ORBCoN
Ontario Regional Blood Coordinating Network

Inspiring and facilitating best transfusion practices in Ontario.

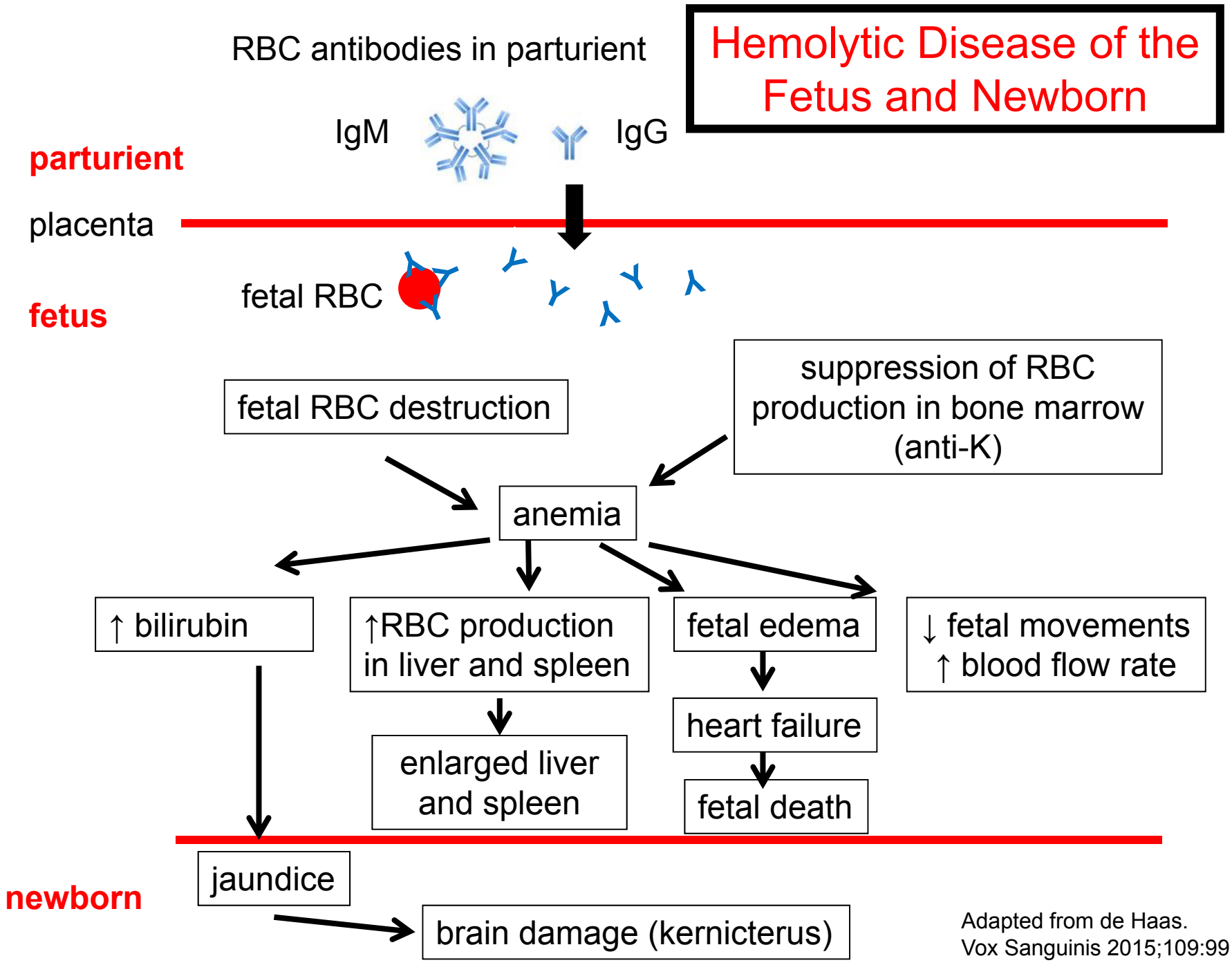
Transfusion Medicine Topics for Midwives

