Blood Product Utilization in Obstetrics

Elianna Saidenberg

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Objectives

- ✓ Blood product utilization in massive hemorrhage
- ✓ Complications of massive transfusion
- ✓ Unique complications of post-partum massive hemorrhage
- ✓ Use of RhIg in pregnancy/ post-partum

- ⊗ Surgical management of post-partum hemorrhage
- ⊗ Ante-natal management of the alloimmunized pregnancy

Post-Partum Hemorrhage

- Defined as bleeding within 24 hours of delivery
- Occurs in ~5% of deliveries
- Leading cause of maternal mortality world wide
  - Majority of deaths due to PPH within 4 hours of delivery
- Non fatal consequences of PPH include:
  - Further interventions (incl hysterectomy)
  - Iron deficiency anemia
  - Pituitary infarction (Sheehan's syndrome)
  - Poor lactation
  - Exposure to blood products
  - Coagulopathy, and organ damage with associated hypotension and shock

PPH-2

- Risk factors for PPH- the 4 T's
  - Abnormalities of uterine contraction (Tone)
  - Retained products of conception (Tissue)
  - Genital tract trauma (Trauma)
  - Abnormalities of coagulation (Thrombin)
    - Pre-existing coagulaopathy (ie hemophilia carrier, vWD)
    - Therapeutic anticoagulation for VTE
    - Pregnancy-associated coagulopathy
      - ITP
      - HELLP
      - DIC
        - » Pre-eclampsia
        - » Intra-uterine fetal demise
        - » Severe infection
        - » Abruption
        - » Amniotic fluid embolus
- RECALL: Most women will *not* have identifiable risk factors prior to delivery
- SOGC Clinical Practice Guideline October 2009

Signs and Symptoms of Shock Resulting from Blood Loss

Degree of Shock	Blood Loss	S & S	Likelihood of transfusion
Mild	<20%	Diaphoresis ↑Capillary refill Cool extremities Anxiety	Possible
Moderate	20-40%	As above + ↑HR ↑Resp rate Postural hypotension Oliguria	Almost always necessary
Severe	>40%	As above + ↓BP Altered mental status Anuria	Anticipate possible massive transfusion

When is transfusion “massive”?

- TM definition:
  - Replacement of a patient's total blood volume in less than 24 hours
- OB definition:
  - EBL >1500 mL, ≥40 g/L drop in Hgb or transfusion of >4 units PRBCs
- My definition…

When is massive transfusion encountered?

- Trauma
- Surgeries: Cardiac, vascular
- Upper GI bleeds
- Obstetrical catastrophe
- Vascular catastrophe
- Surgical misadventure

Why is massive transfusion different than other transfusion scenarios?

- More blood is needed, units are needed faster
  - Uncrossmatched units
  - Group switching
  - Different lab challenges
  - Different complications

Challenges

- Lab challenges
  - Lab tests are out of time sync
    - CBC, INR, aPTT, fibrinogen
  - Lab tests represent *in vitro* phenomena and may not adequately represent *in vivo* situation
- Co-ordination challenges- Multidisciplinary Care
  - Massive transfusion requires seamless efforts from clinical team (may involve more than one service), core lab, transfusion lab and blood bank, porters etc

