Blood Groups – Kell Group

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History

- Discovered in 1946: an antibody was identified in Mrs. Kellacher, the antibody reacted with her newborn infant, her older daughter, her husband, and about 9% of the white population. Antigen is named after her, called Kell
- In 1949, k antigen was discovered by Levine, called Cellano antigen
- Kpa, Kpb antigens were discovered in 1957, 1958
- Jsa, Jsb antigens were discovered in 1957, 1963
- Inheritance patterns and statistics confirmed these antigens are related to the Kell system
History

- $K_0$ (null phenotype) was discovered in 1957. It helped to figure out the relationship between $K$, $k$, $Kpa$, $Kpb$, $Jsa$, $Jsb$ antigens, because anti-$K_0$ reacted with these antigen positive cells.

- McLeod phenotype was discovered by Allen and coworkers in 1961: weaken expression of Kell antigens.
**KEL** gene codes for the entire **Kell system glycoprotein**, some 720 amino acids. It also codes for the Km antigen.

**Kx** is NOT a Kell system antigen - but there is interaction between the Kell protein and the Kx antigen. The Xk gene is located on the X chromosome.

Kell system glycoprotein: Kell Ag’s reside here.
Kell Antigens

- Routinely tested Kell antigens: K, k, Kp\textsuperscript{a}, Kp\textsuperscript{b}, Js\textsuperscript{a}, Js\textsuperscript{b}

- Other Kell antigens: Ku, Ula, Wka, Kx, Km, Kp\textsuperscript{c}, (only exist on Kp\textsuperscript{a}-, Kp\textsuperscript{b}- cells), Cent, Callais...

- Ku – an universal Kell antigen present on all cells except K\textsuperscript{0} cells (K null phenotype)

- Total 25 antigens, designated as KEL or 006 by ISBT

- Kell antigens are present at birth – cause severe HDN
Kell Antigens

- Not affected by routine blood bank enzymes - papain, ficin
- DTT and ZZAP denature all Kell antigens, but not Kx.
- Immunogenicity: strongly immunogenic - One unit of K+ blood transfused to K- patients -70% of patients will have anti-Kell (in comparison to 80% for D- patients receiving D+ blood)
High frequency antigens: $k$, $Js^b$, $Kp^b$

Low frequency antigens: $K$, $Js^a$, $Kp^a$

$K^+ = 9\%$ and $3.5\%$  
$Kp^a = 2.3\%$ and Rare  
$Js^a = $ Rare & $20\%$

$k^+ = 99.8\%$ and $100\%$  
$Kp^b = 100\%$ and $100\%$  
$Js^b = 100\%$ & $80\%$

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Whites (%)</th>
<th>Blacks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K^-$ $k^+$</td>
<td>91.0</td>
<td>96.5</td>
</tr>
<tr>
<td>$K^+$ $k^+$</td>
<td>8.8</td>
<td>3.5</td>
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<tr>
<td>$K^+ k^-$</td>
<td>0.2</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>$Kp (a^+ b^-)$</td>
<td>&lt;0.1</td>
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</tr>
<tr>
<td>$Kp (a^+ b^+)$</td>
<td><strong>2.3</strong></td>
<td>Rare</td>
</tr>
<tr>
<td>$Kp (a^- b^+)$</td>
<td>97.7</td>
<td>100</td>
</tr>
<tr>
<td>$Js (a^+ b^-)$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>$Js (a^+ b^+)$</td>
<td>Rare</td>
<td>19</td>
</tr>
<tr>
<td>$Js (a^- b^+)$</td>
<td>100</td>
<td>80</td>
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McLeod Phenotype

Weakened expression of Kell system antigens - **Loss of Kx and Km**

$k, Kp^b, Js^b$
McLeod phenotype

- No Kx and Km antigens
- XK gene is on X chromosome: Xp21.1
- Associated with x-linked CGD (chronic granulomatous disease): repeated catalase+ bacteria, such as Staph aureus infection due to lack of NADPH oxidase deficiency
- Hemolytic anemia with acanthocytes
- Transfusion should be avoided because they can produce **anti-Kx and anti-Km** which making future transfusion almost impossible, but will not produce anti-K or anti-k if they express weakly.
Kell Null ($K_0$) Phenotype

