

## IX. Other Blood Group Systems

### A. Introduction

1. In addition to antigens previously discussed, over 500 others can be detected on human rbc's.
2. Antigens that are carried by a particular cell line of almost all persons are known as **high-incidence** or **public antigens**.
3. Antigens carried by few individuals are called **low-incidence** or **private antigens**.
4. Each of the known antigens described in this lecture were initially identified through detection of its specific antibody in a serum.
5. Knowledge of the serologic behavior and characteristics of the major blood group antibodies is critical for identification.
  - a. Characteristics of the **antibodies** to blood group antigens is very important when evaluating panel workups in the identification of irregular antibodies.
  - b. Consideration should be given to *phase of reactivity, antibody class involved, and its ability to cause HDN and/or hemolytic transfusion reactions*.

### B. I/i

1. The I blood group system is related to the ABO and the Lewis systems by its biochemical structure.
2. Antigenic development
  - a. Fetal RBCs are rich in **i** antigen, and lack **I** antigen.
  - b. During the first 2 years of life, the **I** antigen gradually develops, and there is a concomitant loss of **i**.
  - c. Thus the RBCs of most adults react strongly with anti-I while cord cells (baby cells) are non-reactive with anti-I.
  - d. In rare instances, the I antigen never develops. These individuals, known as i adults, retain the I=i+ phenotype throughout their lives.
3. Antibodies to I/i
  - a. The **unexpected antibodies most frequently encountered** when serologic test are performed at RT are those directed against the I and i antigens.
  - b. Anti-I is a common cause of non-specific agglutination encountered at RT when performing antibody screens, crossmatches and may even cause ABO discrepancies by agglutinating the reverse cells.
  - c. Anti-I can be detected in the serum of most normal adults if the serum is tested at 4 C.
  - d. Anti-I is also associated with **atypical pneumonia** caused by *Mycoplasma pneumoniae*. Cold agglutinin titers are used to monitor their progress and aid in diagnosis.

- e. Anti-i is classically associated with certain viral disorders, such as **infectious mononucleosis**, caused by the Epstein-Barr virus, and cytomegalovirus (CMV).

#### 4. Clinical Significance

- a. Anti-I is usually seen as a benign, naturally occurring cold-reactive autoantibody.
- b. Clinically significant examples of anti-I are very rare and occur in Cold Agglutinin Syndrome
  - 1) Antibodies are of high titer (greater than 1000).
  - 2) Have high thermal amplitude.
  - 3) Cause hemolytic anemia.
  - 4) Patient's blood must be given through a blood warmer.
- c. The antibody class involved is IgM, so anti-I does not cause HDN.
- d. Anti-I does not cause HTRs, but can cause severe autoimmune hemolytic anemia.

#### 5. Serological Testing to Confirm

- a. Test the patient's serum against three group O adult cells (which are I positive), three group O cord cells (which are i positive), and an autocontrol.
- b. Agglutination of the I positive adult cells and the autocontrol along with negative or very weak reactions with the cord cells proves the presence of anti-I.
- c. Additional confirmation is obtained by negative reactions when the prewarmed technique is used in the antibody screen. Anti-I will be undetectable when the test is performed strictly at 37 C.
- d. In unusual cases the anti-I may be so strong that reactivity will be obtained at AHG. Autoabsorption or absorption using rabbit erythrocyte stroma (REST) may have to be done.

### C. The Lewis System

- 1. First identified in 1946, when Mourant discovered an antibody that he named anti-Le<sup>a</sup>, that he named after the maker, Mrs. Lewis. Anti-Le<sup>b</sup> was discovered in 1948.
- 2. Le<sup>a</sup> and Le<sup>b</sup> are the major antigens of the Lewis system; other antigens in the system include Le<sup>c</sup>, Le<sup>d</sup>, and Le<sup>x</sup>.
- 3. Antigenic development
  - a. Lewis antigens **are not** intrinsic to RBCs, but are carried on plasma glycosphingolipids that are **adsorbed** from the plasma and inserted into the RBC membrane.
  - b. The genetic control of the two antigens appear to reside in a single gene, called Le. Individuals who inherit at least one Le gene will have Lewis antigens, individuals who are le/le (amorph) will not have Lewis antigens.
  - c. The Le gene causes production of a transferase which causes attachment of L-fucose to the subterminal chain of precursor chain to form the Le<sup>a</sup> antigen.