Multi-Disciplinary Care for PPH

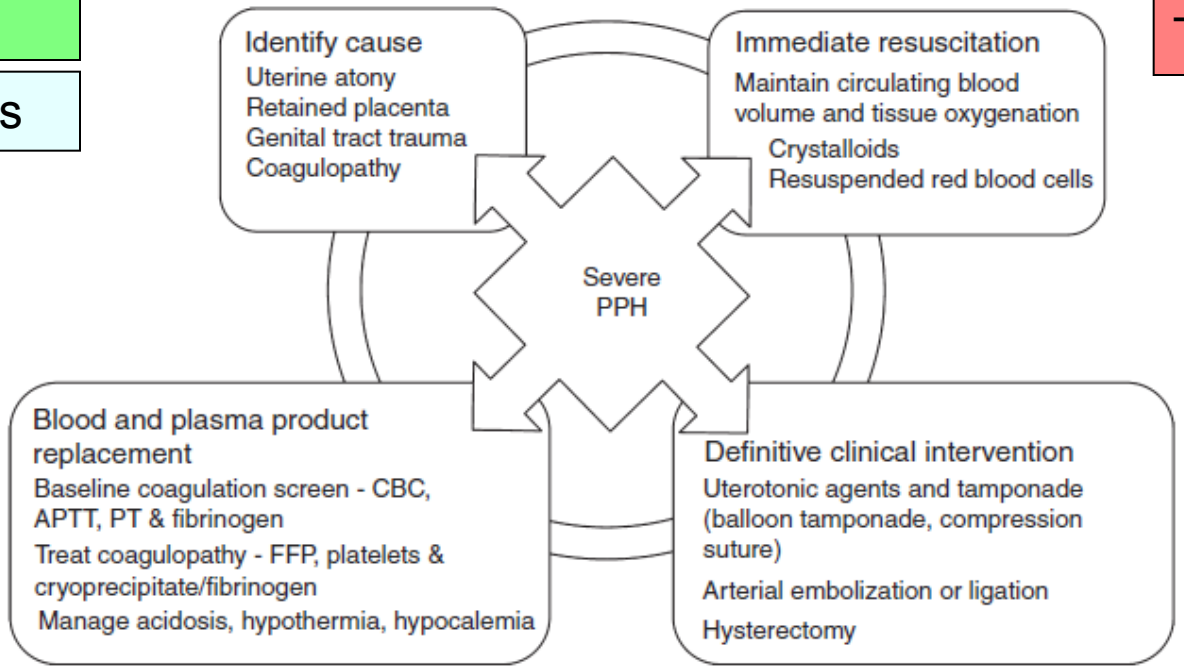
Obstetrician

Core lab

OB nurses

Anesthetist

TM lab



Anesthetist

Obstetrician

OB nurses

Core lab

TM lab

Obstetrician

OB nurses

Surgical nurses

Anesthetist

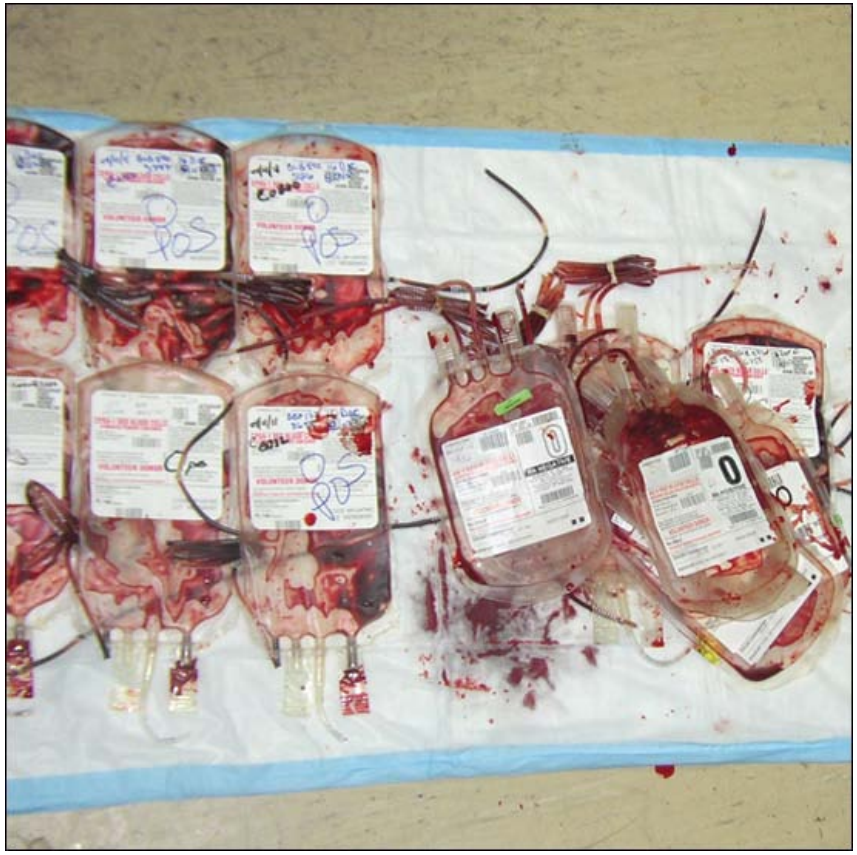
Portering Service

Interventional radiology

Complications of Transfusion

Fever	FNHTR, acute hemolysis, sepsis
Dyspnea	TRALI, TACO, others
Allergic	Mild → anaphylaxis
Antibodies	Acute & delayed hemolytic reactions, pregnancy complications
Infectious	Viruses, Bacteria, Prions
Others	

