

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Rh (D) (Screening and Preventive Medication)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) strongly recommends Rh (D) blood typing and antibody testing for all pregnant women during their first visit for pregnancy-related care.¹

The USPSTF also recommends repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative women between 24 and 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative.¹

Evidence Rating: A (Strongly Recommend/Good Evidence)

The USPSTF found good evidence that Rh (D) blood typing, anti-Rh (D) antibody testing, and intervention with Rh (D) immunoglobulin, as appropriate, prevents maternal sensitization and improves outcomes for newborns. The benefits substantially outweigh any potential harms.¹

B (Recommend/At Least Fair Evidence)

The USPSTF found fair evidence that repeated antibody testing for unsensitized Rh (D)-negative women (unless the father is also known to be Rh [D]-negative) and intervention with Rh (D) immunoglobulin, as appropriate, provides additional benefit over a single test at the first prenatal visit in preventing maternal sensitization and improving outcomes for newborns. The benefits of repeated testing substantially outweigh any potential harms.¹

The American Academy of Family Physicians (AAFP) concurs with the USPSTF.

Other Recommended Guidance American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists (ACOG) concurs with the U.S. Preventive Service Task Force (USPSTF) recommendations, with the exception that ACOG strongly recommends that clinicians administer immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chronic villus sampling or fetal blood sampling.²

ACOG further recommends that immunoglobulin be administered following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

Evidence Rating:

Expert Consensus

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- American Academy of Pediatricians (AAP)
- The American College of Obstetricians and Gynecologists (ACOG)
- National Institutes of Health (NIH)
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Rh (D) incompatibility refers to a condition that develops when a pregnant women with Rh-negative blood type carries a fetus with an Rh-positive blood type. In reaction to what is perceived to be a foreign substance, the woman's body makes antibodies that attack fetal red blood cells (isoimmunization). Since it takes time to build up antibodies, first pregnancies are typically not affected by Rh incompatibility. However, in subsequent pregnancies, Rh incompatibility may cause destruction of fetal red blood cells (hemolysis), which leads to anemia and an accumulation of bilirubin in the fetus's bloodstream (hyperbilirubinemia) that produces jaundice. Extreme jaundice leads to kernicterus, a form of brain damage associated with cerebral palsy and mental retardation. The hemolytic destruction of red blood cells can also lead to hydrops fetalis, a severe anemia resulting in fetal heart failure, total body swelling, respiratory distress or total circulatory collapse, and often death.³

Rh incompatibility occurs in approximately 10% of all pregnancies, depending on the race of the pregnant woman and her fetus. Without treatment, 25% to 30% of these fetuses will show various degrees of hemolytic anemia and hyperbilirubinemia. An additional 20% to 25% will be hydropic and will either die *in utero* (resulting in a stillbirth) or shortly after birth. Hemolytic disease of the fetus accounts for 4 to 5 deaths per 100,000 births in the United States.³

Condition/Disease Risk Factors

Only Rh-negative women are at risk of having a baby with Rh disease. If an Rh-negative woman and Rh-positive man conceive an Rh-positive fetus, there is a chance that some of the fetus's Rh-positive red blood cells may enter the woman's blood stream, which stimulates the woman's immune system to produce antibodies against the fetus's Rh-positive cells. The risk of Rh disease becomes greater with each subsequent pregnancy.⁴

Value of Prevention

Economic Burden of Condition/Disease

No data exist that estimate the total direct or indirect costs of Rh (D) incompatibility in the United States.

	<p>The value of life years lost due to fetal loss, stillbirth, neonatal and post-neonatal deaths, and productivity loss associated with disability constitute the major components of the economic burden of Rh (D) incompatibility. Costs would be even higher if the additional medical care costs and productivity losses of working pregnant women are considered.</p>
Workplace Burden of Condition/Disease	<p>In addition to the incremental medical care utilization costs due to complications from Rh (D) incompatibility, there can be significant productivity losses at the workplace when working parents need to take time off from work to care for short- or long-term health problems of their children.</p>
Economic Benefit of Preventive Intervention	<p>Early identification of Rh (D) incompatibility allows clinicians to begin treatment before damage is done to the fetus. This prevents otherwise expensive medical treatment, lifelong disability, and even death.</p>
Estimated Cost of Preventive Intervention	<p>In 2004, the private-sector cost of screening for Rh (D) incompatibility averaged \$15 per screen; approximately 95% of all paid claims fell within the range of \$0 to \$38. The cost of immune globulin averaged \$111 and approximately 95% of all paid claims fell within the range of \$0 to \$178.⁵</p>
Estimated Cost of Treatment	<p>Not Provided</p>
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	<p>A review undertaken on behalf of the National Institute of Clinical Excellence in the United Kingdom, the governmental unit responsible for producing evidence-based recommendations for the UK, found that routine antenatal anti-D preventive medication (immunoglobulin) provides a cost-effective intervention for preventing the incidence of hemolytic disease of the newborn in pregnancies of Rh (D)-negative women.⁶</p>

