

Blood Bank I

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I. Get the party started!

A. Blood Bank I

- Blood Groups

B. Blood Bank II

- Blood Donation and Autologous Blood
- Pretransfusion Testing

C. Blood Bank III

- Component Therapy

D. Blood Bank IV

1. Transfusion Complications
 - * Noninfectious (Transfusion Reactions)
 - * Infectious (Transfusion-transmitted Diseases)

E. Blood Bank V (available at www.bbguy.org)

- Hematopoietic Progenitor Cell Transplantation

F. Blood Bank Practical

- Management of specific clinical situations
- Calculations, Antibody ID and no-pressure sample questions

Blood Bank I

Blood Groups

I. Basic Antigen-Antibody Testing

A. Basic Red Cell-Antibody Interactions

1. Agglutination
 - a. Clumping of red cells due to antibody coating
 - b. Main reaction we look for in Blood Banking
 - c. Two stages:
 - 1) Coating of cells (“sensitization”)
 - a) Affected by specificity of antibody, electrostatic charge of RBCs, temperature, relative amounts of antigen and antibody
 - b) Substances like Low Ionic Strength Saline (LISS) and Polyethylene glycol (PEG) aid in sensitization by helping to overcome physical barriers to let antigens and antibodies get closer to each other.
 - 2) Formation of bridges
 - a) Lattice-like structures formed by antibodies and red cells
 - b) IgG isn’t good at this; it is usually too small to bridge the gap between red cells by itself.

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- c) IgM is much better at forming bridges.
- 2. Hemolysis
 - a. Direct lysis of a red cell as a result of antibody coating is uncommon, but is just as much a “positive” as agglutination.
 - 1) Requires complement fixation
 - 2) IgM antibodies do this more than IgG.

B. Tube testing

- 1. **Immediate spin “phase”**
 - a. Serum and 2-5% RBC solution together in tube, centrifuge for 15-30 sec and examine.
 - 1) Most common: 2 drops serum, 1-2 drops RBCs.
- 2. **37 C “phase”**
 - a. Take above mixture and incubate at 37 C for specified time, centrifuge and examine.
 - 1) 10-15 minutes if LISS used to potentiate
 - 2) 15-30 minutes if albumin or PEG used
 - 3) 30-60 minutes if no potentiation used
- 3. **Indirect antiglobulin** (a.k.a., “antihuman globulin”) “phase”
 - a. Wash above mixture to remove unbound globulins.
 - b. Add antihuman globulin, centrifuge and examine.

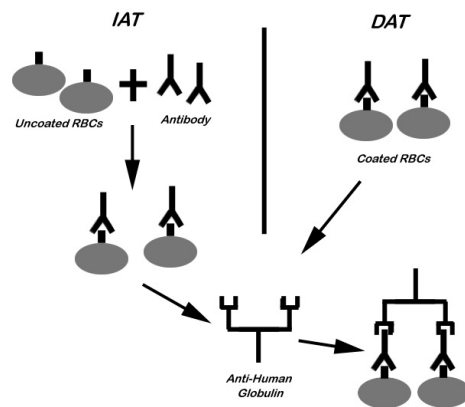
C. Alternatives to tube testing

- 1. **Column agglutination technology (Gel testing-Ortho)**
 - a. Multiple microtubes filled with gel particles and anti-IgG reagent
 - 1) Gel particles separate red cell clusters by size (ie, larger clumps of cells are stopped from migrating through gel while individual cells cruise right on through to the bottom).
 - 2) Anti-IgG grabs onto red cells coated by IgG.
 - b. Add red cells and plasma to top of tube, incubate, then centrifuge.
 - c. More coating of red cells by antibody = larger agglutinates and more attraction to antiglobulin in gel = less transport through gel
 - 1) Negative gel tests show cells in a button at the bottom of the microtube.
 - 2) Positive tests have cells spread in varying degrees through the microtube.
 - d. Can be automated (ProVue machine)
- 2. **Solid-phase Red Cell Adherence Testing (Immucor Gamma)**
 - a. Uses binding of antibody to RBCs that are themselves bound to the sides of microwells
 - b. Manufacturer binds RBCs carrying antigens we are interested in to small wells.
 - c. Lab adds patient serum, incubates, washes: antibody binds to test RBCs.