Complications of Massive Transfusion



- HYPOTHERMIA
- HYPERKALEMIA
- HYPOCALCEMIA
- COAGULOPATHY

In a perfect world…

- Special code called when there is life-threatening bleeding in a peri-partum patient

- **Code Lead: Anesthetist**
  - Ensures blood work Q1hour
    - CBC
    - INR/ aPTT/ Fibrinogen
    - Calcium
    - Lactate
    - ABG (on ice)
  - Orders other blood work as indicated (ie electrolytes, creatinine)
  - Ensures use of blood warmer, adjunctive hemostatic agents, cell salvage device as indicated
  - Co-ordinates medical efforts to maintain:
    - Hgb > 70 g/L
    - Platelets >50 x 10^9/ L
    - INR <2.0
    - Fibrinogen >2 g/L
    - Calcium >1/15 mmol/L
    - Lactate <2 m,mol/L
    - Base deficit <3 mmol/L
    - Temperature> 36 C
    - Systolic BP 70-90 mmHg

- **Communication Lead: Charge nurse (L&D, maternity ward or OR)**
  - Responsible for calling blood bank and other labs with patient name and MRN and key facts; provide phone extension of clinical area
  - Assign RN for patient care and another RN for documentation
    - These RNs must manage blood products for transfusion, collect and label blood samples, assess patient needs
  - Directs porter
  - Contacts OR, interventional radiology or other services as indicated
  - Communicate lab test results to lead physician

- **Transport**: A single porter is assigned to the case for the duration of the code
  - Reports to charge nurse to obtain blood bank requisition
  - Delivers blood products from blood bank to clinical care area
  - Delivers samples to appropriate labs
  - Delivers equipment to patient care area as needed
  - Takes direction from charge nurse
  - NO BREAKS!

- **Blood bank**: Single contact person assigned to case
  - Notifies charge nurse of contact person
  - Issues blood products STAT
  - Mobilize additional lab staff as needed
  - Inform physician on call for TM as needed
  - Check results of laboratory tests Q20 minutes

- **Other laboratories**:
  - Assign contact person, notify charge nurse of contact person
  - Prepare for STAT samples
  - Communicate results of tests to in charge nurse via telephone

- **Terminating a Code**
  - Medical lead:
    - Inform immediate care team that bleeding under control
    - Order tests needed for follow up of patient
    - Conduct debriefing within 72 hours
  - Communication lead:
    - Notify blood bank and laboratories that code terminated
    - Prepare unused blood products for return to blood bank
    - Notify blood bank of any needs for additional products
  - Assigned nurses:
    - Prepare patient for transfer and communicate with receiving RN
    - Review record and complete documentation
  - Porter:
    - Return coolers and unused blood products to blood bank
    - Deliver last blood samples to lab
    - Transport patient and equipment as needed
    - Does not resume regular activities until so instructed by charge nurse
  - Blood bank
    - Replace blood bank stock as needed

