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RHD Genotyping for Prenatal Patients with a Serologically Weak D Phenotype

Patients with Partial D or Weak D antigens can have weaker reactions or discrepant reactions on Rh typing. An estimated 0.2% - 1.0% of Caucasians inherit such weak D phenotype. Furthermore, approximately 80% of persons with a weak D phenotype are subsequently identified to have a weak D type 1, 2 or 3 upon *RHD* genotyping. Persons with a weak D type 1, 2 or 3 can be managed safely as Rh-positive, i.e. can be transfused with Rh positive red blood cells and do not require perinatal Rh immunoglobulin (RhIG). On the other hand, persons with Partial D are at risk for alloimmunization when exposed to a wild type D antigen (present in the majority of Rh positive persons) and therefore should be treated as Rh negative, i.e. receive Rh negative red blood cells and receive perinatal RhIg. Unfortunately, routine serological testing is unable to differentiate patients with Partial D vs. weak D. For that, RHD genotyping must be performed.

Although no Canadian data are available, a recent CAP survey revealed a lack of standard practice in the United States for laboratory testing and interpreting the Rh blood type of patients, including pregnant women, with a weak D phenotype. To ensure safe and uniform practice, in 2015 CAP and AABB issued a Joint Statement on Phasing-In RHD Genotyping for Pregnant Women and Other Females of Childbearing Potential with a Serologic Weak D Phenotype.

Currently, in Canada there is no standard or guidance on further investigation and management of patients who present with a weak D phenotype on pre-transfusion or prenatal testing. Depending on the individual institutional policy, such patients may be labeled Rh positive or Rh negative. If a female patient with Partial D is erroneously labeled as Rh positive, she may be transfused with Rh positive RBC or not offered perinatal RhIG, both possibly leading to alloimmunization and hemolytic disease of the fetus and newborn. On the other hand, a female patient with Weak D may be erroneously labeled as Rh negative and receive unnecessary perinatal RhIG. Such practice also leads to unnecessary utilization of Rh negative RBC when Rh-positive red blood cells could be transfused safely. AABB estimates that if all pregnant women in the United States with a weak D phenotype were identified and their *RHD* genotype determined, an estimated 13,360 pregnant women who are currently managed as Rh-negative could be managed as Rh-positive, avoiding 24,700 injections of Rh immune globulin annually.

At present, RHD genotyping is offered by the Canadian Blood Services for “prenatal patients with discrepant, weak or inconclusive serological RhD test results where RHD genotyping may modify RhIG or blood product requirements”. In the Western Canada, where prenatal testing is centralized, RHD genotyping is performed automatically for eligible patients. However, in the rest of Canada, the decision to send for further testing rests with the individual institution.

To provide safe and appropriate care for prenatal patients with serologically Weak D phenotype and to standardize care across Canada, we support the implementation of the following guidance statement: **Prenatal patients with discrepant, weak or inconclusive serological RhD test results should be further investigated with RHD genotyping to determine Rhlg candidacy and optimal Rh type for transfusion.** This improvement in practice is unlikely to result in a significant cost increment in terms of RHD testing for the provinces since it is already an established practice in some provinces. Moreover, prenatal patients with a serologically Weak D phenotype are rare (<1%). Furthermore, since the majority of patients with serologically Weak D phenotype have Weak D and thus can be regarded as Rh positive, the increased cost of testing will likely be outweighed by the savings derived from not administering unnecessary RhIG.