- d. Indicator RBCs (coated with monoclonal anti-IgG) attach to test RBCs via bound antibody.
- e. Centrifuge and interpret
 - 1) Negative solid phase tests have cells in a button at the bottom of the microplate, because the indicator cells don't bind to the test RBCs on the microplate wall.
 - 2) Positive solid phase tests have cells spread in a "carpet" all along the microplate wall, because the indicator cells have bound to test RBCs all along the wall.
- f. Can be automated (Galileo and Galileo Echo machines)

D. The Antiglobulin Test ("Coomb's Test")

1. Indirect: described above; checks for *in-vitro* coating of RBCs with antibody or complement.
2. Direct: red cells taken directly from patient, washed, then mixed with antihuman globulin; checks for *in-vivo* coating of RBCs with antibody and/or complement.



3. IAT variations
 - a. Can be used to check for an unknown antibody by using red cells with a known antigen profile, as in an antibody screen
 - b. Can be used to check for an unknown red cell antigen by using serum with known antibody specificity, as in RBC antigen testing
 - c. Can be used to check for a reacting unknown antigen *and* unknown antibody, as in the crossmatch procedure
4. Specificity possibilities for the antiglobulin
 - a. Anti-IgG, -C3d ("polyspecific")
 - 1) Will detect red cells coated with either of the above and may also detect other immunoglobulins (because the anti-IgG is not specific)
 - b. Anti-IgG and anti-IgG (heavy chains)
 - 1) Both detect IgG-coated red cells; anti-IgG may also detect light chains associated with other antibody classes (IgA, IgM).

- c. Anti-C3b, -C3d
 - 1) Detects either of the above complement components
 - 2) Useful in evaluating IgM-related hemolysis, cold agglutinin disease and certain warm autoimmune hemolysis without IgG
- 5. IgG-coated red cells (“Coomb’s control”)
 - a. Used after *negative* DAT or IAT to ensure proper functioning of antiglobulin reagent
 - b. IgG-coated RBCs added to AHG-cell mixture
 - c. Negative = bad AHG or no AHG added
 - d. Other errors in the process (leaving out the test serum, bad processing technique, etc) would not be detected by Coomb’s Control test.

E. Dosage

- 1. Certain antibodies do not react as strongly with RBCs that have antigens coded for by a single gene.
- 2. For example, imagine a hypothetical anti-Z
 - a. Patient 1 genotype: ZZ (Homozygous for Z)
 - b. Patient 2 genotype: ZY (Heterozygous for Z)
 - c. If anti-Z shows dosage, it will react stronger with patient 1’s RBCs (see below).

RBC Genotype	Reaction with anti-Z
ZZ	3+
ZY	1+

- 3. Most common in Kidd, Duffy, Rh and MNSs blood groups

F. Neutralization

- 1. A particular substance, when mixed with an antibody, eliminates the activity of that antibody against test red cells.
- 2. Some of these are pretty weird! (See table below)

Neutralization of Antibodies	
ABO	Saliva (secretor)
Lewis	Saliva (secretor for Le ^b)
P ₁	Hydatid cyst fluid Pigeon egg fluid
Sd ^a	Urine
Chido, Rodgers	Serum

II. Blood Groups

A. General characteristics

- 1. Guidelines
 - a. “Clinically significant” = blood group antibody which causes HTRs or HDN

- b. Most significant antibodies are “warm reactive”; meaning they react best at 37 C or IAT.
- c. Most insignificant antibodies are “cold reactive”; meaning they react best below 37 C.
- d. Warm antibodies are most often IgG, while colds are usually IgM.
- e. IgM antibodies are usually “naturally occurring”, meaning no transfusion or pregnancy is required for their formation.

“WARM-REACTIVE” ANTIBODIES	“COLD-REACTIVE” ANTIBODIES
IgG	IgM
Require exposure	Naturally occurring
Cause HDN	No HDN*
Cause HTRs	No HTRs*
“Significant”	“Insignificant”*

- f. *Note that the ABO blood group is the exception in the table above.

