

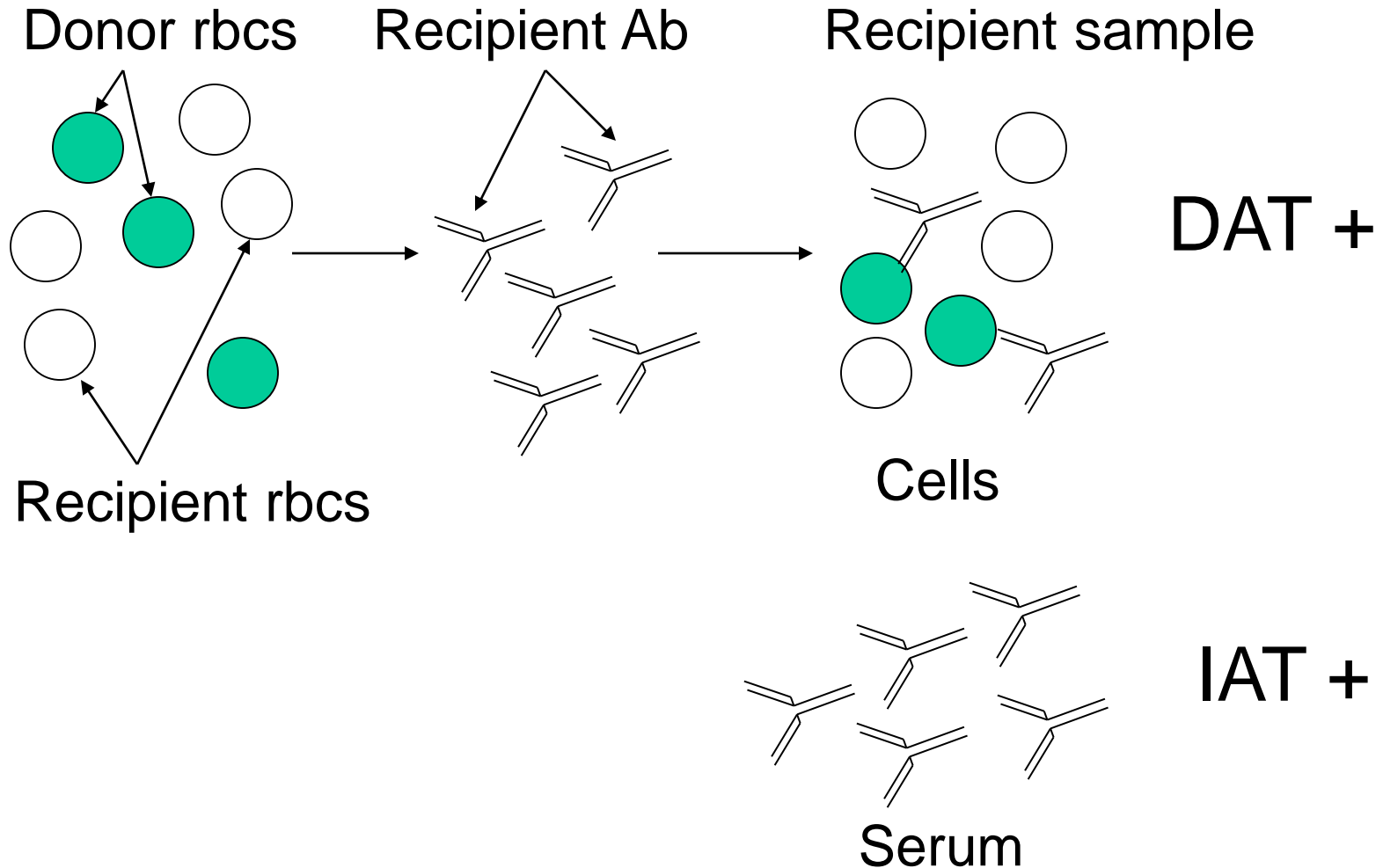
Hemolytic Transfusion Reactions (HTR) / Hemolytic Disease of the Newborn (HDN)

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Immune Response



Intravascular Hemolysis

- IgM antibodies
- Activate complement cascade
- Red cell lysis
- Hemoglobinemia
- ↓ haptoglobin
- Hemoglobinuria

Extravascular Hemolysis

- IgG antibodies
- Removed by RES
- Bilirubinemia
- ↑ urobilinogen

Transfusion Reaction

Any unfavorable response by a transfused recipient to a transfused blood product

Hemolytic

- Intravascular
- Extravascular
- Non-immune

Non-hemolytic

Intravascular HTR

- Due to
 - Antibodies that activate complement (IgM)
 - ABO, Vel, PP₁P^k, Le^a
 - Clerical errors
- Clinical symptoms
 - Immediate, severe
 - Fever, chills, hypotension, pain, shock

