



# e-Network Forum

## CALIFORNIA BLOOD BANK SOCIETY

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### ***A case report of the mysterious development of anti-D in pregnancy***

**A Canadian blood banker** wonders if colleagues might offer input regarding a 25 year old, 144 pound, group B Rh-negative woman, who was in the 33rd week of her first pregnancy when prenatal antibody screening with an MTS Gel method showed a weak alloantibody, without obvious specificity. She had no history of transfusions. She received an antepartum dose of RhIg (300ug) on March 6, 2001 and delivered her baby on May 2, 2001. At the time of the delivery her ABO/Rh was verified as B negative, but her antibody screen increased in strength to 4+, caused by anti-D, which was identified in her serum using an MTS Gel method. There was no history of additional RhIg administration since the March 2001 dose of RhIg. The woman's infant was group O Rh positive with a negative direct antiglobulin test (using a cord blood specimen). In spite of anti-D being identified at 4+ strength in her serum, since she had received antepartum RhIg, she was given a post partum dose of RhIg. A year later in May of 2002 the woman became pregnant again, and at her first prenatal visit, her prenatal antibody screen was negative using an Immucor solid phase method. In October of 2002, at approximately the 27th week of her pregnancy, her antibody screen was positive with anti-D. According to the Canadian blood banker, the anti-D reacted with a 3+ to 4+ 'mixed field' type pattern with an MTS Gel method. The Canadian commented that in his experience the MTS-Gel system has a "distinct way of showing mixed field and this often an indication that the antibody present is IgM". Ficin-treated cells showed 4+ anti-D only. A saline indirect antiglobulin test method revealed an anti-D with a titer of 1. DTT treatment abolished the antibody reactivity, again suggesting that the anti-D was an IgM class antibody. The DTT testing was performed with controls; a 6% albumin control was run in parallel for dilution and tested by the Gel method. 3+ results were obtained in the DTT control, while the DTT test was negative. Rh-negative umbilical cord red cells were non-reactive when reacted with untreated serum in an MTS Gel method. Two examples of ficin-treated D+ LW- cells reacted 4+ in an MTS Gel method. The woman denied receiving RhIg during her current pregnancy. The inquiring Canadian is curious as to why this patient seems to have an IgM anti-D at this point in time, and he wants to know if they should continue to administer RhIg to this patient.

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The following replies were submitted in response to the above case description.

- 1. A transfusion medicine physician in Pennsylvania** wrote that assuming sample identity has been confirmed, (potentially checking ABO and serum pregnancy test), and assuming the specificity of the current antibody is truly confirmed as recurrent anti-D, then patient history of recent transfusion, IV needle use or drug exposure (IVIg, etc.) must be excluded. According to the responding physician, a staged review of patient social history beginning with legal drugs and progressing through marijuana, cocaine and then IV injectables has been reported by colleagues at the NIH to be the most effective way to get this data in blood donors interviewed for hepatitis C notification. If all exogenous sources of anti-D are excluded, and it is proven that the patient is experiencing true sensitization to the D-antigen, then additional D injections are contraindicated. (**Editor's comment:** If there is any doubt about the exogenous nature of the anti-D in this case, then continued injections of RhIg **would** be prudent). The responding physician believes that anti-D injections in this setting are particularly hazardous because they confuse monitoring for a rising titer of anti-D and may contribute to a falsely elevated anti-D which might be inappropriately above the critical titer. Alloimmunization, despite appropriate RhIg therapy has been documented in the Canadian literature.
- 2. The medical director of the Manitoba Rh program**, which is a prenatal red cell serology laboratory, reports that if the antibody is clearly an anti-D, they do **not** offer prophylactic RhIg as there is no evidence that treating will decrease the strength of antibody or affect the clinical course of the fetus. The responding colleague does not have a clear explanation as to why there should be an IgM component at this time other than to wonder if the anti-D detected at the end of the previous pregnancy was **passively acquired** (gel methodology may be more sensitive in picking up the antibody and remain positive longer) and if the sensitization is occurring during this pregnancy. The negative antibody screen at the onset of this pregnancy would support this possibility.

**ADDENDA** Nov. 12, 2002

3. **A blood banker from New York** suggests that one should rule out the possibility that the developing antibody might actually be **anti-G**, and that an umbilical cord sample should be phenotyped for C, once the baby is born. If the mother became immunized with anti-G during her current pregnancy, it could represent a primary response. This might explain why the antibody appears to be IgM class. (**Editor's note:** The inquiring colleague who originally submitted this case reports that the antibody identified was anti-D ONLY, **not anti-D+C, or anti-G**. However, it will be interesting to learn the extended Rh phenotype of the soon-to-be-born neonate (including the C typing), if the information becomes available to the e-Network.)

**ADDENDA** Nov. 13, 2002

4. **A Pennsylvania transfusion medicine physician offers another anti-D case**, but with a slightly different twist.