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

Hemolytic Disease of the Fetus and Newborn



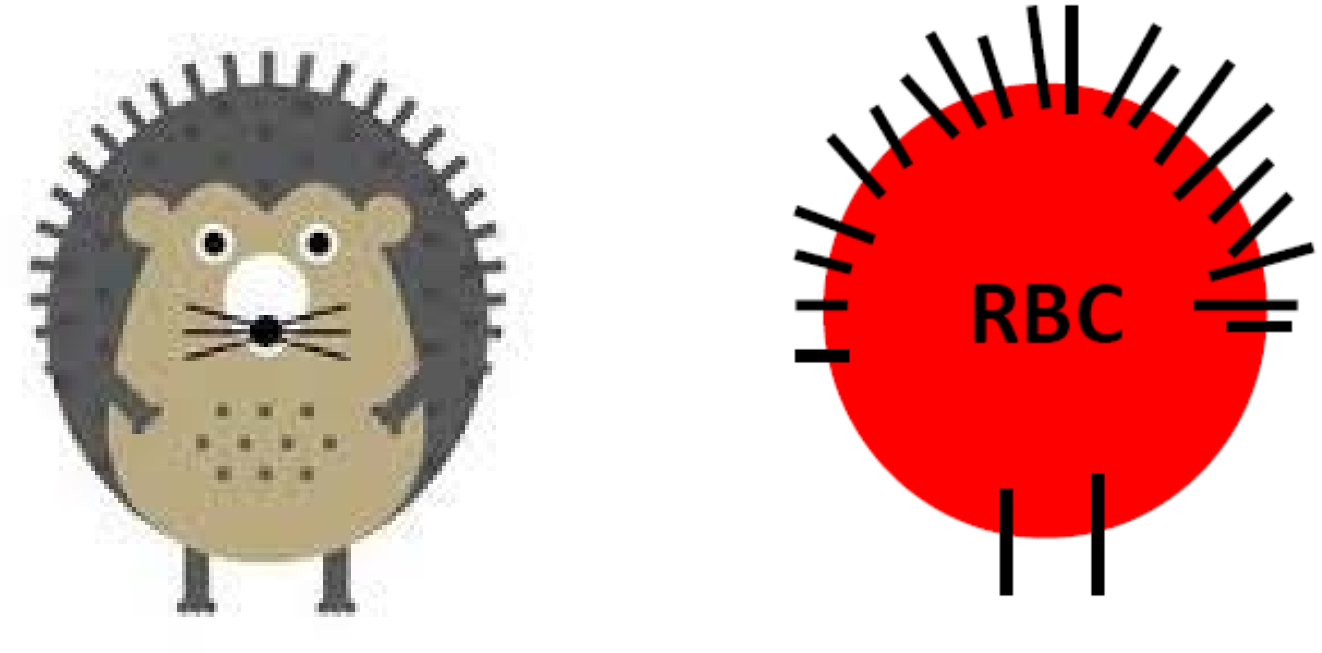
Adapted from de Haas.
Vox Sanguinis 2015;109:99

Potentially Sensitizing Events

Amniocentesis, chorionic villus biopsy and cordocentesis
Antepartum hemorrhage/Uterine bleeding in pregnancy
External cephalic version
Abdominal trauma
Ectopic pregnancy
Evacuation of molar pregnancy
Intrauterine death and stillbirth
Intrauterine intervention (transfusion, surgery, etc.)
Miscarriage, threatened miscarriage
Therapeutic abortion
Spontaneous vaginal birth, assisted vaginal birth, Caesarean section

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).

Pinterest.com

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)

Anti -	Causes HDN? (Y/N)
D	Y
C	Y
E	Y
c	Y
e	Y
K	Y
k	Y
Fya	Y
Fyb	Y
Jka	Y
Jkb	Y
S	Y
s	Y

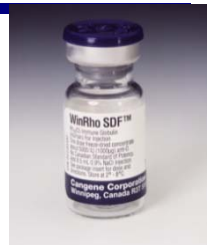
Antibodies Which do NOT Cause HDFN	
Anti-Le	Anti-Dombrock
Anti-Lu	Anti-LW
Anti-Yt	Anti-Ch/Rg
Anti-Xg	Anti-Cromer
Anti-Scianna	Anti-Knops

AABB Technical Manual 18th edition 2014

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

Photo credits: Dr.Zipursky thestar.com published Feb 21, 2016

RhIG Transportation

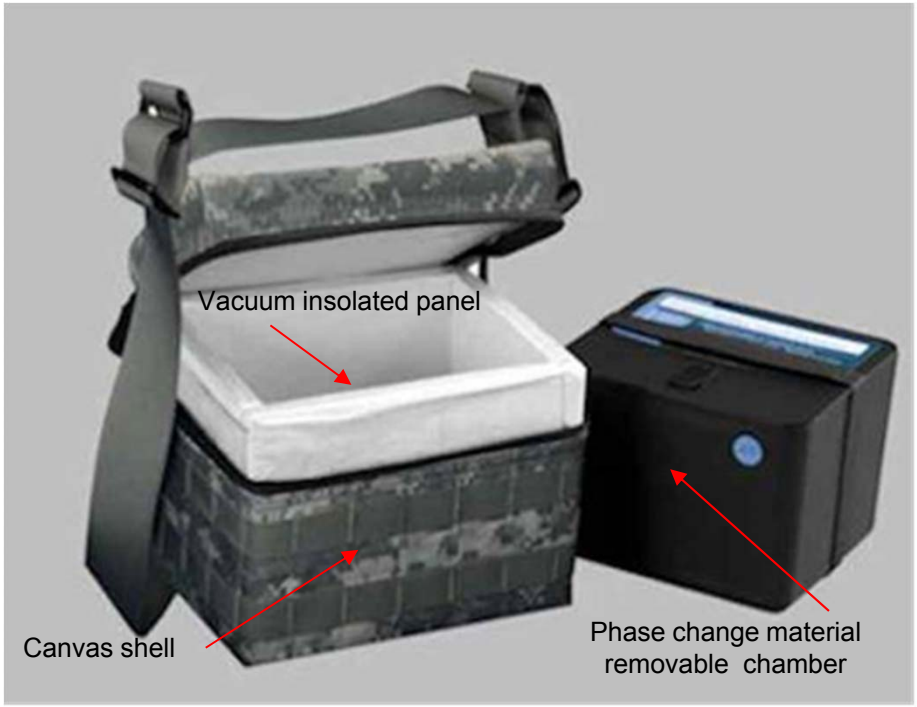
Credo Promed (formerly Golden Hour Box)

- Pelican Biothermal
- 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.)

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

Best to have it stored at the hospital blood bank

  - 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.)