1. $K^0$ is a silent Kell allele

2. When homozygous $K^0K^0$ inherited no Kell system antigens are expressed.

3. $K_x$ antigen expression is enhanced

4. Very rare

5. Develop antibodies against any or all Kell antigens and anti-Ku. Ku is an universal Kell antigen present on all cells except $K^0$ cell, very difficult to find compatible blood.
**K\text{mod} Phenotype**

- Very weak expression of Kell antigens
- Can make antibody resembles anti-Ku, but differs from anti-Ku by being nonreactive with K\text{mod} cells
- Are homozygous fro missense mutation of Kell gene
Kell Antibodies

- Anti-K, anti-k: IgG, significant, warm-reacting, exposure-requiring

- Anti-K is one of the most common alloantibodies we identify in the lab, because K is a low frequency antigen (in 10% of whites, 2% of blacks)

- Anti-k is a very rare antibody, because k (cellano antigen) is a high frequency antigen (in 99.8% of population), very difficult to find compatible blood (freeze compatible units)
Kell Antibodies

- Anti-Jsb is usually seen in black patients (Jsb antigen is negative in 20% of blacks and <1% of whites)
- It is usually seen in sickle cell disease patient with multiple alloantibodies
- Need to search Red Cross national vare blood type database to find compatible RBCs and usually frozen units
- Delaying providing blood: takes 2-3 hours to thaw, then deglycelize the RBCs
Why anti-K and anti-E are most common antibody identified in US?

- Antigen frequency in patient and donor population
- Antigen immunogenicity
Case #1

- A 60 y o female came to Cedars ER due to weakness, fatigue, headache. She has history of CLL with chronic anemia on transfusion support
- CBC showed severe anemia, Hb 5.5
- Patient was telling everybody in the ER “I have blood at UCLA”, ER physicians thought it was a symptom of “mental status change” due to disease and severe anemia
Case #1

- Type and crossmatch 2 units of RBCs was ordered
- BB: panel reactive at 3+ or 4+ on gel panel, autocontrol is negative – no autoantibody – alloantibody causing strong reaction
- Patient was transfused in the last 90 days – cannot do autoabsorption – needs alloabsorption (R1R1, R2R2, rr) – takes at least 2-3 hours
- BB attending decided to talk to the patient about her history of transfusion and where was last transfused
Case #1

- Patient: Last transfusion was at UCLA and “I have blood at UCLA”
- Q: Why?
- A: I have special antibody
- Called UCLA BB: anti-k, 2 units of k- RBCs frozen at UCLA
- Ship to Cedars – thaw (at 37C) – deglycelization
- One phone call saved hours of testing.
Case #2

- 37 y o African American male with sickle cell disease
- Transferred to Santa Monica Hospital for complex hip surgery, expect bleeding during the surgery to be over 1000ml
- Ordered 10 units of RBCs: Hb 6, want to transfuse 4 RBCs before surgery to raise Hb A and decrease Hb S, 6 units in OR
- Type & Screen: panel reactive 2+, 3+, 4+
- Called Red Cross for previous workup: anti-K, E, Fya, Jkb, S, Jsb
Case #2

- Phenotype: negative for these 6 antigens (He produced all the antibodies he possibly could produce)
- Red Cross has 4 matched units frozen – immediately reserved for him.
- National data search found 3 matched units in Atlanta
- Called hematologist, primary care, surgery, anesthesiologist – many phone conversations about the best way to manage him
Case #2

- Final decision: transfuse 1 unit the night before, transfuse 1 unit the morning of surgery, take 2 units to OR, order stat shipment of 3 units from Atlanta
- Will use cell saver – collecting blood from surgical field – filter it – wash it – transfuse back to patient
- Sickle cells will break during the process – usually don’t use cell saver in this population – for this patient it is last ditch
- I ordered 2 units of 5 antigen matched but Jsb + RBCs as back up in case patient bleeds massively – secret (not telling other physicians)
Case #2

- On the day of surgery – we were thawing 3 units of frozen RBCs – 1 unit container broke – loss of 1 unit
- Only 1 unit available for OR use
- Surgeon tried to minimize bleeding.
- Anesthesiologist tried everything she can to maintain oxygenation, hydration,
- Bleeding 1000 ml, only had 100 ml packed RBCs, smear made before, during, after cell saver showed minimum increase of sickling – 100ml autologous cell transfused back to patient
- Post-op: managed without more transfusion, Hb 5.5