Preventive Intervention Information

Preventive Intervention: Purpose of Screening and Preventive Medication	<p>Early identification of Rh (D) incompatibility allows clinicians to begin treatment before damage is done to the fetus. This prevents otherwise expensive medical treatment, lifelong disability, and even death.</p>
Benefits and Risks of Intervention	<p>Early detection of Rh (D)-negative blood type in a pregnant woman is of substantial benefit (when the woman is not yet isoimmunized and the father of the fetus is not known to be Rh (D)-negative) because it makes prevention of isoimmunization possible. Clinicians can administer anti-D immune globulin to Rh (D)-negative pregnant women, thereby preventing the maternal isoimmunization that would adversely affect subsequent pregnancies. This course of treatment prevents isoimmunization in 96% of women at risk.⁴ Screening and treatment with immunoglobulins have few adverse affects.⁴</p>
Initiation, Cessation, and Interval	<p>The USPSTF strongly recommends that all pregnant women undergo Rh (D) blood typing and antibody testing at their first prenatal visit. Furthermore, the</p>

USPSTF recommends that women known to be Rh (D)-negative and unsensitized undergo a repeat Rh (D) antibody test between 24 and 28 weeks' gestation to determine their degree of sensitivity. This second step is unnecessary if the fetus's father is known to be Rh (D)-negative.

A full dose (300mg) of immunoglobulin should be administered to^{1,2}:

- All unsensitized Rh (D)-negative women after their repeated antibody screen between 24 and 28 weeks' gestation.
- D-negative women within 72 hours of delivering a Rh (D)-positive infant.
- D-negative women following amniocentesis or either induced or spontaneous abortion (a 50 mg dose should be administered when abortion occurs prior to 13 weeks).

Clinicians have discretion regarding the provision of immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chorionic villus sampling or fetal blood sampling and/or following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

Intervention Process

Rh (D) blood typing and antibody testing is conducted via an analysis of the blood. Immunoglobulin is administered to those at risk of Rh disease through an injection.

Treatment Information

Health benefit coverage should include provisions for follow-up and treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The U.S. Preventive Services Task Force (USPSTF)
Strength of Evidence: A (Strongly Recommended/Good Evidence),
B (Recommended/At Least Fair Evidence)

A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence to support Rh (D) blood typing and antibody testing for all pregnant women during their first visit for pregnancy-related care.¹

B (Recommended/At Least Fair Evidence)

- The USPSTF found fair evidence to support Rh (D) antibody testing for all unsensitized Rh (D)-negative women between 24 and 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative.¹

This recommendation is supported by the:

- American Academy of Family Physicians (AAFP)

Recommended Guidance:

The American College of Obstetricians and Gynecologists (ACOG)
Strength of Evidence: Expert Consensus

- The ACOG concurs with the USPSTF recommendations, with the exception that ACOG strongly recommends that clinicians 1) administer immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chorionic villus sampling or fetal blood sampling, and 2) administer immunoglobulin following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

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Campbell KP, Chattopadhyay S. Rh (D) incompatibility evidence-statement: screening and preventive medication. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Rh (D) Incompatibility (Screening and Preventive Medication)

1. U.S. Preventive Service Task Force. Screening for Rh (D) incompatibility: Recommendations statement. November 2004. AHRQ Pub. No. 05-0566-A.
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3. Medical Encyclopedia: Rh incompatibility. Available from: <http://www.nlm.nih.gov/medlineplus/ency/article/001600.htm>.
4. March of Dimes. Quick reference and fact sheets. Rh Disease. [cited 2006 Jul 18]. Available from: http://www.marchofdimes.com/professionals/681_1220.asp.
5. Thomson Medstat. MarketScan. 2004.
6. Chilcott J, Lloyd Jones M, Wight J, Forman K, Wray J, Beverley C, et al. A review of the clinical effectiveness and cost-effectiveness of routine anti-D antibiotic prophylaxis for pregnant women who are rhesus-negative. *Health Technol Assess* 2003;7(4).