I. The Lutheran System (ISBT #005)

A. Inheritance

1. Co-dominant alleles $Lu^a$ and $Lu^b$ on chromosome 19.

2. Discovered in 1945. In 1951 the $Lu$ and $Se$ loci were shown to be linked - The first example of autosomal linkage in man.

3. Null phenotype categorized as:
   a. Inheritance of recessive homozygous amorphic gene, $LuLu$
   
   b. Inherited as dominant trait; not expressed due to an inhibitor gene, $In(Lu)$

B. Antigens -

1. Characteristics
   a. Poorly developed at birth
   b. Not destroyed by papain and ficin, but destroyed by trypsin, AET, DTT
   c. Show variable antigen expression

2. Frequency: $Lu^a$ is low prevalence; $Lu^b$ is high prevalence

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Lu(a+b-)$</td>
<td>0.15</td>
</tr>
<tr>
<td>$Lu(a+b+)$</td>
<td>7.5</td>
</tr>
<tr>
<td>$Lu(a-b+)$</td>
<td>92.25</td>
</tr>
<tr>
<td>$Lu(a-b-)$</td>
<td>very rare</td>
</tr>
</tbody>
</table>

C. Antibodies- Found infrequently

1. Anti-$Lu^a$
   a. Most examples are insignificant. Antigen positive units have been reported to have normal or near-normal survival in a patient with the antibody.
b. Usually naturally occurring. May be IgM (usually), IgG or IgA.

c. React best at room temperature (IS phase); loose, weak mixed field reactivity noted

d. May activate complement

e. Can show dosage

f. Rare reports of mild, delayed HTR, rare cause of HDFN

2. Anti-Lu

   a. Very rare, immune, IgG

   b. Most react at the 37°C and AHG phases

   c. Some activate complement

   d. Can show dosage

   e. May cause mild HDFN

   f. May initially cause accelerated destruction of antigen positive RBCs (HTR), followed by slow clearance of remaining positive RBCs. Should be considered significant.

II. The Xg System (ISBT # 012)

A. Inheritance

   1. Discovered in 1962

   2. Sex-linked: carried on X chromosome

   3. No known antithetical allele

   4. Useful in tracing transmission of genetic traits

B. Antigen - Xg

   1. Destroyed by enzymes
2. Frequency %:

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
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</thead>
<tbody>
<tr>
<td>Xg(a+)</td>
<td>65.6</td>
<td>88.7</td>
</tr>
<tr>
<td>Xg(a-)</td>
<td>34.4</td>
<td>11.3</td>
</tr>
</tbody>
</table>

C. Antibody: Anti-Xg\(^a\):

1. Rare IgG antibody that reacts in AHG only
2. Capable of complement activation
3. No allele, so does not show dosage
4. Not implicated in HDFN nor HTR

III. Low Prevalence Antigen

A. Definition - an antigen possessed by less than 10% of the general population.

B. Antibodies:

1. Usually encountered by chance; antibody screen cells are usually negative for these antigens
2. May be IgM, saline agglutinins or IgG, reactive only by AHG
3. Can cause HDFN (if IgG); detected only when infant presents with positive DAT
4. May be unsuspected contaminant in blood grouping reagents prepared from human serum
5. Serum containing autoantibodies often also contains a mixture of alloantibodies directed at low-prevalence antigens
6. Virtually never cause difficulties in selecting blood for transfusion, since most individuals are antigen negative.

IV. High Prevalence Antigens

A. Definition: antigens occurring in 99.9% or more of the population. Also known as high incidence or high frequency.
B. Examples include:

1. **Vel** - Anti-Vel is known for activating complement and causing severe immediate HTRs.

2. **Sd<sup>a</sup>**
   
   a. Antigens are carbohydrate structures found on RBCs and in secretions – particularly high concentration in urine
   
   b. Variable antigen expression on RBCs
   
   c. Depressed antigen expression noted in pregnancy; transient antibodies maybe present
   
   d. Antibodies are mainly IgM
   
   e. Distinctive mixed-field agglutination with large, refractile agglutinates.

3. **Wr<sup>b</sup>** – A member of the Diego system; anti-Wr<sup>b</sup> is a common autoantibody.

C. Antibodies

1. Antibodies are rarely encountered, as most individuals possess the antigen.

2. May be exceedingly difficult to find compatible blood; may check siblings or the American Rare Donor Program for antigen negative RBC units.

3. Usually react best at the antiglobulin phase; suspect when all RBCs on the antibody identification panel are positive in the same phase and at the same strength, but the auto control is negative.

V. Formerly Known As “High Titer Low Avidity (HTLA)”

A. Antigens

1. Fairly high prevalence in the population

2. Weak reactivity with antibodies is most likely due to the low number of antigen sites per RBC and not poor avidity as originally thought

3. Examples include:

   a. Chido (Ch) and Rodgers (Rg) – not true RBC antigens; part of the C4d portion of complement
b. York (Yk\(^a\)), and McCoy (McC\(^a\)) – Part of the Knops system; located on the red blood cell complement receptor-1 (CR-1)

c. Cost (Cs\(^a\)) – Related to the Knops system, but not located on CR-1

B. Antibodies

1. IgG

2. Weak reactions seen in the AHG phase (originally thought to be due to low avidity)

3. Reactions seen with undiluted serum often persist despite considerable dilution (i.e. high titer)

4. Reactions are variable and irreproducible; not stable during storage

5. Questionable clinical significance; seen more as an interfering substance when attempting to detect significant antibodies.

6. Seen in multi-transfused patients, 25% of patients with an HTLA have additional alloantibody(-ies).

7. Chido and Rogers may be neutralized using fresh serum containing complement.