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

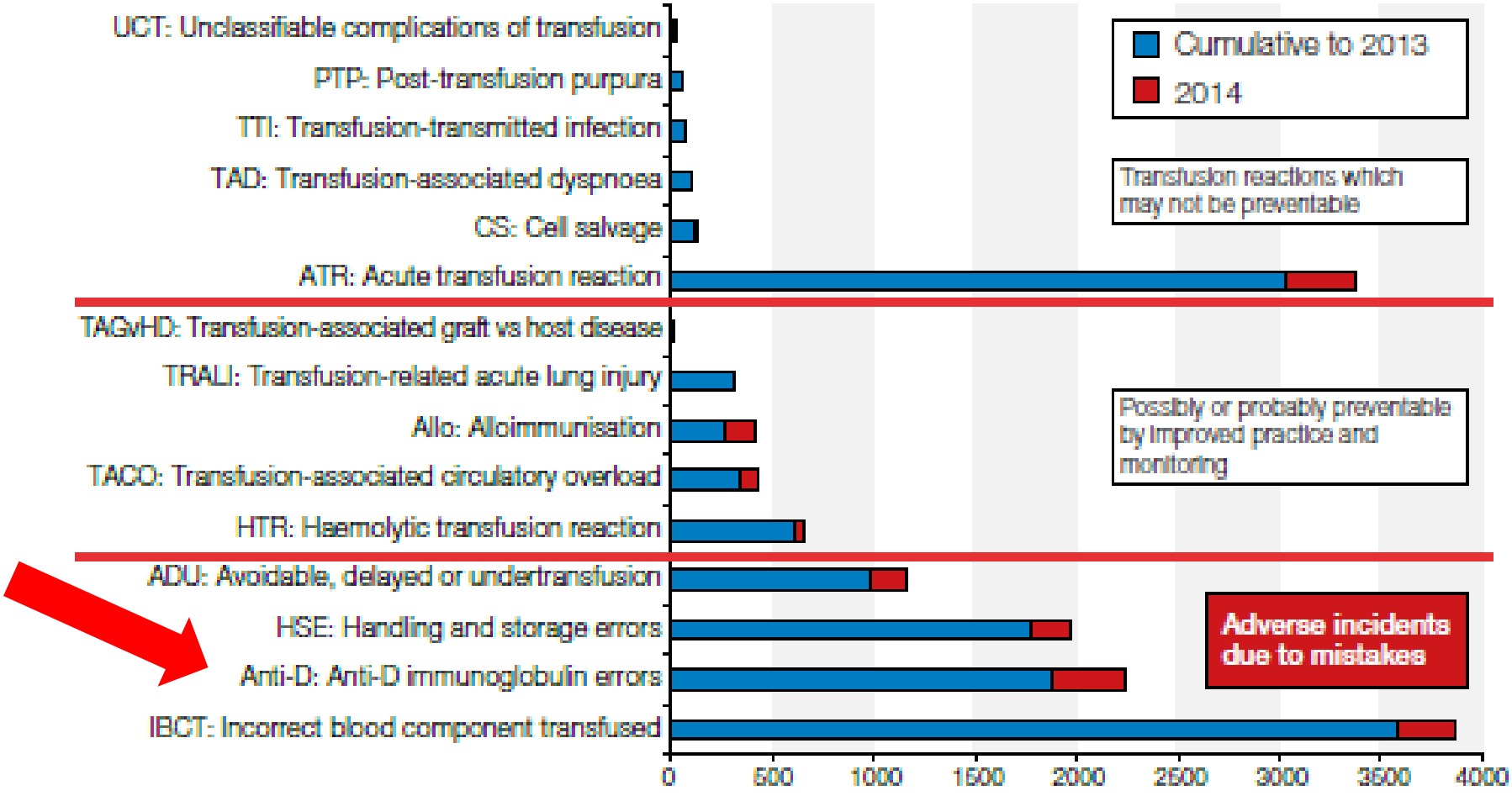
- Group and screen (G&S) at first prenatal visit
  - group the red cells for ABO and Rh(D)
  - screen the plasma for other red cells antibodies
  - also called ‘type and screen’
- **Do not give RhIG** before this testing is done
- Second group and screen at 28 weeks
- If Rh negative, obtain sample for 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)

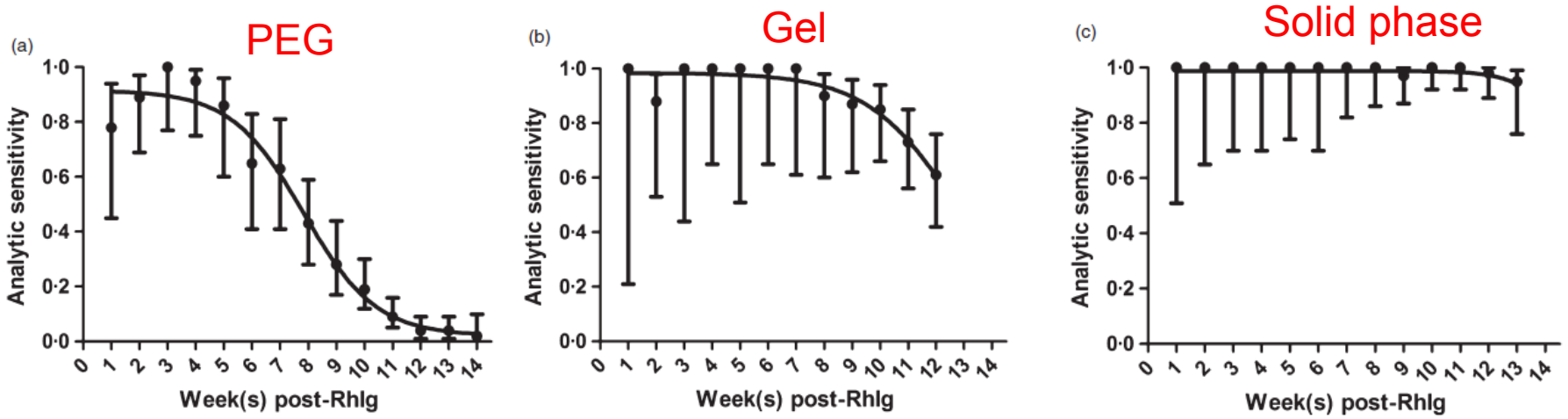
359 cases: 76% were omission or late administration of RhIG



