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Antibody titer studies in pregnant women at risk for bearing an infant with hemolytic disease of the newborn

A blood banker in Wisconsin is re-evaluating his hospital's practices for determination of antibody titers in pregnant women where there is risk for hemolytic disease of the newborn. The inquiring blood banker states that an article originating from the Scientific Section Coordinating Committee of AABB (Transfusion 2001;41:1445-1452) it was suggested that the antibody titer should be determined using a 60-minute incubation at 37 degrees centigrade, using homozygous expressing cells (in the case of anti D, c or E, it was suggested to use an R2R2 cell). According to the inquiring blood banker the article goes on to state that a "critical titer" for first pregnancy is 16 for anti-D, possibly 64 for Duffy antibodies, but does not state a "critical titer" for anti-Kell. At a recent Wisconsin Association of Blood Banks annual meeting, the inquiring blood banker learned that there was not uniformity of practice within that state. He reports that an AABB certified reference lab in his area does not use a 60-minute incubation or R2R2 cells to titer anti-D. Before changing the parameters of this assay at his own hospital he desires input on the following questions:

- What are the details of the **methodology** that resulted in definition of 16 as a critical titer?
- Is the recommendation proposed by the AABB's publication an "**industry standard**" or is there wide variation in method?
- Have other labs switched to the use of **homozygous cells** for either Rh or non-Rh
- antigens?

The following responses have been submitted.

ADDENDA June 18, 2002

1. **A blood banker/immunohematologist** offers the following: "The concept of a **critical titer** originated from a paper by VJ Freda in 1965 Am J Obstetr Gynecol 1965;92:341. Freda noted that for 771 pregnancies in which anti-D was present for the first time, there were no intrauterine deaths when the titer was 16 or less, and only 1 when the titer was 32. These were '**Coombs**' titers, and done prior to the advent of LISS and PEG. There is some discussion about albumin titers, but they relate to a direct agglutination method and not albumin-antiglobulin tests that were once popular in the USA. As for a **saline-antiglobulin titer** being an 'industry standard', the method is given in the AABB Technical Manual. The method (saline, 60' incubation, anti-IgG) was proposed in the Transfusion 1990;30:175-183 report. Readers are referred to the College of American Pathologists 1995 Comprehensive Transfusion Medicine Survey J-C for compliance with this method, and the wide range of values (2-2048) reported for a single anti-D). **R2R2 red cells** are recommended for anti-D titration because - among all of the D-positive phenotypes - they show the least variation in D antigen expression from one individual to another. Finally, it should be noted that **each laboratory should establish their own critical titer**. The value proposed by Freda applies only to **first affected** pregnancies. A more conservative approach has been suggested by Spinnato JA Obstetr Gynecol 1992;80:873-7. For an update on the management of the alloimmunized pregnancy, Dr. Ken Moise provided an excellent handout for Workshop 503-TC at the 2000 AABB Annual Meeting."

ADDENDA June 19, 2002

2. **A hospital transfusion service physician** wrote that although recommendations and guidelines are helpful, laboratories should **be careful before abruptly changing**

methodologies which may affect the clinical interpretation of titer results in their institution. He cautions "If your obstetricians have a concept of what the current critical titer is, parallel testing with old and new methods should probably be done for numerous cases before switching methods. For most facilities, even with a high-risk OB service, it would take several years to develop this type of experience. Perhaps frozen stored samples could be used for this purpose if available."

ADDENDA May 7, 2008

3. **A transfusion medicine physician who works at a large county teaching hospital in the Lone Star State** reports that their Obstetrics department delivers over 17,000 babies annually. Because of the patient population that they serve, a significant number of women do not receive prenatal care and are initially seen when they go into labor. The blood bank **does not perform antibody titer studies for patients whose first sample is received at the time of labor.** The reason for this policy is that there is no previous titer for comparison, and even if the titer was determined, in most cases the baby is born before the titer studies are completed. The institution is considering whether or not to update the aforementioned policy, because some practitioners wonder **if the titer information could prove useful when counseling the parents in regards to future pregnancies.** The inquiring colleague wonders how other institutions address similar clinical scenarios.
4. **A colleague located at an academic medical center in North Carolina** reports that there is **no pressing need to determine a titer at the time of delivery** as the titrations are generally used in making decisions about the timing of invasive procedures during the pregnancy. Nevertheless, he acknowledges that a titer **might be of some benefit in attempting to assess the risk of a subsequent pregnancy** if the newborn's red cells express the antigen at which the maternal antibody is directed. High titers and/or a baby with HDFN would not bode well for subsequent pregnancies. The North Carolina hospital's practice is to **not do a titer at delivery unless the physician asks for a titer.** During pregnancy, a titer is reflexively ordered.
5. **A Transfusion Medicine physician in a large general teaching hospital in Boston** would **support what has been the policy of the hospital at the Lone Star State.** In the Bostonian's opinion, rather than do titers after the delivery, it would seem better to identify those mothers who have antibodies capable of causing hemolytic disease of the newborn at the time of a subsequent pregnancy, and then counseling those mothers that it would be especially important to come for prenatal care at the time of their next pregnancy. This approach has three advantages: first, titers may change over time and you would really want to know the maternal titer at the time of the future pregnancy rather than now. Second, the antigen status of the father would be important and the father might change for the next pregnancy. Third, and most important, the **medical needs of the future high-risk pregnancy are only served if the mother comes for prenatal care.** It does little good to know titers now if the mom will not come until the time of delivery of the next pregnancy. **If the special needs are explained to the mother, she will be more likely to return for prenatal care** at the time of the next pregnancy.

Please submit comments to the [e-Network Forum](#).

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Addenda: June 18 & 19, 2002;
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