- d. This can then be modified by the Lewis active enzyme to form Le<sup>b</sup> antigen.
- 1) When Le<sup>b</sup> is produced, it is adsorbed preferentially over Le<sup>a</sup> to RBC membranes.
  - 2) Because Le<sup>b</sup> antigen is produced in much greater quantities than Le<sup>a</sup> antigens only Le<sup>b</sup> can be routinely demonstrated.
- e. *The Lewis phenotype of RBCs depends on the phenotype of the plasma in which they are suspended and **can be changed** by incubating the cells in plasma containing different Lewis-active glycolipids.*
- 1) If Le(a-b-) RBCs are incubated with plasma containing Le<sup>a</sup> or Le<sup>b</sup> glycolipid, they *will take up the antigen from the plasma*. They will subsequently type as positive for the Le antigen they were incubated in.
  - 2) If Le positive cells are incubated in plasma from an lele person, the cells *will lose their Lewis antigens* and type as Le(a-b-).
- f. **Lewis phenotypes and their frequencies**

	<u>Whites</u>	<u>Blacks</u>
Le(a+b-)	22%	23%
Le(a-b+)	72%	55%
Le(a-b-)	6%	22%
Le(a+b+)	rare	rare

4. Le antigens are **absent or extremely weak at birth**.
- a. Cord blood specimens are essentially Le(a-b-).
  - b. Expression of the Le<sup>b</sup> antigen develops gradually, and the infant who is genetically Le(a-b+) may type as Le(a+b+) during the transition period.
  - c. Thus, the newborn who appears to be Le(a-b-) at birth can type as Le(a+b-) at two months of age, Le(a+b+) by 12 to 18 months and Le(a-b+) by 2 or 3 years of age.
  - d. Lewis typing cannot be done on babies for paternity testing.
5. Lewis antigens during pregnancy.
- a. Lewis antigen strength may decline dramatically during pregnancy.
  - b. The transiently Le(a-b-) pregnant woman may produce Lewis antibodies during pregnancy
  - c. These antibodies disappear after delivery as the normal Lewis phenotype is restored.
6. Interactions of Le, Se and H genes.
- a. Interactions of 3 genetic loci influence the production of the Le<sup>a</sup> and Le<sup>b</sup> antigens.
  - b. People who type as lele do not produce Le<sup>a</sup> or Le<sup>b</sup> antigens, type as Le(a-b-) and do not have Lewis antigens in their plasma or secretions. But if the Se gene is present they will have the appropriate A, B and H substances in their secretions.

- c. Nonsecretors (genotype sese) who have at least one Le gene will produce only the Le(a) antigen, their RBCs will type as Le(a+b-) and their plasma and secretions will contain the Le(a) antigen.
- d. Expression of the Le(a-b+) phenotype depends on the presence of at least one Le gene, one Se gene, and one H gene. These individuals will have both Le<sup>a</sup> and Le<sup>b</sup> antigens in their secretions as well as the appropriate A, B, and H substances in their secretions.

### Lewis Phenotypes and ABH Secretions

RBC Lewis Phenotype	ABH Secretor Status	Lewis Secretor Status
Le(a+b-)	All ABH non-secretors	All secretors of Le <sup>a</sup>
Le(a-b+)	All ABH secretors	All secretors of Le <sup>a</sup> and Le <sup>b</sup>
Le(a-b-)	80% ABH secretors 20% ABH non-secretors	None

