeopardy. His question is best answered by quoting directly from that technical bulletin. "In general, it is believed that, if the antibody titers remain less than 1:16 in an initial immunized gestation, the fetus is not in serious jeopardy. *It is important to know, however, that this value is somewhat dependent on local laboratory methods, skill of laboratory personnel, and previous experiences related to titers within that institution* [emphasis added]."

Spinnato is not the first to have missed this point. With the decreasing incidence of fetal hemolytic disease, experience with the entity has shrunk. Our critical titer has been and remains 1:8 and is the result of many years of experience in one laboratory with a wide referral area. All physicians involved in the evaluation of fetal hemolytic disease should find the critical titer in their individual laboratories. Obviously this is impossible in a small hospital; regionalization is required.

In our experience patients have frequently been referred with a low indirect Coombs' titer from the local laboratory, only to have a much higher titer when tested by the University of Iowa Hospitals and Clinics blood bank. Whether this reflects a change in sensitization or differences in laboratories, I cannot state.

Our data base does not include information as to whether the pregnancy under evaluation was the first sensitized pregnancy. As a rule we monitored each patient during her first sensitized pregnancy with serial indirect Coombs' titers. We require a titer ≥1:8. Ten nulliparous women have undergone cordocentesis for red blood cell isoimmunization. Two of those fetuses had anemia when first evaluated. In one, sensitization was to D and the indirect Coombs' titer was 1:1024. In the other, sensitization was to Kell and the indirect Coombs' titer was 1:8. However, most of the patients who have required transfusion with low indirect Coombs' titers were not in their first sensitized pregnancies. Thus our observation of severe hemolytic disease with a titer of 1:8 is mostly, but not exclusively, explained by its occurrence in a subsequent sensitized pregnancy. As Spinnato notes, other have had similar experiences with their laboratories.

Spinnato refers to a case report by MacGregor et al., who observed an abrupt increase in antibody titer within weeks of cordocentesis. However, I note that the fetus in question was already anemic when the titer was 1:8. This raises an important point. Cordocentesis is but a procedure. One must not only know what the normal values are, but what to do with them. With our management scheme we have tried to supply a course of action. The procedure can also be misused. To prevent worsening of disease we avoid the placenta in patients with low-grade sensitization by sampling from a midsegment.

In summary, the 1:16 guideline in the American College of Obstetricians and Gynecologists Technical Bulletin was never intended to be engraved in stone. It is clear that at the University of Iowa our critical titer is 1:8. Our experience is that these fetuses are at risk and benefit from accurate testing.

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