Use of Rh Immunoglobulin in Pregnancy

These are not trick questions

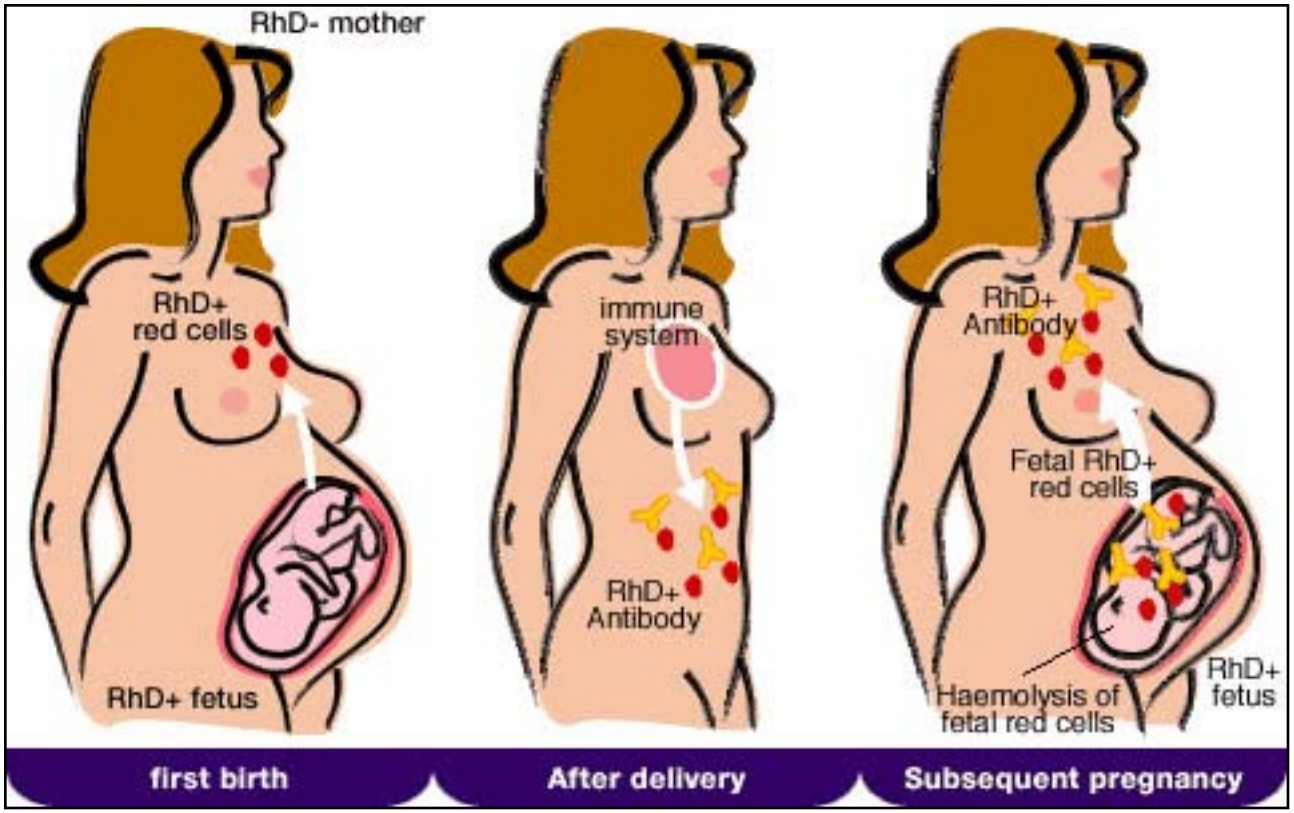
- When you order a blood group and screen what blood groups are tested?
- Why?
- Why not determine other blood groups?