2. The “Enzyme Classification”

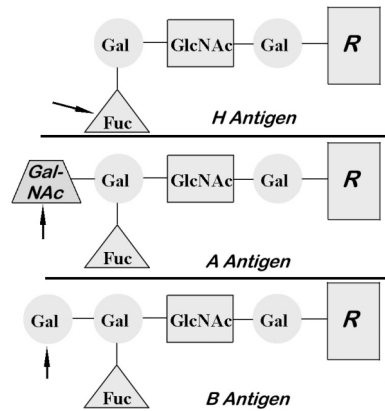
Enzyme-enhanced	Enzyme-decreased	Enzyme-unaffected
ABO Family ABO Blood Group Lewis Blood Group I/i Blood Group P Blood Group Rh Blood Group Kidd Blood Group	MNSs Blood Group Duffy Blood Group	Kell Blood Group

B. ABO Blood Group

- 1. Basic biochemistry (see figure below)
 - a. Type I and II chains
 - 1) Type I: Think of them as primarily glycoproteins in secretions and plasma carrying free-floating antigens
 - 2) Type II: Think of them as primarily glycosphingolipids carrying bound antigens on RBCs.
 - b. *Se* gene (FUT2)
 - 1) “Secretor” gene on chromosome 19
 - a) A secretor is a person able to make A or B antigens in their secretions (saliva, etc).
 - 2) Codes for a fucosyltransferase (FUT) enzyme that adds fucose to *type I* chains at terminal galactose; **product is type I H antigen**
 - 3) 80% gene frequency
 - c. *H* gene (FUT1)
 - 1) Closely linked to *Se* on chromosome 19

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- 2) FUT enzyme adds fucose to terminal galactose of *type II* chains; **product is type II H antigen.**
- 3) Virtually 100% gene frequency (lack of *H* = “Bombay phenotype” (more to follow).
- d. H antigen is required before A and/or B antigens can be made either on red cells (type II H) or in secretions (type I H).
 - 1) A single sugar is added to a type I or II H antigen chain to make A or B antigens; when this happens, the chain no longer has H activity.
 - a) Group A sugar: **N-acetylgalactosamine**
 - b) Group B sugar: **Galactose**



- 2) Relationship is reciprocal; the more A or B is made, the less H remains.
 - a) Relative amounts of H by blood group
 - $O > A_2 > B > A_2B > A_1 > A_1B$
- 2. ABO antigens and antibodies
 - a. Antigens based on combinations of three genes on chromosome 9: **A, B and O.**
 - b. Antibodies are clinically significant and “naturally occurring.”
 - c. ABO antigens begin to appear on fetal RBCs in utero (6 weeks gestation); reach adult levels by age 4.
 - d. ABO antibodies do not begin to appear until after 4 months of age; reach adult levels by about 10 years
 - 1) Conflicting reports about falling titers in elderly patients; most believe there is a decline with advanced age.
 - e. **Group O**
 - 1) Generally the most common blood group
 - 2) Genotype: *OO*
 - 3) Antigen: H
 - a) O gene is nonfunctional; no sugars transferred
 - b) Lectin of *Ulex europaeus* agglutinates cells with abundant H antigen.
 - c) Note lectin chart for various specificities

Lectin	Specificity
<i>Dolichos biflorus</i>	A ₁ , Sd ^a
<i>Ulex europaeus</i>	H
<i>Vicia graminea</i>	N

- 4) Antibodies: anti-A, anti-B and anti-A,B
 - a) Anti-A and anti-B antibodies in group A and B patients are characteristically IgM, and react strongly at body temperatures.
 - b) Those antibodies in group O people have a strong **IgG component**, so they may cross the placenta to cause mild HDFN (most common HDFN).
 - c) Anti-A,B is also IgG, and reacts against both A and B cells (reactivity can't be separated into individual specificities).
 - f. **Group A**
 - 1) Genotypes: AA, AO
 - 2) Antigens: A, H
 - 3) Antibodies: anti-B (primarily IgM).
 - 4) A subgroups
 - a) A₁ (80%) and A₂ (~20%) most important
 - b) A₁ red cells have about 4 times more A antigen on RBC surfaces than A₂ cells (quantitative difference).
 - c) Qualitative differences also exist in the forms of the antigenic chains.
 - d) Small % of A₂'s (1-8% of A₂ and 25% of A₂B) form anti-A₁.
 - Anti-A₁ is usually a clinically insignificant IgM but it can cause discrepancies in ABO testing.
 - If reactive at 37C, patients should not receive A₁ red blood cells.
 - e) Lectin of *Dolichos biflorus* agglutinates A₁ RBCs, to differentiate A₁ from A₂.
 - g. **Group B**
 - 1) Genotypes: BB, BO
 - 2) Antigens: B, H
 - 3) Antibodies: Anti-A (primarily IgM).
 - 4) B subgroups: usually unimportant and less frequent
 - h. **Group AB**
 - 1) Least frequent ABO blood type (about 4%)
 - 2) Antigens: A and B (very little H)
 - a) Can be further subdivided into A₁B or A₂B depending on the status of the A antigen
 - 3) Antibodies: none
3. ABO testing
 - a. Cell typing ("forward grouping")