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



Increasing sensitivity

The more sensitive the test,
the longer post-injection of RhIG the result will be positive

Significance: Passive vs Immune anti-D

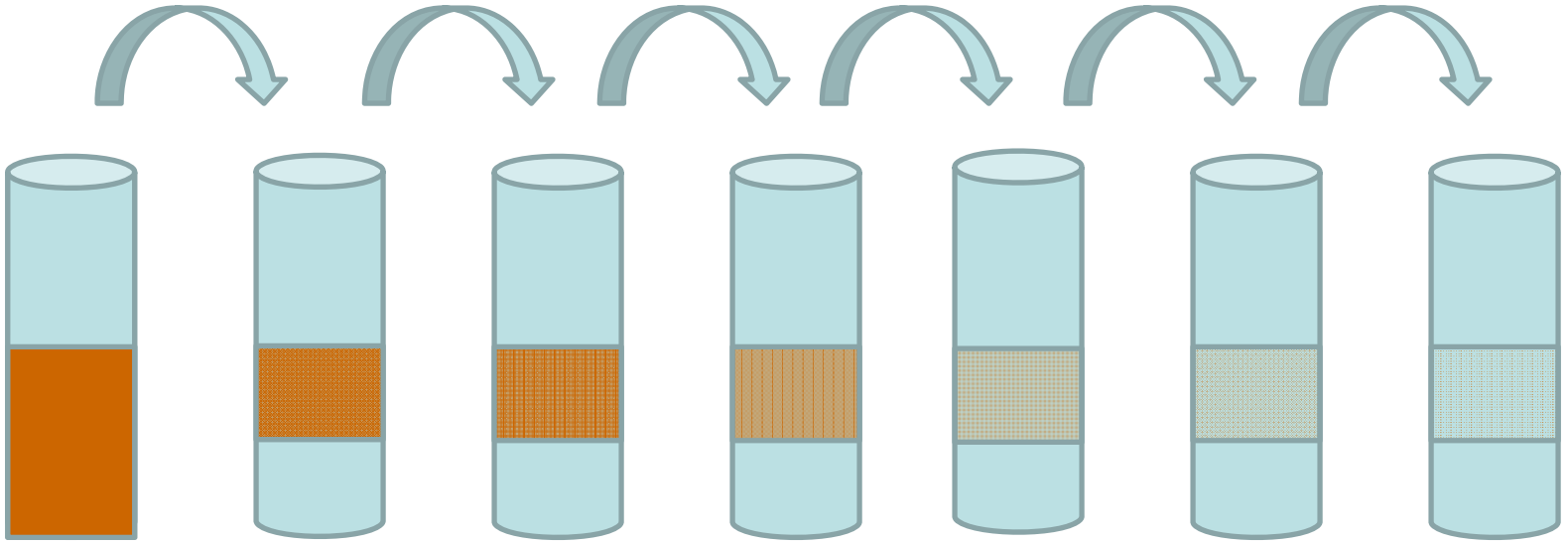
- If the anti-D is passive anti-D then RhIG is still indicated postpartum
- If the anti-D is immune anti-D then RhIG is no longer indicated (will be ineffective)
- CLINICAL HISTORY is critical - has client had RhIG ?
- If yes, when was it given?