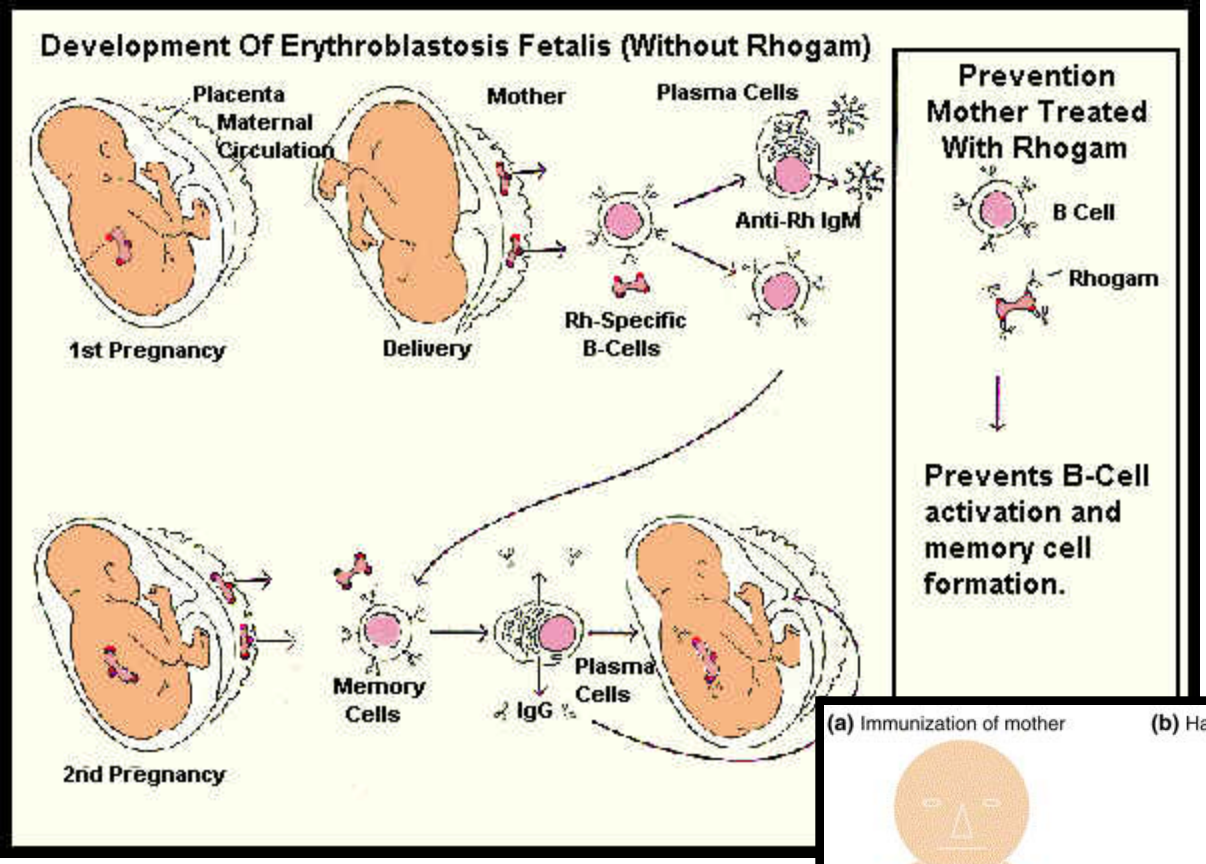
Also not a trick question

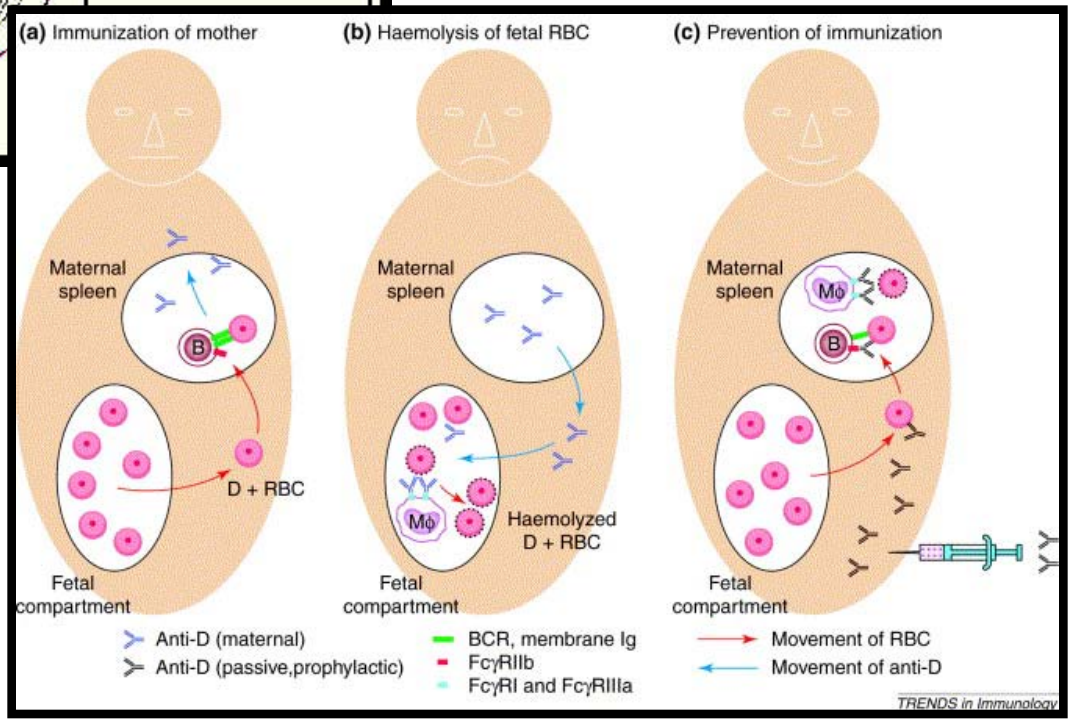
- What is weak D?
  - Weakened form of the D antigen that in routine D typing will react with some anti-D reagents but not with others (when an immediate spin or 37° incubation is done).
- Who should be tested for weak D?
  - Blood donors
  - RhD negative neonates born to RhD negative mothers
- Why not test all transfusion recipients and pregnant women?