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- 1) Patient red cells agglutinated by known sera (anti-A, anti-B).
- b. Serum typing (“reverse grouping”, “back typing”)
 - 1) Patient serum (or plasma) against A₁ and B RBCs.

Red Cell		Serum		ABO Group
Anti-A	Anti-B	A ₁ cells	B cells	
4+	0	0	4+	A
0	4+	4+	0	B
4+	4+	0	0	AB
0	0	4+	4+	O

- c. Note the opposite reactions!
 - 1) If forward reactions are not opposite of reverse, an ABO discrepancy is present.
 - d. Both serum and cell typing are required unless testing babies < 4 months of age or reconfirming ABO testing done on donor blood (requires cell typing only).
4. ABO discrepancies
- a. Disagreement between the interpretations of forward and reverse grouping (eg, forward grouping looks like group A, reverse like group O); caused by either antigen or antibody problems or technical errors.
 - b. Antigen problems
 - 1) Lack of expected antigens
 - a) A or B subgroups
 - b) Transfusion or transplantation
 - c) Leukemia or other malignancies
 - 2) Unexpected antigens
 - a) Transfusion/transplantation out-of-group
 - b) **Acquired B phenotype** (more below)
 - c) **Recent marrow/stem cell transplant.**
 - d) Autoagglutination
 - c. Antibody problems
 - 1) Lack of expected antibodies
 - a) Immunodeficiency
 - b) Neonates, elderly, or immunocompromised
 - c) Transplantation or transfusion
 - d) ABO subgroups
 - 2) Unexpected antibodies
 - a) Cold auto- or alloantibodies
 - b) **Anti-A₁**
 - c) Rouleaux (false positive)
 - d) Transfusion or transplantation
 - e) Reagent antibodies

- d. Technical errors
 - 1) Errors in preparation of samples, sample mix-ups, or interpretation errors
- 5. Weird stuff about ABO
 - a. **Acquired B phenotype**
 - 1) Seen in contact with enteric gram negatives: Colon cancer, intestinal obstruction, gram-negative sepsis
 - 2) AB forward (with weak reactions with reagent anti-B), A reverse

Forward Grouping			Reverse Grouping		
Anti-A	Anti-B	Interp	A ₁ cells	B cells	Interp
4+	1-2+	AB	0	4+	A

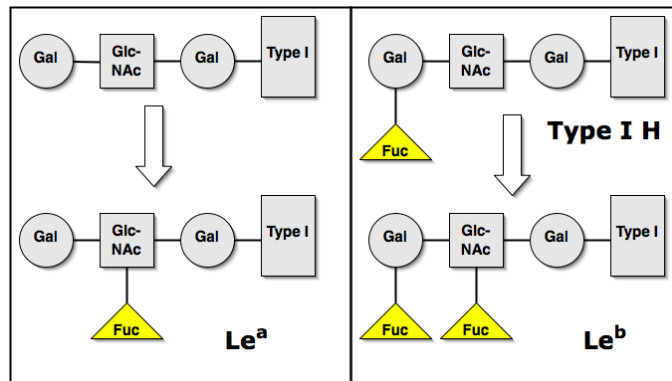
- 3) Bacteria deacetylate group A sugar (GalNAc); remaining galactosamine cross-reacts with **reagent** anti-B.
 - 4) Acidify serum (no reaction with anti-B), add acetic anhydride (re-acetylates), autoincubation (no reaction), BS-1 lectin (no reaction).
 - b. **B(A) phenotype**
 - 1) Similar to acquired B, but with group B (ie, they are really group B but forward test like an AB, with a weak reaction with anti-A).
 - 2) Problem is a cross-reaction with a particular form of monoclonal anti-A; testing using a different anti-A it shows the patient truly to be group B.
 - c. **Bombay (O_h) phenotype**
 - 1) Total lack of H, A and B antigens due to lack of *H* and *Se* genes (genotype: *hh, sese*)
 - 2) Naturally occurring strong anti-H, anti-A, anti-B
 - 3) Testing: O forward, O reverse, but antibody screen wildly positive and all units incompatible
 - 4) Require other Bombay donors
 - 5) Para-Bombay phenotype
 - a) Similar, but these patients have *Se* to partially compensate for their lack of *H*.
 - b) Phenotypes: A_h, B_h, AB_h
 - c) Red cells may type like Bombays, but serum/secretion testing shows free H and A or B antigen (unless group O).
 - d) These patients have anti-H in serum.
- 6. Consequences of ABO incompatibility
 - a. Severe acute hemolytic transfusion reactions
 - 1) Among most common blood bank fatalities
 - 2) Clerical errors
 - b. Most frequent HDFN; usually mild, however

