DO YOU DO D\textsuperscript{u}?
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Introduction

The D\textsuperscript{u} phenotype of the Rh system has made things difficult since it was described 35 years ago. It is a problem for the blood banker, for the clinician, and for the blood donor and recipient. In early descriptions, D\textsuperscript{u} was a red cell sample agglutinated by some but not all Rh\textsubscript{o}(D) antisera. That is still the working definition and the root cause of the problem. The identity of D\textsuperscript{u} was never defined by the character of the red cells tested, but rather by the properties of the antisera used for the testing, ie, specificity, titer, and strength of binding. With some antisera, a D\textsuperscript{u} blood is called Rh-positive and with other antisera it is called Rh-negative. Thus, every time D\textsuperscript{u} blood is typed, a different answer can be obtained, and the clinician and the subject are sure that the blood banker is not only indecisive but also inept. It is time to reevaluate and perhaps change the concepts and the rules of 1950 regarding D\textsuperscript{u}.

D\textsuperscript{u} Varieties

There are a number of scientific reasons why certain red cells will have a weak expression of D and be called D\textsuperscript{u}. There can be inheritance of only a segment of the complex chemical that usually expresses as D, ie, a qualitative difference; there can be inheritance of an inadequate amount of the total chemical, ie, a quantitative difference, or there can be a normal amount of D but simultaneous inheritance of suppressor genes that prevent the full expression of the D phenotype. It is the qualitative variants\textsuperscript{2} that can present the confusing picture of Rh-positive cells with a serum antibody that reacts with most Rh-positive and D\textsuperscript{u} samples, but is not an autoagglutinin.

Currently, more potent anti-D reagents are obtained by plasmapheresis from stimulated donors than from whole blood collected from naturally immunized donors. One donor can supply huge quantities of starting material, whereas older reagents consisted of pools of raw serum with a blend of many specificities. In addition, IgG Rh antisera are modified chemically to act as direct agglutinins. That further obscures the difference between "high-grade" D\textsuperscript{u} cells previously characterized by direct reactivity with some anti-D reagents, and "low-grade" D\textsuperscript{u} cells, identified only by the indirect antiglobulin test (IAT).\textsuperscript{3} D\textsuperscript{u} cells are much rarer than they were in the past, not because genetics are different, but because D\textsuperscript{u} today is a function of the more potent anti-D reagents used.

D\textsuperscript{u} Decisions and Indecisions

There are three types of subjects affected by D\textsuperscript{u} decisions and indecisions: Blood donors, transfusion recipients, and pregnant women.
Blood donors

Blood donors are tested for D\textsuperscript{n} because there is a fear that D\textsuperscript{n} donor red cells will stimulate anti-D if given to D-negative recipients. With primitive testing, that was true, but it was not a problem even 20 years ago when D\textsuperscript{n} was defined with the IAT. It was demonstrated in 1962 that donor cells negative with slide test sera, but positive in the IAT, were less immunogenic to transfusion recipients than cells positive for K or E.\textsuperscript{4} Even if D\textsuperscript{n} red cells are randomly given to a population already stimulated, there is less chance of an acute hemolytic reaction in 1987 because there is proportionately less anti-D and more anti-K and anti-E in the modern transfusion recipient population. Blood banks, however, are still required to search for D\textsuperscript{n} and to apply an Rh-positive label. That confuses the public and requires 1,500,000 antiglobulin tests annually in the United States for initial testing. There is a further requirement that a D\textsuperscript{n}-negative test be verified in the hospital before transfusion, requiring another 1,500,000 tests.\textsuperscript{5} Although that confirmation was challenged\textsuperscript{6} and is no longer required, it is probably still performed in most hospital laboratories.

Transfusion recipients

Currently, D\textsuperscript{n} testing is not recommended in the United States for prospective transfusion recipients. It is safer theoretically for the D\textsuperscript{n} patient to be called Rh-negative and to receive D-negative blood. The best way to accomplish that is by not doing D\textsuperscript{n} testing on patients. Unfortunately, old Medicare regulations included a requirement for the test. Although the requirement was not enforced, the test is still performed by many hospital blood banks.

Pregnant women

D\textsuperscript{n} testing of pregnant women presents the greatest confusion. Prenatal testing usually includes D\textsuperscript{n} testing for a number of reasons. First, the testing is often done in laboratories that do not wish to be caught in the trap of miscalling an Rh type. Second, there has been controversy over whether a D\textsuperscript{n} woman should or should not get immunoprophylaxis with Rh immune globulin (RhIG). The confusion has been amplified by the introduction of antenatal prophylaxis with RhIG. The same woman may be tested (and treated) three times in one pregnancy. If the first test early in pregnancy says she is D\textsuperscript{n}, the obstetrician may or may not decide to give immunoprophylaxis at 28 weeks.\textsuperscript{7} When she is admitted for delivery, she may be found to be D\textsuperscript{n} by the hospital laboratory and will probably be called Rh-positive, but if she is one of the 20 percent of women who is to be delivered by caesarian section, she will also become a potential recipient of blood. So, does she or does she not get RhIG postpartum? Finally, she may seemingly become D\textsuperscript{n} postpartum because of a large fetal-maternal bleed. The resultant controversy between obstetrician and laboratory is not beneficial to either party or to the patient.

Trends

To allay some of the confusion, some experts would like to forego D\textsuperscript{n} testing on any patient admitted to the hospital, including women for delivery. The latter proposal was considered but rejected for the eleventh edition of the standards for blood bankers.\textsuperscript{8} When a D-negative or D\textsuperscript{n} patient comes to delivery in the hospital, what should a transfusion service do if it has no information on antenatal testing? That problem has been solved in Tampa by providing RhIG for all women who type as D-negative in the appropriate clinical obstetrical situation: We do not do an initial antiglobulin test for D\textsuperscript{n}, nor do we search to see if the mother is already immunized (actively or passively) to D or to anything else. We issue the RhIG and then search for evidence of a fetal-maternal hemorrhage of a size requiring more than one dose of RhIG by performing the "rosette" test.\textsuperscript{7} That test is designed not only to detect a larger than normal fetal-maternal bleed of Rh-positive fetal cells, but also to detect D\textsuperscript{n}. We have thus fulfilled the requirement for D\textsuperscript{n} testing and for testing for fetal-maternal hemorrhage by doing one test instead of two. If the test is positive, we can go back and sort out the differences. Meanwhile we have made some reduction in testing and confusion, albeit by giving RhIG to a few D\textsuperscript{n} mothers who may not need it. They will not be injured by the RhIG. The result has been a reduction in our costs.

The D\textsuperscript{n} test is no longer required on the blood of transfusion recipients. In the opinion of the author, the test could be dropped altogether from the testing of blood donors\textsuperscript{6} and even pregnant women. The end result may be to eventually discard the whole concept of D\textsuperscript{n}, which has long been made irrelevant by modern practice.\textsuperscript{8}

References

2. Broman B. Swedish thoughts on D\textsuperscript{n} nomenclature. Transfusion 1984;24:85.

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