Intravascular HTR

- Clinical complications
 - DIC
 - Renal failure
 - May be fatal
- Serologic findings
 - Hemoglobinemia, bilirubinemia
 - ↓ serum haptoglobin
 - DAT (+ or -)

Extravascular HTR (acute)

- Due to antibodies that do not activate complement (IgG)
- Clinical symptoms
 - Similar to intravascular HTR
 - Not immediate, not as severe
- Clinical complications
 - Rarely fatal

Extravascular HTR (acute)

- Serologic findings
 - May see hemoglobinemia, hemoglobinuria
 - Bilirubinemia
 - ↑ urine urobilinogen
 - No expected ↑ in hemoglobin
 - Spherocytes, red cell fragments
 - DAT positive (mixed field)
 - Re-tested Pre-IAT is positive (if enhanced)

Extravascular HTR (delayed)

- Due to antibodies that do not activate complement (IgG)
 - Anamnestic response
- Clinical symptoms
 - Steadily decreasing hemoglobin
- Clinical complications
 - Rarely severe
 - Considered unpreventable

Extravascular HTR (delayed)

- Serologic findings
 - Post-IAT and DAT positive (mixed field)
 - Re-tested pre-IAT-negative
 - May see
 - Hemoglobinemia, hemoglobinuria
 - Bilirubinemia
 - ↑ urine urobilinogen
 - Spherocytes, red cell fragments

Extravascular HTR (delayed)

- Delayed serologic transfusion rxn (DSTR)
 - Positive DAT (post-transfusion)
 - Newly-formed alloantibody
- Delayed hemolytic transfusion rxn (DHTR)
 - Same as DSTR
 - Clinical and /or lab evidence of hemolysis
- Positive DAT (extended length of time)
- Possible autoantibody production

Non-immune HTR

- Overwarming
- Exposure to cold
- Incomplete deglycerolization
- Mixing with nonphysiological saline
- Use of small-bore needle
- Bacteria

Non-hemolytic Transfusion Reactions

- Febrile
- Allergic
- Anaphylactic
- Bacterial
- Circulatory overload

Febrile Reactions

- Due to
 - Antibodies to white blood cells / platelets
 - Cytokines
 - Pyrogenic plasma substances
- Clinical symptoms
 - Fever
- Prevention
 - Leukocyte-reduced blood products

Allergic Reactions

- Due to
 - Antibodies to plasma proteins
- Clinical symptoms
 - Hives, rash
- Treatment
 - Pre-medication (antihistamine)
 - May need washed red cell products

Anaphylactic Reaction

- Due to
 - Anti-IgA in recipient
- Clinical symptoms
 - Immediate, severe
 - Respiratory distress, hypotension, shock
- Treatment
 - Washed red cell products
 - IgA-deficient plasma products

Bacterial Contamination

- Due to
 - Bacteria in donor product
- Clinical symptoms
 - Immediate, severe fever
 - Hypotension, shock
- Treatment
 - Culture blood product
 - Culture recipient blood sample

Circulatory Overload

- Due to
 - Infusing too much volume
- Clinical symptoms
 - Difficulty in breathing, edema
 - Congestive heart failure
- Treatment
 - Divide blood products

Bedside Responsibility

- Stop infusion
- Check records
- Document clinical symptoms
- Notify physician
- Notify laboratory
- Collect blood and urine samples

Laboratory Responsibility

- Initial work-up
 - Clerical check
 - Observation of post-transfusion sample for hemolysis
 - DAT on post-transfusion sample

Laboratory Responsibility

- Extended work-up
 - DAT on pre-transfusion sample
 - ABO, D, antibody screening, crossmatch
 - Pre-, post- and donor samples
 - Serum
 - Bilirubin, haptoglobin, hemoglobin
 - Urine
 - Hemoglobin, urobilinogen, cultures

Serologically Negative HTR

- Due to
 - Undetectable levels of potent antibody
- Techniques
 - ELAT
 - Polybrene / PEG
 - Compare phenotypes of pre-, post-, donors
 - Determine possible alloantibodies
 - Calculate expected % of transfused donor cells
 - Assess disparities between expected / actual

Hemolytic Disease of the Newborn (HDN)

- Exposure of female to foreign antigen on red cells
- Female produces IgG antibody
- Female becomes pregnant
- IgG antibody crosses placenta
- IgG antibody attaches to antigen on fetal red cells
- IgG antibody destroys fetal red cells