C. Lewis blood group

- 1. Biochemistry (see figure below)

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- a. Type I chains only
- b. One gene: *Le* (FUT3)
- c. FUT enzyme adds fucose to **subterminal GlcNAc** (left side of figure below).
 - 1) This makes **Le^a** (Lewis A) antigen.
 - 2) In a non-secretor, Le^a is the only Lewis antigen possible.
 - 3) Le^a antigens **cannot** be further modified to make Le^b (in contrast to previous thought).
- d. In secretors, *Se* product adds fucose, then *Le* product adds fucose; this makes **Le^b** (Lewis B).
 - 1) In secretors, this interaction shown on the right of the figure below, occurs preferentially over Le^a formation.
 - 2) As a result, the vast majority the chains of secretors who carry *Le* are Le^b rather than Le^a.



- e. Unlike ABO, antigens are not tightly bound (remember, they are made from *type I chains*); rather, they **adsorb** onto the surface of RBCs.
 - 1) Le^b does this better than Le^a, so this is another reason that most adults with both *Le* and *Se* will be Le(a-b+).
 - 2) Le(a-b+) people still have Le^a, just in much smaller quantities that may not show up on RBCs.
 - f. Same chain can carry Le and ABO antigens (unlike the inverse relationship with ABO and H).
2. Lewis phenotypes, antigens, and antibodies
 - a. Phenotypes: Le(a+b-), Le(a-b+), Le(a-b-)
 - b. Le^a, Le^b
 - c. Le^b is seen more frequently.
 - d. **22% of blacks are Le(a-b-), vs. only 6% of whites.**
 - e. Antibodies are naturally occurring.
 - 1) Primarily in Le(a-b-)
 - 2) Cold reacting IgM
 - 3) Neutralize with saliva.
 3. Consequences of incompatibility
 - a. Rare HTRs (more commonly anti-Le^a)

- b. No HDFN (antibody doesn't cross placenta and Le antigens are not present on fetal RBCs).
- 4. Weird stuff about Lewis
 - a. Lewis antigens decrease during pregnancy.
 - 1) Pregnant patients may appear Le(a-b-) and have transient, insignificant Lewis antibodies.
 - 2) Thought to be due to increased plasma volume diluting the antigen
 - b. Le(a-b+) people don't make anti-Le^a.
 - 1) As above, these people still have Le^a, just not visibly on their red cells.
 - c. Children's Lewis type may vary, as antigen chains are converted [they may have more Le^a than Le^b, and have a transient period of Le(a+b+)].
 - d. Helicobacter pylori may attach via Le^b antigen.
 - e. Le(a-b-) in children increases risk of urinary tract infections.

D. I/i Blood Group

- 1. Antigens built on chains related to ABO.
- 2. Expression is age-dependent.
 - a. Simple chains found on neonates make i antigen.
 - b. More branched chains in adults make I antigen.
 - c. "Big I in big people, little i in little people"
- 3. Antibodies
 - a. Cold reacting IgM
 - b. Naturally occurring
 - c. Autoantibodies very common
- 4. Classic associations
 - a. Auto-anti-I
 - 1) Cold agglutinin disease
 - 2) *Mycoplasma pneumoniae* infection
 - b. Auto-anti-i
 - 1) Associated with **infectious mononucleosis**
 - 2) Less often a problem than auto-anti-I

