Transfusion Medicine Topics for Midwives

Ontario Regional Blood Coordinating Network (ORBCoN)
Topics to be Covered

- Brief review of:
  - hemolytic disease of the fetus and newborn
  - the use of Rh Immune Globulin (RhIG)
- Transport, storage, and administration of RhIG
- Laboratory testing
  - the significance of passive anti-D
  - the significance of other red cell antibodies
  - extra doses of postnatal RhIG
- Weak D blood types and their significance
RBC antibodies in parturient placenta

parturient

placenta

fetal RBC destruction

fetus

suppression of RBC production in bone marrow (anti-K)

anemia

↑ bilirubin

↑ RBC production in liver and spleen

fetal edema

enlarged liver and spleen

heart failure

fetal death

↓ fetal movements

↑ blood flow rate

newborn

jaundice

brain damage (kernicterus)

Adapted from de Haas. Vox Sanguinis 2015;109:99
### Potentially Sensitizing Events

<table>
<thead>
<tr>
<th>Event</th>
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<tbody>
<tr>
<td>Amniocentesis, chorionic villus biopsy and cordocentesis</td>
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<td>Antepartum hemorrhage/Uterine bleeding in pregnancy</td>
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<td>External cephalic version</td>
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<td>Abdominal trauma</td>
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<td>Ectopic pregnancy</td>
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<td>Evacuation of molar pregnancy</td>
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<tr>
<td>Intrauterine death and stillbirth</td>
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<td>Intrauterine intervention (transfusion, surgery, etc.)</td>
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<td>Miscarriage, threatened miscarriage</td>
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<td>Therapeutic abortion</td>
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<td>Spontaneous vaginal birth, assisted vaginal birth, Caesarean section</td>
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*About 0.1 mL of baby’s blood may cause immunization*
HDFN caused by other RBC antibodies

There are over 300 blood group antigens in 35 blood group systems (so far).
HDFN caused by other RBC antibodies

- After anti-D, the most common are anti-K, -c, -E
- Refer clients with antibodies to an obstetrician or high-risk pregnancy unit (CMO Standard: Consultation and Transfer of Care)
- Anti-Kell antibodies also suppress the bone marrow in the fetus
- Anti-A, anti-B, and anti-A,B can cause mild HDFN because some is IgG and can cross the placenta
HDFN caused by other red cell antibodies
(this list is not comprehensive)

<table>
<thead>
<tr>
<th>Anti -</th>
<th>Causes HDN? (Y/N)</th>
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<td>D</td>
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<td>Antibodies Which do NOT Cause HDFN</td>
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<td>Anti-Ch/Rg</td>
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<td>Anti-Xg</td>
<td>Anti-Cromer</td>
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<td>Anti-Scianna</td>
<td>Anti-Knops</td>
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Management of HDFN

• Fetus
  – non-invasive monitoring of by ultrasound: size of liver, spleen and heart, edema, velocity of blood flow in middle cerebral artery (Doppler)
  – intrauterine transfusion of fetus

• Newborn
  – phototherapy to reduce bilirubin level
  – exchange transfusion, top-up transfusion
  – maternal antibodies may persist for months
RhIG (WinRho®)

- each vial contains 300µg anti-D in 1.3 mL
- contains traces of IgA
- when given prenatally and post-delivery (≤ 72 hrs), reduces the chance of anti-D formation in D neg clients by 99.9%
- RhIG is not indicated or effective if a D neg client has already formed anti-D
- RhIG does not protect against any red cell antibodies other than anti-D
RhIG Transportation

Credo Promed (formerly Golden Hour Box)

- Pelican Biothermal
- [Link to Credo Promed v6 0915.pdf](http://www.pelicanbiothermal.com/sites/default/files/9-credo_promed_v6_0915.pdf)
- Contact: Mark.Jezierski@pelican.com
- Consists of a removable chamber made of phase change material which sits in a vacuum insulated panel
- Dimensions 9.5in x 8.25in x 8in
- Must precondition phase change material to meet external temperature conditions.
- Summer and Winter profiles
  - Summer: -18°C to -40°C freezer for minimum 8 hours, then to room temperature for 30 minutes
  - Winter: 4-8°C for minimum of 6 hours
- Full validation performed nationally available through ORBCoN
- Yearly validation done on individual site
RhIG Transportation