#### 7. Lewis antibodies

- a. They are almost always **IgM** and may react strongly at RT, even causing ABO discrepancies if the reverse cells are positive for the appropriate Lewis antigen.
- b. Lewis antibodies occur almost exclusively in the sera of Le(a-b-) persons, and usually without known RBC stimulus (**naturally occurring**).
- c. Persons whose RBC phenotype is Le(a-b+) do not make anti-Le<sup>a</sup> because small amounts of unconverted Le<sup>a</sup> are present in their saliva and plasma.
- d. Anti-Le<sup>a</sup> is a very commonly encountered antibody but it is unusual to find anti-Le<sup>b</sup>.
- e. It is not unusual to find anti-Le<sup>a</sup> and -Le<sup>b</sup> together in the sera of Le(a-b-) individuals.
- f. Most examples of these antibodies **react best at room temperature**, but reactivity may be seen at 37 C but is much weaker than that seen at RT. They also may be detected weakly at the AHG phase if polyspecific coombs is used as the AHG reagent.
- g. The antibody **can bind complement and cause in-vitro hemolysis**. Hemolysis is more often seen with enzyme treated cells.
- h. Because Lewis antibodies do not cross the placenta and the antigens are poorly developed at birth, the antibodies **have not been implicated in HDN**.
- i. Lewis antibodies can be neutralized in-vitro by the addition of soluble **Lewis substance** the patient's serum.
  - 1) This procedure is very helpful when multiple antibodies are suspected and one of them is a Lewis.
  - 2) The Lewis antibody activity is eliminated leaving only "other" antibody activity, if present.

## 8. Transfusion Practice

- a. Lewis antigens readily adsorb to and elute from RBC membranes. Transfused RBCs assume the Lewis phenotype of the recipient within a few days of entering the circulation.
- b. Lewis antibodies in the recipient's serum are readily neutralized by Lewis blood group substance in donor plasma.
- c. For these reasons, it is **exceedingly rare** for Lewis antibodies to cause in-vivo hemolysis.
- d. It is **not necessary to type donor blood for the presence or absence of Lewis antigens prior to transfusion or crossmatching.**
  - 1) Reactions obtained in the crossmatch with the donor blood provide a good index of transfusion safety.
  - 2) If agglutination and/or hemolysis are observed at 37 C or AHG, then the blood should not be given.

## D. The P Blood Group System

1. The P blood group system was discovered in 1927, when Landsteiner immunized rabbits with human RBCs and used the resulting immune serums to test for antigenic differences between individual RBC donors.
  - a. Landsteiner named the new antigen P, but in the following years, as the complexity of the system began to unfold, the terminology was changed.
  - b. Landsteiner's P antigen is now called P<sup>1</sup>, with the name P being reassigned to an antigen present on almost all human RBCs.
  - c. RBCs lacking P<sup>1</sup>, but shown to possess P, are of the P<sup>2</sup> phenotype.

### Phenotypes and Frequencies Of P<sup>1</sup> and P<sup>2</sup>

	<u>Whites</u>	<u>Blacks</u>
P <sup>1</sup>	79%	94%
P <sup>2</sup>	21%	6%

- d. Other P phenotypes exist, but are exceedingly rare (<1%) and include: P, P<sup>1</sup>k, and P<sup>2</sup>k.
2. **Anti-P<sup>1</sup>**
    - a. The sera of P<sup>2</sup> persons commonly contain anti-P<sup>1</sup>.
    - b. The antibody reacts **optimally at 4 C** but may occasionally be detected at 37 C.
    - c. Rarely may cause **in-vitro** hemolysis.
    - d. **As it is nearly always IgM, it does not cross the placenta and has not been reported to cause HDN** (it is poorly expressed on fetal cells).
    - e. In general, anti-P<sup>1</sup> has little clinical significance unless it is reactive at 37 C.

- f. Anti-P<sup>1</sup> **has rarely** been reported to cause hemolysis in vivo.
- 3. The **strength** of the P<sup>1</sup> antigen **varies** among different RBC samples, and antigen strength has been reported to diminish when RBCs are stored.
  - a. These characteristics sometimes creates difficulties, both in testing RBCs for the antigen and in the identification of the antibody.
  - b. Anti-P<sup>1</sup> blood typing reagents are usually sufficiently potent to detect weak forms of the antigen.
- 4. An antibody that is weakly reactive at RT testing can often be shown to have anti-P<sup>1</sup> specificity by lowering the incubation temperature or using enzyme treated RBCs.
- 5. **Hydatid cyst fluid or P<sup>1</sup> substance derived form pigeon eggs inhibits the activity of anti-P<sup>1</sup>.**
  - a. *Inhibition* is a useful aid to the identification of anti-P<sup>1</sup>, especially if the antibody is present in a serum with multiple antibodies.
  - b. The anti-P<sup>1</sup> is *neutralized* (becomes non-reactive) revealing other specificities (if present).
- 6. *Do not have to confirm antigen negative for transfusion.*

E. The MN Blood Groups

- 1. The M and N antigens (MNS1 and MNS2 in ISBT terminology) were discovered in 1927 by Landsteiner and Levine.
- 2. Studies of inheritance indicates the genes behave as allelic pairs that are closely linked: MM, MN or NN.
- 3. Frequencies of the MN genotypes.