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

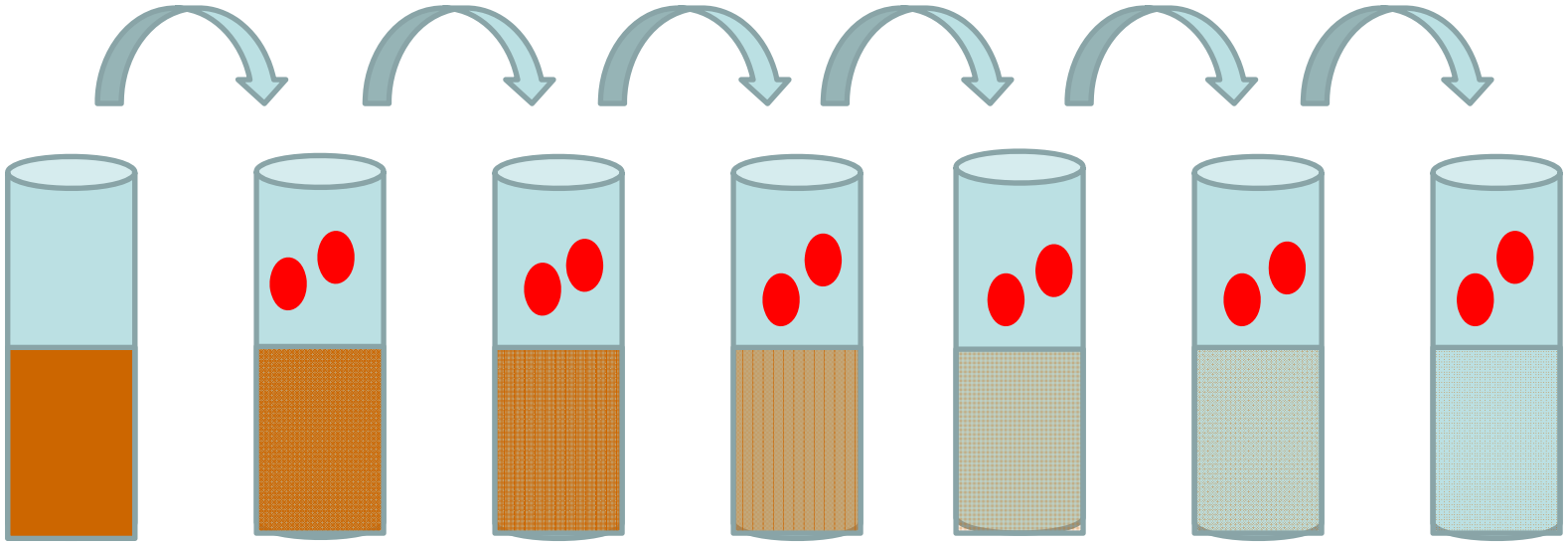
Serial dilutions are made of client serum with saline.



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.



neat client serum | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64

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

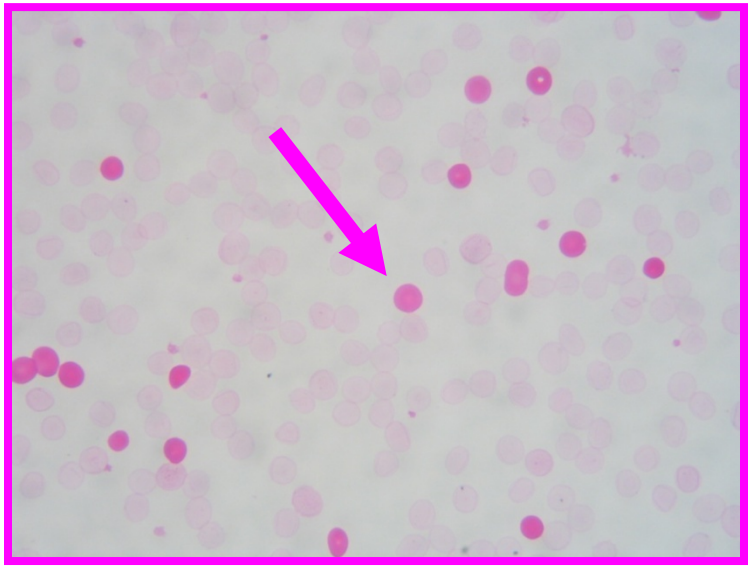
SOGC Clinical Practice Guideline No.133, September 2003

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)

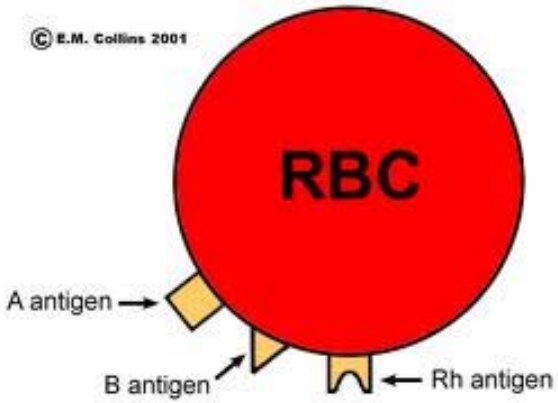
- treat sample of mother's blood with acid
- fetal red cells contain Hb F, which is acid resistant
- stain treated sample and count fetal cells
- assume maternal blood volume of 5 L
- estimate size of FMH
- estimate dose of RhIG needed ("round up")