Effects of HDN

- In utero
 - Red cell destruction
 - Severe anemia
 - Cardiac problems
- Post delivery
 - Hyperbilirubinemia
 - Kernicterus
 - Brain damage

Clinical Symptoms of HDN

- Subclinical
 - Mild
 - ABO antibodies
 - Slight anemia
 - DAT weak
 - Phototherapy
- Clinical
 - Moderate to severe
 - Other IgG antibodies
 - Moderate to severe anemia
 - DAT strong
 - Intrauterine or exchange transfusions

ABO-HDN

- Group O females
 - IgG forms of anti-A, anti-B, anti-A,B
- May be seen in first pregnancy
- Rarely severe
 - Determine father's genotype

Rh-HDN

- Female with anti-D
- Moderate to severe
- Rarely seen in first pregnancy
 - Primary immunization--at delivery
 - Secondary immunization--next pregnancy
- Severity increases with each pregnancy

Rh Immunoglobulin (RhIG)

- Manufactured IgG anti-D
- Administered to female within 72 hours of delivering D positive infant
- Mechanism
 - Binds to D positive infant red cells
 - Clears them from maternal circulation
 - Keeps female from making immune anti-D

RhIG Exception

- 1-2% of D negative pregnant females
 - Primary immunization--during pregnancy
 - Secondary immunization--at delivery
- Immune anti-D detected at delivery
- No need for RhIG
- Antenatal dose of RhIG

Other Common Causes of HDN

- Due to
 - Other Rh antibodies
 - Kell
 - Kidd
 - Duffy
- Not often
- Not as severe

Less Common Causes of HDN

- Antibody to low incidence antigen
 - Not detected in pre-natal testing
 - Deliver symptomatic infant
 - Test serum / eluate with father's red cells
- Antibody to high incidence antigen
 - May need to collect maternal blood for infant transfusion

Role of Laboratory in HDN

- Recognize females at risk
- Determine potential for antibody to cause HDN
- Monitor condition of fetus
- Provide blood products for intrauterine or exchange transfusions

Prevention of HDN

- Pre-natal testing
 - ABO
 - Group O Potential for ABO-HDN
 - D
 - D negative Potential for Rh HDN
 - Antibody screening
 - Positive Potential for HDN due to IgG antibody

Prevention of HDN

- Antenatal RhIG
- Post-partum RhIG
- Criteria for administration
 - Female is D negative and weak D negative
 - No immune anti-D in serum of female
 - Delivery of D positive or weak D positive infant

Dosage of RhIG

- Depends on fetal-maternal hemorrhage
- 20 micrograms RhIG for 1 ml red cells
- Typical dose--1 vial of 300 micrograms
- Exception
 - Larger than normal fetal-maternal hemorrhage
 - Detection--qualitative tests
 - Determination of adequate dosage--quantitative test

Large Fetal-maternal Hemorrhage

- Detection
 - Qualitative tests
 - Weak D--mixed field
 - Rosette test
 - Tagged antibodies--flow cytometry
- Determination of dosage
 - Quantitative test
 - Kleihauer-Betke test

Formula to calculate fetal bleeding:

$$\frac{\text{Fetal cells x maternal blood volume (ml)}}{\text{Total cells counted}} = \text{Fetal hemorrhage (ml)}$$

Total cells counted

1 Vial RhIG suppress 30ml of fetal whole blood

Other Uses of RhIG

- Pregnant female
 - Ectopic, miscarriage, abortion
- Transfusion of D positive product to D negative recipient
 - Red cells
 - Platelets
- Patients with ITP
 - If patient is D positive

Identification of HDN

- IgG antibody detected in antibody screening test
- Perform antibody titration
 - Baseline titer and score
 - Subsequent titer and score
 - Results not always conclusive
- Phenotype father's red cells
 - Genotype statistics

Treatment of HDN

- Determine condition of fetus
 - Amniocentesis
 - Bile pigment indicates red cell destruction
 - L / S ratio indicates lung maturity
 - Ultrasound
 - PUBS (percutaneous umbilical blood sampling)
- May need intrauterine transfusions

Treatment of HDN

- Determine condition of infant
 - Cord blood
 - ABO, D, DAT
 - Hemoglobin, bilirubin, reticulocytes, smear
- May need phototherapy
- May need transfusion
 - Exchange
 - Aliquots

Laboratory Investigation of HDN

- False negative
 - Blocked antigen sites
- False positive
 - Potentiator in antisera
 - IAT method
- Dissociate IgG before antigen typing
 - DTT, chloroquine