	Whites	Blacks
M+N-	28%	26%
M+N+	50%	44%
M-N+	22%	30%

- 4. Anti-M
  - a. Detected quite frequently in human sera, usually occurring as a naturally occurring saline agglutinin in antibody tests performed at RT.
  - b. Most examples occur without RBC stimulus.
  - c. *Weak antibody reactivity by anti-M can be enhanced by lowering the pH of the test system to 6.5.*
  - d. Anti-M sera are predominantly IgM, but rare examples have been found that are partly or wholly IgG. The M antigen occurs in sufficient density on the RBCs that agglutination in a saline test may occur even when the antibody is wholly IgG.
  - e. Rarely clinically significant, although examples that react at 37 C or AHG should be considered potentially significant.
  - f. Has rarely been associated with HDN or HTR.
  - g. *Do not need to confirm units are M negative, must be crossmatch compatible.*

5. Anti-N
  - a. Comparatively rare.
  - b. Invariably IgM and typically behave like weakly reactive cold agglutinins.
  - c. Usually considered clinically insignificant although some powerful and potentially significant IgG examples have been observed.
6. Antibodies Showing Dosage
  - a. Some individual examples of anti-M and anti-N demonstrate dosage, showing significantly greater reaction strengths with homozygous cells than with heterozygous cells.
  - b. Examples of anti-M that react **only** with RBCs carrying a double dose of the M antigen are frequently encountered.
  - c. Anti-N showing dosage are rare encountered.
  - d. Problem arises due to the specificity not being immediately apparent from the reaction patterns obtained with a panel of RBCs.
7. The M and N antigens are denatured when the cells are with enzymes, and are useful in antibody identification.
8. Blood grouping reagents are available from a variety of sources: human, rabbit, and monoclonal.
  - a. The most widely used *lectin reagent* is the anti-N-like extract of ***Vicia graminea*** seeds.
  - b. Interpretation of reactions with anti-M and anti-N reagents always requires special care, and it is particularly important that the manufacturer's instructions be followed carefully.
9. A very rare variant of the MN blood group system is M<sup>s</sup>.
  - a. Person with the genotype M<sup>s</sup>N will give the reactions M-N+, leading to the false conclusion that the genotype is NN.
  - b. Of primary importance in paternity testing.

F. S, s and U Antigens

1. The antigens S (MNS3) and s (MNS4) are produced by a pair of allelic genes found at a locus closely linked to the MN locus.
2. Frequencies of the S, s and U Phenotypes

	<u>Whites</u>	<u>Blacks</u>
S+s-U+	11%	3%
S+s+U+	44%	28%
S-s+U+	45%	69%
S-s-U-	0	Less than 1%

3. Antibodies to S, s and U usually occur following RBC stimulation. *All are considered clinically significant and capable of causing HDN and HTRs.*

- a. A few saline reactive examples have been reported, but the antibodies are **usually detected by the IAT.**
  - b. Anti-S occurs about as infrequently as anti-N.
  - c. Anti-s is seen even less often, partly because the s- phenotype is less frequently than the S-, but also because the antigen is less immunogenic than S.
  - d. Anti-U is rare but should be considered when serum from a previously transfused or pregnant Black person contains an antibody to a high-incidence antigen. Established as U negative by proving they are S-s-.
4. S antigen is denatured by ficin treatment, the s antigen may or may not be denatured, depending upon the enzyme used.
  5. *Must confirm that units for transfusion are antigen negative as well as crossmatch compatible.*

G. Lutheran Blood Group System

1. The first example of anti-Lu<sup>a</sup> was found in 1946.
2. Antigens are Lu<sup>a</sup> (LU1) and Lu<sup>b</sup> (LU2) and have the following phenotypic frequencies in the white population:

