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Commentary

Foregoing Rh testing and anti-D immunoglobulin for women presenting for early abortion: a recommendation from the National Abortion Federation's Clinical Policies Committee

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Early abortion continues to expand outside of traditional clinics, through telemedicine, self-managed medication abortion, or in smaller offices that do not specialize in obstetrical care. Consequently, requiring Rh testing and anti-D immunoglobulin as part of abortion care is becoming a barrier. As of early 2019, the Society of Family Planning [1], the American College of Obstetricians and Gynecologists [2], and the Society of Obstetricians and Gynecologists of Canada [3] recommend that all Rh D-negative women receive anti-D immunoglobulin after an induced abortion, regardless of gestational age or type of procedure. However, the evidence of clear benefit in early pregnancy, the gestational age at which sensitization might occur, and the differences between aspiration, sharp curettage, or medication abortion, are not well established [4]. Indeed, other guidelines vary. The World Health Organization recommends that where Rh D-negative status is prevalent and anti-D immunoglobulin is routinely provided, it should be administered. However, Rh testing is not a requirement for abortion in any setting [5]. Dutch guidelines do not recommend testing and treating Rh D-negative women until the pregnancy is greater than 49 days from the last menstrual period [6]. The British Committee for Standards in Hematology recommends no treatment for spontaneous complete miscarriage below 12 weeks but treatment for therapeutic termination of pregnancy regardless of gestational age [7]. Danish guidelines state that routine anti-D immunoglobulin treatment does not appear to be necessary for pregnancies of less than 8 weeks gestation [8]. In 1997, the Swedish Board of Health and Welfare recommended against the use of anti-D immunoglobulin in early spontaneous or medication abortion [9].

Each expert body acknowledges the lack of evidence in making the recommendation for Rh testing and treatment in the context of early abortion. Evidence about fetal-maternal hemorrhage in early pregnancy that has supported Rh testing and treatment relies on older studies with unclear gestational age dating, outdated methods of abortion including sharp curettage, and Kleihauer-Betke testing, which has methodological limitations [10]. In addition, although some studies may detect fetal-maternal hemorrhage, they do not follow patients to assess development of Rh antibodies or future pregnancy outcomes [11]. In the single randomized controlled trial of 57 patients who were Rh D-negative with Rh D-positive partners who had pregnancy loss or abortion in the first-trimester and received either anti-D immunoglobulin or placebo, no subject in either the treatment or control group became sensitized [4, 12]. Although encouraging, this trial was underpowered for the rare outcome of sensitization.

Experts justify the universal use of anti-D immunoglobulin because it is safe. However, anti-D immunoglobulin is a pooled human blood product and consequently is not without risk. A cluster of Hepatitis C cases resulted from anti-D immunoglobulin given to women in Ireland in the late 1970's [13]. Although screening has improved since then, emerging bloodborne pathogens may place patients who receive anti-D immunoglobulin at risk. Anti-D immunoglobulin is also expensive, and the cost is a barrier for many women and health systems. In the United States, typical anti-D immunoglobulin costs are around $30 for a 50 mcg dose and $90 for a 300 mcg dose. Finally, shortages of anti-D immunoglobulin have occurred [14]. Because there is clear benefit later in pregnancy and at the time of delivery, the product should be used only by women who need it and not wasted on those who do not [15]. In Denmark and the Netherlands, in an effort to only provide anti-D immunoglobulin to those who need it, Rh D-negative patients

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have fetal screening using cell-free fetal DNA in the maternal plasma and are only given anti-D immunoglobulin in the third trimester and after birth if they are known to carry an Rh D-positive fetus [16].

When during an induced abortion might the fetal-maternal hemorrhage volume be enough to cause maternal sensitization? A volume of 0 .1mL of fetal Rh D-positive cells (0.2 mL of fetal blood) has been shown to cause sensitization both after delivery and in experimental studies on Rh D-negative non-pregnant volunteers [17,18]. In a study of 483 patients presenting with spontaneous and induced abortion through the second trimester, 11.6% had evidence of fetal-maternal hemorrhage before the abortion and 23% had evidence after. In this study, only three of the 23 patients presenting below 8 weeks had detectable fetal-maternal hemorrhage and none had a volume greater than 0 .1mL [19]. Further, historical studies of fetal-maternal hemorrhage may have exaggerated the amount of blood volume because the Kleihauer-Betke test detects maternal F cells as well as fetal cells in the maternal circulation.

Recent research using flow cytometry is more sensitive to low volumes of fetal cells, gives precise estimates of cell number, and accurately distinguishes fetal cells from maternal F cells. A pilot study by Sarah Horvath from the University of Pennsylvania presented at the 2018 North American Forum on Family Planning used flow cytometry to measure the fetal cells in maternal circulation before and after induced and spontaneous abortion in 28 patients from 5 to 12 weeks [20]. All patients had a uterine aspiration procedure. Patients with pre-procedure bleeding were excluded from the study. The majority had no detectable fetal cells, and no patient either before or after the procedure was even close to the threshold for sensitization (0 .1mL fetal cell volume). A larger clinical trial investigating the volume of fetal-maternal hemorrhage in patients using medical abortion up to 10 weeks has been funded by the Society for Family Planning, with results anticipated in two to 3 years.

Epidemiologic data from the Netherlands supports the policy of foregoing Rh testing and anti-D immunoglobulin provision in early pregnancy. A study by Ellen Wiebe and colleagues compares the rates of positive anti-D antibody in women from Canada and the Netherlands [21]. Canada's policy states that all women with spontaneous or induced abortion should be tested and given Rh D immunoglobulin if they are Rh D-negative [3]. In the Netherlands, women having induced abortion under 7 weeks and spontaneous abortion under 10 weeks are not tested or treated. The two populations' Rh D-negative rate, abortion, and fertility rates are similar. The study found that despite not testing or treating, the Netherlands' clinically significant anti-D antibody rate was not statistically different from that of Canada. The authors conclude that the Netherland's policy is safe and that testing and treating at early gestational ages can be dropped.

The evidence around the need for Rh testing and anti-D immunoglobulin in early pregnancy is evolving. Physiologically and epidemiologically, little evidence exists to support the idea that testing and treating in early pregnancy improves outcomes, as the likelihood of sensitization is low. Direct evidence in a pilot study related to fetal-maternal hemorrhage is encouraging, and a large study of medication abortion up to 10 weeks is forthcoming.

The challenge for current abortion providers is changing a time-honored clinical practice with dubious benefits. Recent changes in cervical and breast cancer screening could serve as a model both for educating providers and patients about the reason for change and supporting patients who are affected. Carefully explaining that testing and treating patients with anti-D immunoglobulin early in pregnancy has no demonstrated benefit and carries risk, is not practiced in other countries, and adds cost and complexity to the abortion procedure, will be critical steps in changing practice. The established risk and cost of providing anti-D immunoglobulin for women having abortion in early pregnancy outweighs the potential benefits.

For this reason, the National Abortion Federation's Clinical Policies Committee recommends that it is reasonable to forgo Rh testing and anti-D immunoglobulin for women having any type of induced abortion before 8 weeks from the last menstrual period. Prior to 8 weeks, the likelihood of fetal-maternal hemorrhage adequate to cause sensitization is negligible. Given that medication abortion is more similar to spontaneous abortion with less risk of fetal-maternal hemorrhage, forgoing Rh testing and anti-D immunoglobulin for medication abortion under 10 weeks may also be considered. As evidence continues to emerge, these gestational age limits may also change. NAF's Clinical Policies Committee looks forward to putting that evidence into practice.

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