E. P Blood Group (the cool one)

- 1. Also built on ABO-related chains
- 2. P1 only P group antigen
 - a. P, P^k not officially in P system anymore
 - 1) Still, combination of these three antigens defines the P phenotype.
 - 2) Most common P phenotype is P₁ (positive for P1 and P and negative for P^k).
 - b. Very rare people lack all three and make anti-PP1P^k.
 - 1) Associated with acute HTRs, HDFN and early, spontaneous abortions
 - c. P antigen is **parvovirus B19** receptor.
 - d. P^k antigen is receptor for various bacteria and toxins
- 3. Antibodies (anti-P1)
 - a. Cold reacting, naturally occurring, insignificant IgM

- b. Titers elevated in those with hydatid cyst disease (*Echinococcus*) and bird handlers
 - 1) Bird feces has P1-like substance.
- c. Neutralized by hydatid cyst fluid and pigeon egg fluid (Really! I'm not kidding!)
- 4. Association with paroxysmal cold hemoglobinuria
 - a. Biphasic IgG with anti-P specificity
 - 1) Binds in cold temps, hemolyzes when warmed
 - 2) "Donath-Landsteiner biphasic hemolysin"
 - b. Classically associated with syphilis, now with viral infections in children

F. Rh Blood Group

- 1. Second most important blood group (after ABO)
- 2. Terminology systems
 - a. **Fisher-Race (DCE or CDE)**
 - 1) Five major antigens: D, C, E, c, e
 - a) "Rh positive" really means "D positive."
 - b) Absence of D designated "d" (later found not to be a real antigen)
 - 2) Eight potential combinations ("haplotypes") named based on presence of genes for above antigens (ie, "DCe", "dce", etc.)
 - b. **Wiener (Rh-Hr)**
 - 1) Used different names for the five main antigens; these are not used very often by non-geeky people.
 - 2) Believed that main Rh genes (for presence or absence of D, for C or c and for E or e) were inherited as one genetically linked group, or "haplotype."
 - 3) Gave shorthand names to the eight potential combinations alluded to above; this nomenclature is still in use and is essential to know (even though his theory of how these are inherited has been disproven).

Wiener's "Haplotypes" (with DCE Equivalents)
R₁: DCe r' : dCe
R₂: DcE r'' : dcE
R₀: Dce r : dce
R_z: DCE r^y : dCE

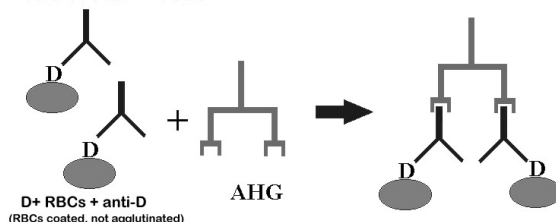
- a) Rules for converting Wiener's shorthand into Fisher-Race terminology:
 - "R" = D, "r" = d
 - "1" or "prime" = C
 - "2" or "double prime" = E
 - "0" or "blank" = ce
 - Any superscript letter = CE

- c. "The Big Four"
- 1) Fortunately, only four of the above combinations occur frequently enough to memorize their relative order: **R₁, R₂, R₀ and r**. (~97% of blacks and whites use only these four).
 - a) How to remember?
 - R₀ is most common in blacks, least common in whites.
 - r is always second in frequency.
 - R₁ always comes before R₂.

"The Big Four"
Whites: R₁ > r > R₂ > R₀
Blacks: R₀ > r > R₁ > R₂

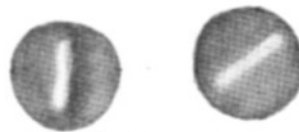
- 2) FYI, Asians have much less r; the order in that group is R₁ > R₂ > r and R₀.
- d. The real story of Rh inheritance
 - 1) Two main genes: *RHD* and *RHCE*, on chromosome 1 code for main Rh antigens
 - 2) D type determined by presence/absence of *RHD*
 - 3) CE combination by which variants of *RHCE* are present (four combinations: CE, Ce, cE, ce)
3. Rh antibodies
 - a. Exposure required
 - b. Warm-reacting IgG
4. Consequences of Rh incompatibility
 - a. Very immunogenic blood group, with D inducing the most antibodies, then c and E
 - b. Up to 80% (reported as wide range of 30-85%) of D-negative patients make anti-D with a one unit D-pos RBC transfusion.
 - c. Exposed: HTRs with extravascular hemolysis
 - d. Most severe and prototypical HDN
5. Weird stuff about Rh
 - a. **Weak D phenotype (formerly known as D^u)**
 - 1) D testing is typically done with monoclonal antibodies today and most truly D+ people test that way.
 - 2) Some D+ individuals, however, require an Indirect Antiglobulin Test (IAT) to detect D antigen.