- FMH can also be tested by flow cytometry

Weak D blood types

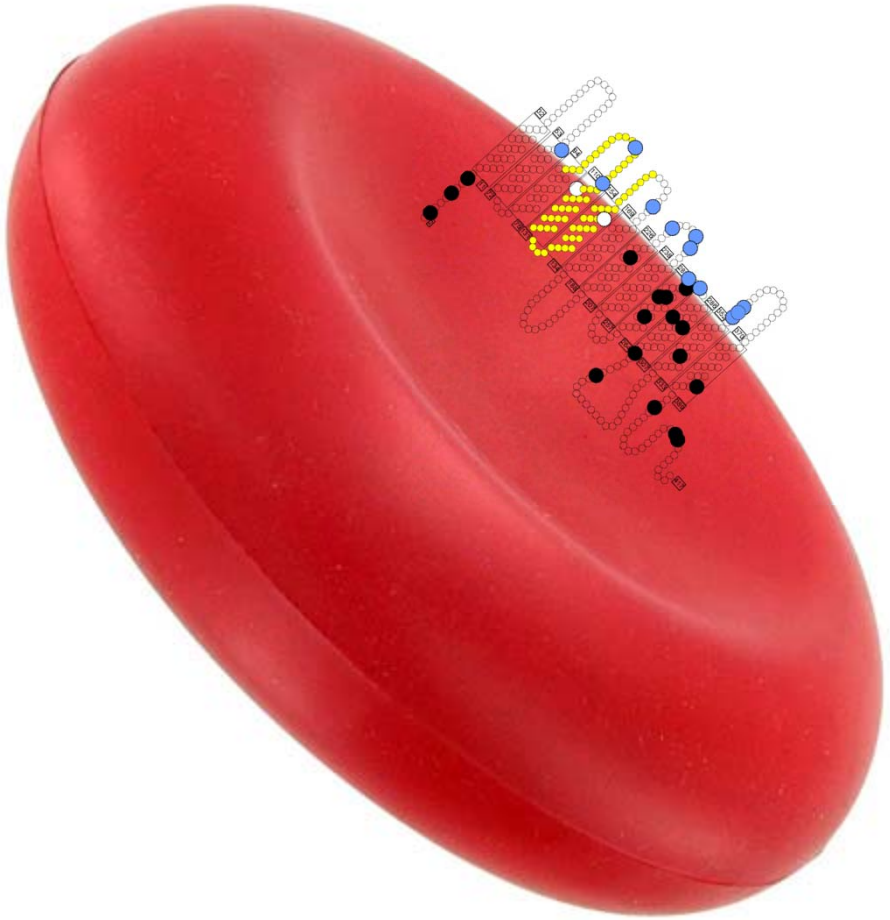
- There are over 100 genetic variants of *RHD*
- D is the most antigenic blood group antigen after the ABO blood group
- that's why routine blood typing (blood grouping) includes ABO *and* RhD