	Can be alloimmunized	Can alloimmunize others	Should receive RhD- blood	Should receive RhIG
True RhD+	NO ⊗	YES ☑	NO ⊗	NO ⊗
True RhD-	YES ☑	NO ⊗	YES ☑	YES ☑
WeakD	YES ☑	YES ☑	YES ☑	YES ☑

Pathophysiology of HDFN




Development Of Erythroblastosis Fetalis (Without Rhogam)
Placenta
Maternal Circulation
Mother
Plasma Cells
Anti-Rh IgM
Rh-Specific B-Cells
1st Pregnancy
Delivery
Memory Cells
IgG
Plasma Cells
2nd Pregnancy
Prevention Mother Treated With Rhogam
B Cell
Rhogam
Prevents B-Cell activation and memory cell formation.


(a) Immunization of mother
(b) Haemolysis of fetal RBC
(c) Prevention of immunization
Maternal spleen
B
D + RBC
Fetal compartment
Mϕ
Haemolyzed D + RBC
Anti-D (maternal)
Anti-D (passive,prophylactic)
BCR, membrane Ig
FcγRIIb
FcγRI and FcγRIIIa
Movement of RBC
Movement of anti-D
TRENDS in Immunology

Scope of the Issue

- Anti-D allloimmunization still occurs in 0.4/ 1000 births
  - 1-2% of RhD negative women in Canada
  - Due to failure to administer RhIg
    - Without post-partum prophylaxis incidence of sensitization in subsequent pregnancy is 12-16%
    - With post-partum prophylaxis- <2%
    - With routine antenatal prophylaxis- 0.1%
  - Or insufficient RhIg dose
    - 300 mcg of RhIg protects against 30 mL fetal blood

JOGC September 2003

TABLE I

SYNOPSIS OF QUALITY OF EVIDENCE REGARDING ANTI-D IMMUNOPROPHYLAXIS*

Recommendations	Strength of Recommendations	Quality of Evidence
Postpartum Prophylaxis		
• Anti-D 120–300 µg within 72 hours of delivery	A	I
• Anti-D up to 28 days after delivery	B	III
• Routine FMH testing after delivery	C	Insufficient
Antepartum Prophylaxis		
• Anti-D 300 µg at 28 weeks	A	I
• Repeat antibody screening at 28 weeks	C	III
• Routine paternal testing	C	III
• Anti-D for "weak D" (e.g., D^u)	D	III
• Repeat anti-D at 40 weeks	C	III
Early Pregnancy Loss and Termination		
• Anti-D 120–300 µg after spontaneous/induced abortion	B	II-3
• Antibody screening prior to anti-D after abortion	B	III
• Ectopic pregnancy: 120–300 µg Rh immune globulin	B	III
• Molar pregnancy: 120–300 µg Rh immune globulin	B	III
Invasive Fetal Procedures		
• Amniocentesis: 300 µg Rh immune globulin	B	II-3
• CVS: 120–300 µg Rh immune globulin	B	II
• Cordocentesis: 300 µg Rh immune globulin	B	II-3
APH, Abdominal Trauma, ECV, FMH		
• Quantitative FMH testing	B	III
• Anti-D 120–300 µg following placental trauma	B	III
Consent		
• Informed consent prior to administration of anti-D	C	III

*CVS: chorionic villous sampling; APH: antepartum hemorrhage; ECV: external cephalic version; FMH: fetomaternal hemorrhage.