Lu(a+b-)	0.15%
Lu(a+b+)	7.5 %
Lu(a-b+)	92.35%
Lu(a-b-)	Very Rare

3. Anti-Lu<sup>a</sup>
  - a. The antibody is uncommon and is usually a naturally occurring *saline agglutinin*.
  - b. *Lutheran antigens are poorly developed at birth*, anti-Lu<sup>a</sup> has not been reported to cause HDN.
  - c. Has not been associated with HTRs and is *not considered clinically significant*.
  - d. May agglutinate saline suspended cells in a MF manner. This is characteristic of reactions with some examples of Anti-Lu<sup>a</sup>.
4. Anti-Lu<sup>b</sup>
  - a. Antibody production caused by exposure to antigen through transfusion or pregnancy and is *considered clinically significant*.
  - b. Has been reported to cause diminished survival of transfused RBCs.
  - c. Has been implicated in **mild** HDN.
  - d. May agglutinate saline suspended cells, although it most commonly reacts at the IAT.
  - e. Very difficult finding antigen negative blood as approximately 99% of the population is antigen positive.

## H. Kell Blood Group System

1. The K (KEL1) antigen was first identified in 1946 as the causative antibody in a case of HDN.
2. The allele of K is Cellano, k (KEL2).
3. Phenotypes frequencies are as follows:

	<u>White</u>	<u>Blacks</u>
K+k-	0.2%	Rare
K+k+	8.8%	2%
K-k+	91 %	98%

4. The **Kell antigen is strongly immunogenic**, and is frequently found in sera from transfused patients.
5. Anti-K and anti-k
  - a. Most examples detected are of immune origin, clinically significant and are reactive by the IAT, some bind complement.
  - b. Anti-K has caused HTRs on numerous occasions, both immediate and delayed.
  - c. Both have been implicated in HDN.
  - d. 90% of donors are K negative, so it is not difficult finding compatible blood.
  - e. Anti-k has clinical and serologic characteristics similar to anti-K but occurs much less frequently because only about one person in 500 lacks the k antigen.
  - f. Donor units must be tested and be negative for the antigen as well as crossmatch compatible.
6. Other antigens of the Kell system.
  - a. Kp<sup>a</sup> (Penney, KEL3), 1957
  - b. Kp<sup>b</sup> (Rautenberg, KEL4), 1958
  - c. Js<sup>a</sup> (Sutter, KEL6), 1958
  - d. Js<sup>b</sup> (Matthews, KEL7), 1963
  - e. K<sub>o</sub> is a null phenotype.
  - f. McLeod phenotype has weakened expression of Kell system antigens and is associated with structural and functional abnormalities of RBCs and leukocytes.
7. Antibodies to other Kell system antigens
  - a. Show similar serologic characteristics and are considered clinically significant.
  - b. May occur following transfusion or pregnancy.
  - c. Frequency influenced by immunogenicity of the antigen and distribution of relevant negative and positive phenotypes among donors.
  - d. These antibodies are rare, suggesting that the antigens are of low immunogenicity.

- e. Patients immunized to high incidence antigens present a problem that may require assistance from a rare donor file.
- f. These antibodies may cause HDN and HTRs.

### I. Duffy Blood Group System

1. The Fy<sup>a</sup> (FY1) antigen was discovered in the serum of a multiply transfused hemophiliac in 1950. The following year Fy<sup>b</sup> (FY2) was discovered in the serum of a multiparous female.
2. In 1955 it was reported that most African Americans lacked both the Fy<sup>a</sup> and Fy<sup>b</sup> antigens produced by what was thought to be codominant alleles.
  - a. Indicated that a third allele, a silent gene called Fy (FY0) was also part of the system.
  - b. Blacks who are Fy(a-b-) are considered to be homozygous FyFy.
  - c. The Fy(a-b-) phenotype *provides resistance to infection with Plasmodium vivax*, a species of malaria.
3. Phenotypes and frequencies of the Duffy System.

	Whites	Blacks
Fy(a+b-)	17%	9%
Fy(a+b+)	49%	1%
Fy(a-b+)	34%	22%
Fy(a-b-)	very rare	68%

4. Antibodies to Duffy antigens.
  - a. *Both anti-Fy<sup>a</sup> and anti-Fy<sup>b</sup> cause immediate and delayed HTRs and HDN*
  - b. Anti-Fy<sup>a</sup> is quite commonly encountered, anti-Fy<sup>b</sup> is considerably less common.
  - c. *The antibodies react best by the IAT.*
  - d. **The antigen sites are destroyed by most enzymes used in serologic tests**, so anti-Fy<sup>a</sup> and anti-Fy<sup>b</sup> antibodies usually give negative reactions in enzyme test procedures.
  - e. Duffy antibodies frequently show dosage affect, sometimes to such an extent that they may be nonreactive with heterozygous cells.
  - f. When Duffy antibodies are encountered it is extremely helpful to search in the right ethnic population for appropriate antigen negative donors to crossmatch.