Immunohematology 2004;20(1):23
Transfusion 2004;44:1663

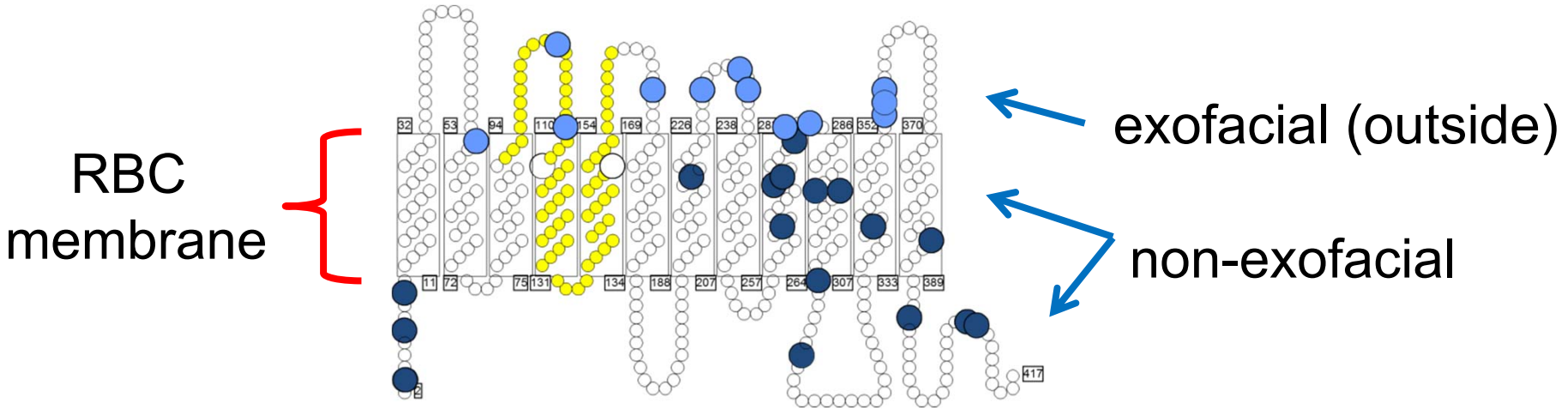
D antigen on RBC

- 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

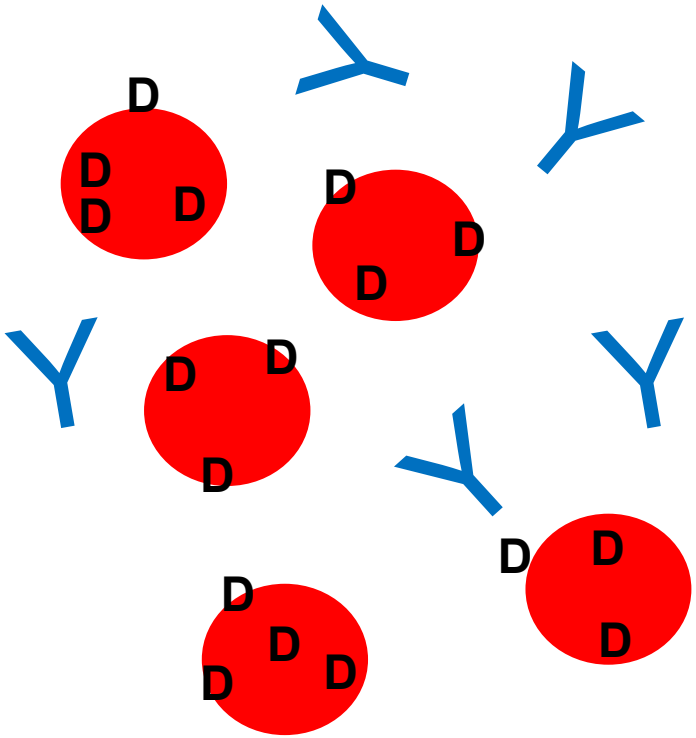


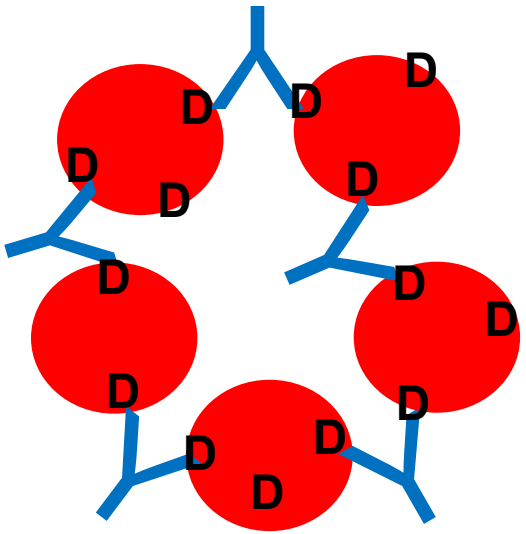
Weak D Testing

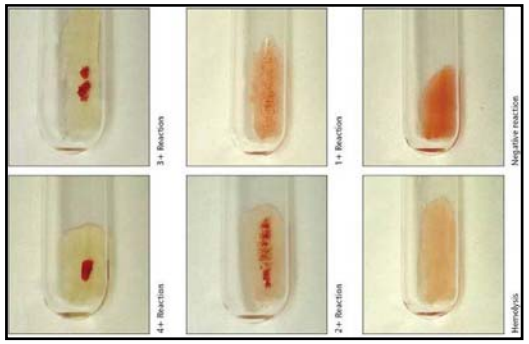
- If a person initially types as D neg, an extra lab test is required to look for weak D in some clinical situations
- The weak D test does not differentiate between weak D and partial D; only genotyping can do that
- weak D
  - incidence varies by ethnicity
  - most (90%) don't make anti-D
- partial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