The Weak D Test



- 3) Possible reasons for weak D

- a) C on opposite chromosome to D (“C in trans”)
 - b) Weak form of *RHD* gene
 - c) Mosaic forms of D antigen (“partial D”, “D mosaic”) lack portions of D antigen.
 - Probably better considered separately from first two.
 - Patients with partial D may develop antibodies against portions of the antigen they lack; this may lead to what looks like an anti-D in a D-positive person.
 - 4) Testing requirements
 - a) Weak D test for all D negative blood donors
 - b) Not required for D negative blood recipients
 - This was previously a concern, for fear of wasting d-negative units on D+ patients
 - Monoclonal antibodies mentioned above make this very unlikely
 - In transfusion services, the only patients who definitely need weak D testing are apparently d-negative babies with d-negative moms.
- b. **Rh_{null} phenotype**
- 1) No Rh antigens whatsoever
 - 2) Hemolytic anemia with stomatocytes



The lovely stomatocyte

- 3) Also associated with altered activity of S, s and U antigens (See MNSs system later)
- c. **Warm autoimmune hemolytic anemia**
 - 1) Antibody seems to have relative specificity to basic Rh structural antigens.
- d. **Compound Rh antigens**
 - 1) **G** = antigen present when either C or D are present.
 - 2) **f** = antigen present when c and e are on the same chromosome (as in r and R⁰).

G. Kidd Blood Group

- 1. Kidd antigens
 - a. Jk^a, Jk^b
 - b. Jk^a slightly more common
- 2. Kidd antibodies
 - a. Exposure required
 - b. Warm reacting IgG
 - 1) Unusually good at fixing complement, in contrast to most IgG antibodies
 - c. **Marked dosage effect**

- 1) A Kidd antibody may not react at all against cells with heterozygous expression of Kidd antigens, but may react very strongly against a homozygous cell.
- d. **Variable antibody expression**
 - 1) Antibody often disappears with time/storage.
- 3. Weird stuff about Kidd
 - a. **Delayed HTRs**
 - 1) Kidd's most famous association
 - 2) Anamnestic response
 - 3) Intravascular and often severe
 - b. **Mild HDFN at worst**
 - 1) Child can only be one antigen different from mom; remember dosage discussion above.

H. MNSs Blood Group

- 1. Basic biochemistry
 - a. Glycophorin A carries M and N antigens.
 - b. Glycophorin B carries S, s and U antigens.
- 2. MNSs antigens
 - a. M frequency roughly equals N
 - b. $s > S$
 - c. If S-s- (as seen in 2% of African-Americans), may also be U negative (U is extremely high frequency).
- 3. MNSs antibodies
 - a. M and N antibodies are mostly opposite of S, s and U antibodies (see below)

Anti-M & anti-N	Anti-S, -s and -U
Naturally occurring	Require exposure
Cold IgM	Warm IgG
Dosage	Minimal dosage
Insignificant	Significant

- b. Enzymes destroy M, N and S antigens, but do not greatly affect s antigens.
 - c. Anti-M is generally insignificant, but has been associated uncommonly with HDFN.
- 4. Weird stuff about MNSs
 - a. **N-like antigen ('N')**
 - 1) Glycophorin B has a terminal 5 AA sequence that matches glycophorin A's last 5 when coding for actual N antigen; this is known as 'N'.
 - a) This is not really true N antigen, but it is close enough that it prevents most M+N- people from making anti-N.
 - 2) Everyone except those who lack glycophorin B (S-s-U-) have 'N'.