### J. The Kidd Blood Group System

1. Anti-Jk( was first recognized in 1951 in the serum of a woman who had given birth to a child with HDN. Two years later, anti-Jk<sup>b</sup> was found in the serum of a patient who had suffered a transfusion reaction.
  - a. The designation for the Kidd system is Jk<sup>a</sup> (JK1) and Jk<sup>b</sup> (JK2)
  - b. The "null" phenotype was discovered in 1959, the individuals type as Jk(a-b-). This is due to a the silent allele Jk. More common in people of Polynesian descent.

2. Phenotypes and frequencies of the Kidd System.

	Whites	Blacks
Jk(a+b=)	28%	57%
Jk(a+b+)	49%	34%
Jk(a=b+)	23%	9%
Jk(a=b=)	Exceedingly Rare	

3. Antibodies to Kidd

- a. Occasionally causes HDN, but it is usually mild.
- b. **These antibodies are notorious for involvement in severe HTRs**, especially in delayed reactions, which occur when antibody, developing rapidly in an anamnestic response to antigens on transfused RBCs, destroy the still circulating RBCs.
  - 1) In some reported cases, retesting the patient's pretransfusion serum has confirmed that the antibody was undetectable.
  - 2) This highlights the importance of checking previous records prior to selecting blood for transfusion. In several cases the antibody had been previously detected and identified.
- c. *Antibodies react best by the IAT*, but saline reactivity has been observed.
- d. *These antibodies are often weakly reactive and lose reactivity upon storage*, even after freezing and some workers feel that RBCs carrying a double dose of Jk<sup>a</sup> or Jk<sup>b</sup> are needed in screening tests to reliably detect these antibodies.
- e. **Rare examples of Kidd antibodies will not be detected unless fresh complement is present and the AHG serum has anticomplementary activity.**
  - 1) Since these are so rare, and due to the number of false positives obtained when using poly coombs, it is best to use IgG.
  - 2) Some workers report no difficulties detecting these antibodies in low ionic tests that incorporate anti-IgG.
- f. Donor units must be tested with specific anti-sera and be negative for the antigen as well as crossmatch compatible.

K. Additional Pairs of Antithetical RBC Antigens

1. The blood group systems previously referred to are the principle ones in which the antibodies may be frequently encountered.
  - a. Other systems of genetically determined antigens also exist and the student should be aware of them.
  - b. These antigens appear to be less immunogenic than those of the other major blood group systems.
  - c. Antibodies directed at these antigens occur rarely, usually in sera containing multiple specificities and are usually clinically significant.

- d. The antigens themselves may be important in genetic investigations and population or family studies.
2. Diego ( $Di^a$  and  $Di^b$ )
    - a. Useful as a racial marker,  $Di^a$  antigen being almost entirely confined to populations of Mongolian origin, including Native Americans.
    - b. One hundred per cent of the white population types as  $Di(a-b+)$ .
  3. Colton ( $Co^a$  and  $Co^b$ ).
    - a. Parallels the incidence of K and k.
    - b. Approximately 89% of the White population is  $Co(a+b=)$  and 10.4% are  $Co(a+b+)$ .
  4. Cartwright ( $Yt^a$  and  $Yt^b$ )
    - a. Parallels the incidence of K and k.
    - b. Approximately 91.9% of the White population is  $Yt(a+b-)$  and 7.9% is  $Yt(a+b+)$ .
  5. Dombrock ( $Do^a$  and  $Do^b$ )
    - a. Parallels incidence of the Duffy system.
    - b. Approximate 49.5% of the White population is  $Do(a+b+)$ , 33.3% is  $Do(a-b+)$  and 17.2% is  $Do(a+b-)$ .