CSTM Standard 5.4.5 (2011)

- Policies, processes and procedures shall be established to ensure that all potential candidates for RhIg therapy shall have their Rh type and antibody screen determined
- A policy shall be established regarding the administration of RhIg to women who type as weak D positive
- RhIg should be administered to each Rh negative woman not known to be immunized to the D antigen in the following situations:
  - At 28 weeks GA
  - Following delivery of an Rh + neonate (including weak D or Rh unknown)
  - Following spontaneous or therapeutic termination
  - Following amniocentesis
  - Following any procedure known to be associated with increased risk of Rh immunization due to fetomaternal hemorrhage

CSTM Standard 5.4.5 cont

- RhIg should be administered within 72 hours of delivery or other potentially immunizing event
  - If 72 hours have passed, RhIg should be administered up to 28 days
- When a weakly reactive anti-D is detected in an Rh negative woman, a determination should be made as to whether she received RhIg in pregnancy
  - If receipt of RhIg cannot be determined, she should be treated as above

How to determine if reactive anti-D due to RhIg adminstration

- HISTORY! HISTORY! HISTORY!
- Following RhIg dosing antibody screen positive
  - Typically low titre, weakly reactive
    - Higher titre antibodies or increasing titres should raise concern for active alloimmunization
- Don’t be blind-sided by passive anti-D
  - Remember to consider active alloimmunization for RhD and other antibodies and ensure sufficient testing is done

CSTM Standard 5.4.5 cont

- A test shall be performed to determine the amount of fetomaternal hemorrhage in an eligible candidate

Qualitative screen- The Rosette test

- Highly sensitive method to detect ≥10 mL RhD+ fetal blood in maternal circulation
  - Anti-D is incubated with maternal blood. The cells are then washed and Rh(D) + indicator cells are added.
  - If fetal cells are present, they will have been coated with anti-D and the Rh(D)+ indicator cells and fetal cells will be bridged by the anti-D forming microscopic rosettes
  - False negative if fetus/ neonate has weak D phenotype
  - False positive if mother has weak D phenotype

Quantitative Screen-1

- Acid Elution (Kleihauer-Betke)
  - Principle: Upon exposure to an acid buffer, fetal Hgb resists elution and appears bright pink but maternal Hgb is eluted and maternal cells appear as “ghost cells”.
  - Percent of fetal cells is determined by counting number of pink cells present out of total of 2000 cells examined. Arbitrary whole blood volume of mother is converted to a percentage for a constant of 50
    - Calculation: (i) % fetal RBC= (# fetal cells/ 2000) x 100, (ii) FMH= % fetal RBC x 50
      - » ex: (i) (40/ 2000) x 100= 2%, (ii) 2 x 50= 100

Quantitative Screen-2

- Flow cytometry
  - Can be done using anti-HbF antibodies or anti RhD antibodies
    - Little data comparing the 2 methods
  - Correlates well with results of acid elution, but has greater inter-test and inter-laboratory precision than acid elution

Dosing RhIg

- One 300 mcg vial offers protection against 30 mL of Rh(D) + whole blood Rounding rules
  - Determine volume of FMH, divide by 30
    - If digit to right of decimal place is <5- round down and add 1 dose
    - If digit to right of decimal place is ≥ 5, round up and add 1 dose
  - Example: FMH= 100 mL
    - 100/ 30= 3.33
    - 3 +1= 4, so 4 doses of 300 mcg of RhIg needed

Summary

- **Management of post-partum hemorrhage**
  - Multidisciplinary care
    - Involve TM lab early
  - Prevent/ manage complications of massive transfusion
  - Early use of adjunctive hemostatic agents
- **Rh immunoglobulin use in pregnancy**
  - When in doubt- give WinRho
  - BUT- not every positive Ab screen in pregnancy is passive anti-D