www.aabb.org/development/awardsscholarships/scholarships/Documents/11er.pdf

Typing for D antigen

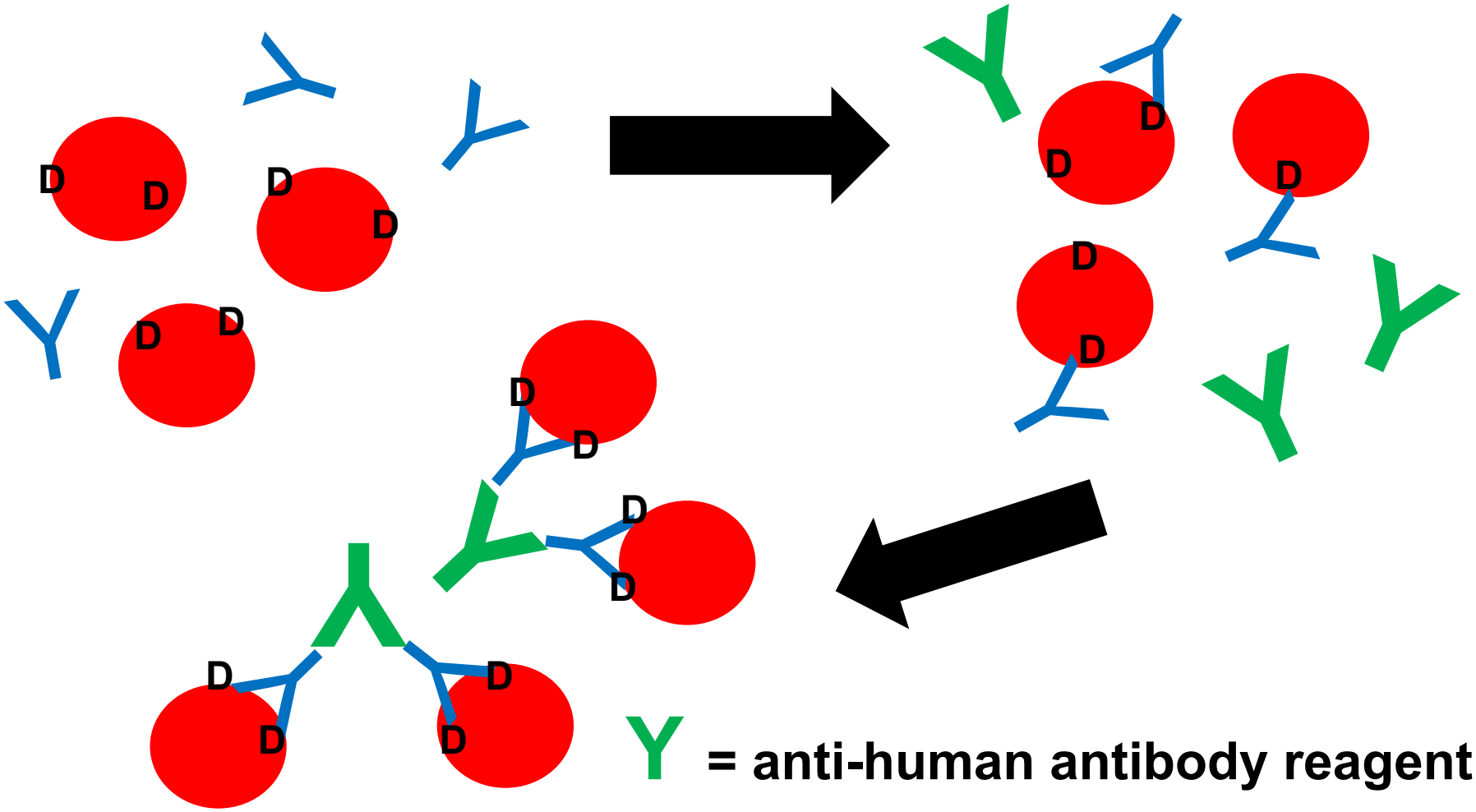






Y = anti-D antibody reagent

The Weak D Test

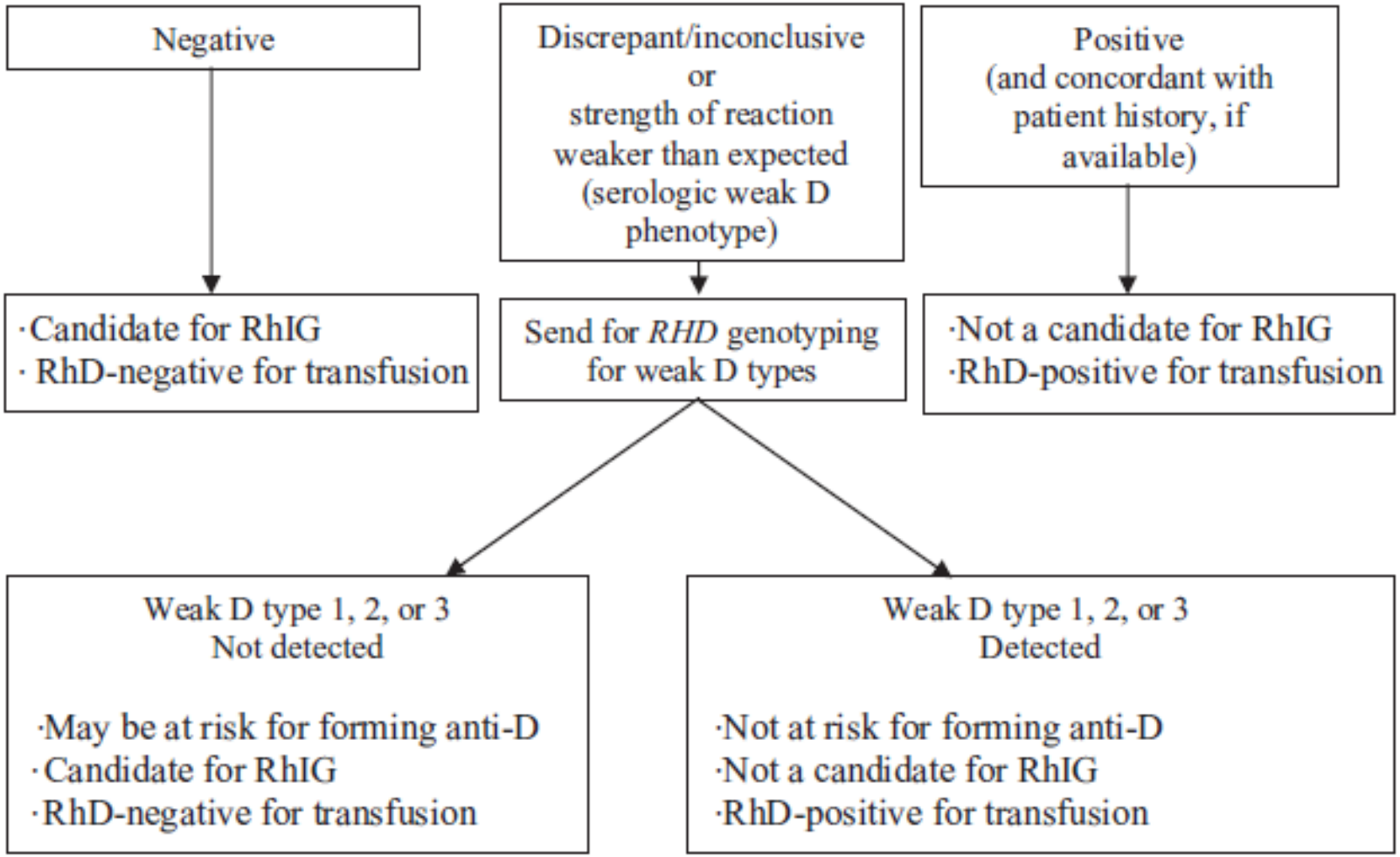


When to Test for Weak D

(★ 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



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

CBS Genotyping Service
(National Immunohematology Reference Laboratory)

Canadian Blood Services

Diagnostic Services Laboratory
8249-114 Street
Edmonton, AB T6G 2R8
Phone: 780-431-8765 Fax: 780-431-8779

Canadian Blood Services
it's in you to give

Request for RHD Genotyping

Requests must be approved by a consultant pathologist or CBS Physician

Testing Information	
Reason Requested	☐ Prenatal testing for weak or partial RhD phenotype ☐ Confirmation of weak or partial RhD phenotype ☐ Other (please provide additional information):_____

This form is available at 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?

Canadian Blood Services
it's in you to give

one match
stem cell and marrow network

Please consider donating blood or bone marrow

www.blood.ca

1-888-2-DONATE