- RhIG is stable when stored at 2-8°C until expiry date
- The Credo Promed box provides a temperature controlled environment during transportation to client
- Validated to maintain temperature for 24 hours
- Training for conditioning of box must be documented
- Cost is approximately $300.00
Storage and Administration of RhIG

- RhIG must be stored according to the package insert directions (at 2-8°C) in a refrigerator with:
  - validation that it maintains the required temperature
  - continuous temperature monitoring, or temperature recorded every 4 hours
  - connection to an emergency power supply
  - an alarm system that signals in a continuously-monitored location
  - the alarm points set at temperatures that allow for correction of the problem before the blood product is compromised
  - the alarm and back-up power system checked at least monthly
  - all equipment records kept for 5 years (validation, maintenance, service, alarm checks, etc.)
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Best to have it stored at the hospital blood bank
Storage and Administration of RhIG

• If there is a product recall all product must be perfectly traceable to the recipient
  – use a tracking log (or alternative) so that you can identify every client who received vial(s) from each lot number

• Document:
  – client identification, date of administration, dose given
  – lot number of vial(s)*

• Note the expiry date on the vial and do not use past the expiry date

*Can Standards Assoc CAN/CSA-Z902-15;11.9
Informed Choice

• Before administering any blood product, including RhIG, an informed choice discussion must take place and be documented according to your MPG protocol and the CMO Standard
Prenatal Laboratory Testing

• Group and screen (G&S) at first prenatal visit
  – group the red cells for ABO and Rh(D)
  – screen the plasma for other red cells antibodies
  – also called ‘type and screen’

• **Do not give RhIG** before this testing is done

• Second group and screen at 28 weeks

• If Rh negative, obtain sample for second G&S **before RhIG**
  – to eliminate confusion by passive anti-D
Prenatal Laboratory Testing

- anti-D in the first pregnancy indicates previous transfusion or undisclosed abortion. NEED CLINICAL HISTORY
- anti-D in subsequent pregnancies indicates a missed anti-D, or RhIG given too late or in insufficient dose
RhIG Errors 2014 (UK)

359 cases: 76% were omission or late administration of RhIG

Passive anti-D

- = anti-D present in client due to previous administration of RhIG (RhIG is anti-D)
- may be picked up by the antibody screen test in the lab, but depends on method used by the lab
- can persist for months after RhIG injection
- can cause difficulty in interpreting a positive antibody screen: is this immune anti-D formed by the client or passive anti-D from a previous RhIG injection?
Anti-D Test Methods

The more sensitive the test, the longer post-injection of RhIG the result will be positive.
Significance: Passive vs Immune anti-D

- If the anti-D is passive anti-D then RhIG is still indicated postpartum
- If the anti-D is immune anti-D then RhIG is no longer indicated (will be ineffective)
- CLINICAL HISTORY is critical - has client had RhIG?
- If yes, when was it given?
Is it Passive or Immune anti-D?

- Passive anti-D due to RhIG is rarely present at a high titre (concentration)
- The titre of passive anti-D is rarely >4
- RhIG is pure IgG (no IgM)
- Immune anti-D is both IgM and IgG, and the lab may be able to tell them apart upon request
- This question may be impossible to answer
- If in doubt, give RhIG if the client would otherwise qualify
Antibody titration

Serial dilutions are made of client serum with saline.

neat client serum 1:2 1:4 1:8 1:16 1:32 1:64 .... to 1:256
Antibody titration

- To each tube reagent red cells with the antigen to be tested are added.
- Agglutination of the reagent red cells indicates antibody present.
- The higher the titre the greater the Ab concentration in the client’s serum.
When to give extra prenatal RhIG

• prenatal: 300µg after each sensitizing event
• prenatal: quantitative testing for FMH may be considered after placental abruption, blunt trauma to the abdomen, cordocentesis, or placenta previa with bleeding. More than one 300µg vial may be required
• prenatal: not required at 40 weeks unless the previous dose was given before 28 weeks

SOGC Clinical Practice Guideline No.133, September 2003
When to give extra postpartum RhIG