L. The Sex-Linked Blood Group antigen  $Xg^a$

1. In 1962, an antibody was discovered that identified an antigen more common among women than among men.
  - a. This would be expected of an X-borne characteristic.
  - b. Females inherit an X chromosome from each parent, whereas male inherit X only from their mother.
2. The antigen is called  $Xg^a$  in recognition of its X-borne manner of inheritance.
3. Anti- $Xg^a$  is an uncommon antibody that usually react only by the IAT, but saline agglutinins have been observed.
4. This antibody has not been implicated in HDN or HTRs.
5. Anti- $Xg^a$  may be useful for tracing the transmission of genetic traits associated with the X chromosome.

M. High-Incidence RBC Antigens

1. ***High-incidence (public) antigen is defined as those antigens occurring in 92 to 99.9% or more of the general population.***
2. Persons make alloantibody to specific blood group antigens due to the fact that their own RBCs lack the offending antigen.
3. For this reason, *antibodies directed at high- incidence antigens are rarely encountered* because by definition, most of the general population will have these antigens present on their cells.
4. When antibodies to high frequency antigens occur it may be *exceedingly difficult to find compatible blood.*

a. *Members of the patient's family , especially siblings, are usually the most promising sources.*

b. May have to have blood center contact the Rare Donor File to find potential units.

5. Antibodies to the corresponding antigens usually react best by the IAT.

#### N. Other RBC Antigens of Comparatively High Incidence

1. Formerly referred to as high-titer, low-avidity (HTLA).

2. Among the most frustrating problems encountered in testing sera for unexpected antibodies are those created by the group of antibodies formed to these antigens.

a. Reactions invariably observed in the AHG phase of testing.

b. They are commonly weakly reactive, variable in reactivity and sometimes irreproducible.

3. **The term HTLA refers to the fact that feeble reactions seen with undiluted serum will often persist in serum subjected to considerable dilution.**

4. Reactions suggests either low affinity of the antibody or weak cellular expression of the antigen, rather than limited antibody concentration.

5. Transfusion practice:

a. These antibodies, though of debatable clinical significance, react with antigens having a fairly high incidence in the population.

b. When the antibody has been identified, blood can normally be issued without delay.

c. Work can then continue to determine the antibody specificity.

#### O. The Sd<sup>a</sup> Antigen

1. This antigen is of fairly high incidence and is widely distributed in mammalian tissues and body fluids.

a. The antigen is variably expressed on the cells.

b. May disappear transiently during pregnancy.

2. Anti-Sd<sup>a</sup> is most frequently detected during the AHG phase when the test is examined microscopically.

a. Most examples would be equally demonstrable if the cell button were examined microscopically at IS after resuspension.

b. **Mixed-field agglutination is the characteristic reaction.**

3. *Urine from guinea pigs and from Sd(a+) humans inhibits the reactivity of anti-Sd<sup>a</sup> (neutralization).*

4. Although reported once as causing an HTR, anti-Sd<sup>a</sup> is widely believed to have **no clinical significance.**

P. Low-incidence RBC Antigens

1. Many low-incidence (private) RBC antigen have been recognized in addition to a growing number that have been assigned to the MN and Rh systems.
2. These antigens occur with a frequency of 1 in 500 or less.
3. Antibodies
  - a. React with so few random blood samples that they virtually never cause difficulties in selecting blood for transfusion.
  - b. They are only encountered by chance in antibody screening or compatibility testing, when a screening cell or donor cell selected happens to carry the corresponding antigen.
  - c. Routine antibody screening tests rarely detect such antibodies, the crossmatch affords the only opportunity to detect an incompatibility, should antigen positive blood be selected.
  - d. The chance of choosing donor blood positive for that antigen, however, is quite remote.
4. The antibodies to these are usually saline agglutinins, but some do occur as IgG reactive at the IAT and have cause HDN.

Q. The Bg Antigens

1. Antibodies directed at certain leukocyte antigens sometimes cause confusing reactions in serologic test with RBCs.
  - a. The Bg antigens are expressed to variable degrees on RBCs.
  - b. Reactions of varying strengths are observed when a serum contains anti-Bg is tested with different Bg+ RBCs.
  - c. Reactivity is most commonly observed at IAT although potent anti-Bg may cause direct agglutination of cells with strong expression of Bg antigens.
2. Antibodies to the Bg antigen are not clinically significant in regard to RBC transfusion practice.