**Assessment:** The patient is a group A Rh negative, 31 y/o Caucasian female (G1P0) with no prior prenatal care. An antibody screen at 12 weeks gestation revealed a weak anti-D that was present in low concentration (1+ in a tube LISS antibody screen, 2+ in a gel-AHG test). The specimen was obtained at 12 weeks gestation during an Emergency Department (ED) assessment of a 3-week long history of vaginal bleeding. Ultrasound in the ED identified probable subchorionic bleed in lower uterine segment near a viable, intrauterine pregnancy. However, no Kleihauer-Betke test of vaginal blood or maternal peripheral blood was done before the patient left against medical advice. RhIg was recommended for IM injection, but the dose was never administered. The patient returned to the ED with pain described as right round ligament pain at 18 weeks plus 5 days gestation. At that followup visit, no anti-D was detected. In fact, anti-D was NOT found in maternal blood specimens at 19, 20 and 23 weeks gestation.

**Discussion:** Because of the rarity of a series of group A Rh negative blood specimens obtained in the ED with appropriately rising beta HCG levels (done retrospectively on each serum specimen, all frozen prospectively), the correct patient identification of all patient specimens appeared to be confirmed. However, according to the Pennsylvanian, down regulation of anti-D production by the immune system is quite uncommon in the absence of generalized immunosuppression (not known to affect this patient). Exogenous anti-D antibody therefore, could not be distinguished from anti-D produced by the patient's immune system. Therefore, in the opinion of the Pennsylvanian physician, one-time detection of anti-D cannot confirm or refute sensitization in this Rh negative patient.

**Recommendations** of the Pennsylvanian physician:

1. Ask patient to definitely **identify the biologic father** of current fetus and ask father to provide a blood specimen for "Father prenatal" test of blood type. (Father is reportedly very non-compliant.)
2. Unless the possibility of anti-D hemolytic disease of newborn is excluded by this testing, **consider monthly maternal antibody screen** to search for recurrence of anti-D until birth.
3. Consider **historical review of patient's exposure to intravenous blood or blood products**, particularly between 8 and 12 weeks gestation. (Anti-D Rx, IVIG Rx, transfusion or use of a needle previously shared with another individual with high titer anti-D may be detectable in this test system up to 4 to 6 weeks after exposure.)
4. Consider **routine Rh(D)Ig prophylaxis at 28 weeks gestation**, hoping that sensitization has not yet occurred. (If patient again refuses intramuscular injection, intravenous injection of WinRho may be offered.) After the Rh(D)Ig injection, continued monthly antibody screens may be able to detect an unexpected, rapidly rising or persistent anti-D titer and possibly allow earlier identification of any increasing risk for anti-D hemolytic disease of newborn during the 3rd trimester.
5. Unless biologic father or newborn lacks D red blood cell antigen, **potential Rh sensitization from vaginal bleeding between 9-12 weeks gestation cannot be reversed.**

**Note:** The mother has not yet been asked directly to confirm or deny IV exposure to blood or drugs that might have occurred prior to 12 weeks gestation.

**Educational note:** This case **calls into question the practice in some hospitals of reporting patients as "Not eligible for Rhogam" following detection of anti-D in a single blood specimen.** That practice may be acceptable **ONLY after careful history has excluded exposure to products which may contain anti-D.** Illicit needle-sharing with a sensitized D negative individual may be very difficult to detect during routine patient questioning but might have the unfortunate side effect of denying potentially effective anti-D prophylaxis.

5. **A highly respected Blood Bank Technical Specialist who works at one of the major transfusion medicine support companies** suggests that **passive anti-D** from recent infusion of IVIG and/or IMIG (such as a gamma globulin injection) should also be considered when seeking explanations for the "mysterious" detection of anti-D.

**ADDENDA** Mar. 25, 2003

6. **A colleague in California** suggests that one possible explanation for an "anti-D" to appear and disappear and reappear may be that it is not anti-D, but a **warm autoantibody with relative anti-D specificity**. Various Rh specificity's have been seen when warm auto antibodies are first detected and either disappear or broaden to react with all red cells. With no explanation for the development of Anti-D, warm auto antibody should be considered a possibility and the administration of RhIg not withheld.

**ADDENDA** Mar. 27, 2003

7. **A colleague in Texas** reports that they have had two cases in the last 9 months of women who had negative antibody screens early in pregnancy, received a 28 week injection of Rh Immune Globulin (a full 300 microgram dose) and then at delivery had a strongly demonstrable anti-D. One woman moved from the area immediately upon discharge after delivery and was lost to followup so that they could not determine her IV drug use status. The other woman, however, denies drug use or prior pregnancy, and 3 months after delivery still had an anti-D titer of 128. She did not have anti-G because her serum failed to show 'anti-C' reactivity. The Texan is concerned, and would like to hear whether others have seen this type of occurrence, in addition to the Canadian colleague who originally raised this discussion.

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

**Ira A. Shulman, MD**  
CBBS e-Network Forum Editor & Moderator



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**Addenda:** Nov. 12 & 13, 2002;  
Mar. 25 & 27, 2003

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