- a) For this reason, the majority of people who make clinically significant anti-N are African-Americans (<1% lack S, s and U).
- b. **Anti-N induced by hemodialysis**
 - 1) Formaldehyde sterilization of machine
 - 2) Modification of N antigen
- c. Another lectin!
 - 1) *Vicia graminea* lectin used commonly as an N-typing reagent

I. Duffy Blood Group

- 1. Duffy antigens
 - a. $Fy^b > Fy^a$
 - b. **Fy(a-b-) is the most common Duffy phenotype in blacks (68%).**
 - c. Fy^a is much more common in Asians than in Caucasians.
- 2. Duffy antibodies
 - a. Anti- Fy^a much more common and significant than anti- Fy^b
 - b. Require exposure
 - c. Warm-reacting IgG
 - d. Marked dosage
 - e. May have variable expression like Kidd antibodies
- 3. Consequences of incompatibility
 - a. Severe HTRs, usually delayed and extravascular
 - b. Generally mild HDFN (for same reason as Kidd above)
- 4. Weird stuff about Duffy
 - a. **Fy(a-b-) and malarial resistance**
 - 1) Fy(a-b-) humans are resistant to *Plasmodium vivax* and *P. knowlesi* infection.

J. Kell Blood Group

- 1. Extremely important group clinically and serologically
- 2. Kell antigens
 - a. Low frequency: **K, also known as “K1” (9% whites, 2% blacks)**, Js^a , Kp^a
 - b. High frequency: **k, also known as “K2” (99.8%)**, Js^b , Kp^b
 - c. Kx: important antigen that may help stabilize RBC membrane (more later); is closely associated with K antigens on the red cell membrane.
 - 1) Kx has a strange relationship to Kell antigens.
 - 2) When Kell antigens decrease in number, Kx increases (as in “Kell null” phenotype, aka K_0); thought to be due to decrease in masking Kell antigens.
 - a) This led to Kx originally postulated as a precursor; not true.

- 3) When Kx decreases (as in “McLeod phenotype”, see later), Kell antigens decrease, too.
 - a) Kx may be required for proper Kell antigen expression.
- d. Kell system antigens destroyed by thiol reagents (2-ME, DTT, ZZAP) but not by enzymes alone.
3. Kell antibodies
 - a. Anti-K
 - 1) Very common (most common non-ABO antibody after anti-D)
 - 2) Warm reacting IgG
 - b. Anti-k
 - 1) Very uncommon due to high antigen frequency
 - 2) Analogous to anti-K
4. Consequences of incompatibility
 - a. Severe HTRs
 - 1) May be acute or delayed; usually extravascular.
 - b. Severe HDN
5. Weird stuff about Kell
 - a. **Kell null phenotype (“K₀”)**
 - 1) Absence of all Kell antigens
 - 2) Kx increased
 - 3) Significant anti-Ku (“universal”) with exposure
 - b. **McLeod phenotype**
 - 1) Absence of Kx
 - 2) Markedly decreased (not absent) Kell system Ags
 - 3) No anti-Ku!



Acanthocyte

- 4) Hemolytic anemia with **acanthocytes**
- 5) Occasional association with **X-linked chronic granulomatous disease**
 - a) NADPH oxidase deficit
 - b) Organisms phagocytized but not killed
 - c) Catalase-positive organisms (*Staph*)
- 6) Also associated with cardiac and nervous system abnormalities

K. A few other antigens (in brief)

1. Lutheran
 - a. Lu^a and Lu^b antigens
 - b. Linked to *Se* on chromosome 19
 - c. Antibodies uncommon and not usually significant
 - d. Enzymes decrease Lu antigen activity.
2. Xg
 - a. Gene carried on X chromosome (“X-linked”)

Pathology Review Course

- 1) Seen in approximately 2/3 of males and 90% of females
- b. Antibody insignificant
3. Diego system
 - a. Two pairs of antigens, Di^a/Di^b , Wr^a/Wr^b (“Wright A” and “Wright B”)
 - b. Anti- Di^a may be significant, but is uncommon.
 - c. Anti- Wr^a is common but is not usually significant.
4. Sd^a (“Sid”)
 - a. High frequency
 - b. Refractile immune complexes
 - c. Lectin of *Dolichos biflorus* agglutinates Sid positive RBCs (like A^1)
 - d. Neutralize with urine of the guinea pig!
5. HTLA (“high titer, low avidity”)
 - a. High frequency
 - b. **Chido, Rodgers** most frequent
 - 1) Complement components (C4)
 - c. Clinically insignificant (no HTRs or HDN)
 - d. Neutralize with serum.