- at birth, baby’s blood group is determined from a cord blood sample
- cord blood sample is not tested if client is D pos
- if baby is D pos or weak D pos, or the Rh status is unknown, client needs at least 1 300µg vial of RhIG
- each 300µg vial contains enough anti-D to protect against 30 mL fetal blood (=15 mL of fetal red cells)
- average bleed at delivery = 1 mL
- 3 in 1000 births will involve a bleed >30mL
- a Kleihauer-Betke test or flow cytometry is done to determine the size of the bleed
Kleihauer-Betke Test to Estimate Fetal-Maternal Hemorrhage (FMH)

- treat sample of mother’s blood with acid
- fetal red cells contain Hb F, which is acid resistant
- stain treated sample and count fetal cells
- assume maternal blood volume of 5 L
- estimate size of FMH
- estimate dose of RhIG needed (“round up”)

FMH can also be tested by flow cytometry
Weak D blood types

• There are over 100 genetic variants of RHD
• D is the most antigenic blood group antigen after the ABO blood group
• that’s why routine blood typing (blood grouping) includes ABO and RhD
D antigen on RBC

- D pos
- D neg
- ‘weak D’
  - weak D
  - partial D
Weak D and Partial D

- weak D = fewer RhD antigens
- partial D = different RhD antigens
Weak D Testing

- If a person initially types as D neg, an extra lab test is required to look for weak D in some clinical situations.
- The weak D test does not differentiate between weak D and partial D; only genotyping can do that.
- Weak D
  - Incidence varies by ethnicity.
  - Most (90%) don’t make anti-D.
- Partial D (also known as variant D)
  - Incidence varies by ethnicity.
  - Can make anti-D.

Garratty. Transfusion 2005;45:1547
Typing for D antigen

\[ Y = \text{anti-D antibody reagent} \]
The Weak D Test

\[ Y = \text{anti-human antibody reagent} \]
When to Test for Weak D

(weak D looks D neg until the test for weak D is done)

• Yes
  – cord blood if client is D neg with no anti-D
    • because you don’t want to type the baby as D neg
      and sensitize a D neg client who needs RhIG

• No
  – prenatal sample in an apparently D neg client
    of childbearing age
    • because you want to identify the client as D neg so
      that RhIG is given
Algorithm for Resolving Weak D

**Negative**
- Candidate for RhIG
- RhD-negative for transfusion

**Discrepant/inconclusive or strength of reaction weaker than expected (serologic weak D phenotype)**
- Send for RHD genotyping for weak D types

**Positive (and concordant with patient history, if available)**
- Not a candidate for RhIG
- RhD-positive for transfusion

**Weak D type 1, 2, or 3**
- Not detected
  - May be at risk for forming anti-D
  - Candidate for RhIG
  - RhD-negative for transfusion

**Weak D type 1, 2, or 3**
- Detected
  - Not at risk for forming anti-D
  - Not a candidate for RhIG
  - RhD-positive for transfusion
Why do Genotyping?

• A client with a weak D type that does not form anti-D does not:
  – need RhIG
  – need to be transfused with D negative RBCs if a transfusion is needed

• Why avoid RhIG?
  – derived from human plasma, costly, risk of infection is not zero, client choice

• Why avoid requirement for D neg RBC?
  – in chronic short supply
This form is available at [www.blood.ca](http://www.blood.ca) > hospitals > diagnostic services > Edmonton > test request forms > request form for RHD genotyping.

You will need to involve your local hospital blood bank. Lab test results are required. Requests must be approved by a consultant pathologist or CBS physician.
Case

- pregnant client MP, typed as D neg at one lab (the hospital) and D pos at another; the attending physician called the hospital blood bank
- genotyping was suggested to resolve the discrepancy
- Genotyping report:
  - blood group RHD, genotype weak D type 1, phenotype weak D
  - comment that weak D types 1, 2, and 3 have not been known to produce anti-D and do not require RhIG prophylaxis
  - the hospital changed the client’s blood group from D neg to D pos in the computer system
- MP had already received prenatal RhIG, but no postpartum RhIG was required after the C-section
- cord blood was not typed because client is now D pos
ORBCoN Toolkit for Midwives

• Presentation slides for education
• Information pamphlets for midwives
• Information pamphlet for clients
• Form to document informed choice discussion (note in client record is another option)
• Log sheets for documentation of RhIG transportation and administration
• Memorandum of Understanding template
• CSA & CSTM standards excerpts, References and published Guidelines
Thank you. Questions?

Please consider donating blood or bone marrow
www.blood.ca
1-888-2-DONATE