AB0-blood group system – Karl Landsteiner
“Wherever a blood transfusion is performed in the world today, wherever a worried mother's threatened child is saved, Karl Landsteiner is virtually present” - Hermann Chiari

1 P. Speiser, F.G. Smekal, Karl Landsteiner. Verlag Brüder Hollinek, Wien
Structure

• Karl Landsteiner – Biography
• The Discovery of the AB0 Blood groups
• Blood Group Systems
• Blood Transfusion
Karl Landsteiner - Biography

- Born on 14 June 1868 in Baden
- 1885-1891 studies medicine at University of Vienna
- Different employments at Hygiene Institute at Vienna and University Department of Pathological Anatomy in Vienna
- Devoted to science - interested in immunology, bacteriology and pathology
- 1900/1901 discovers different blood groups of humans (AB0 blood group system)
- 1923 Landsteiner moves to New York
- 1930 Nobel Price for medicine
- Dies on 26 June 1943 in New York

The Discovery of the AB0 Blood groups

• Before Landsteiner‘s discovery it was well known that if blood of different animals was mixed agglutination would occur

• The idea that blood from two humans would cause the same reaction was novel

2 Figl M et al. Karl Landsteiner, the discoverer of blood groups, Resuscitation, 2004
3 Schwarz HP and Dorner F, KARL LANDSTEINER AND HIS MAJOR CONTRIBUTIONS TO HAEMATOLOGY. British Journal of Haematology. 2004
Beispiel:
Anti-A Antikörper  Erythrozyten mit Antigen A  Agglutination
Landsteiner’s Experiment

- In 1900 Landsteiner crosstested six sera and erythrocytes of his own blood and five coworkers and “accidentally” discovered human blood groups
- Landsteiner’s observations:
  - None of the sera reacted with their own erythrocytes (self-tolerance)
  - Coworker A’s blood reacted with Coworker B’s blood → Agglutination (antibodies involved)
  - Agglutination reaction appeared even with dried blood

2 Figl M et al. Karl Landsteiner, the discoverer of blood groups, Resuscitation, 2004
3 Schwarz HP and Dorner F, KARL LANDSTEINER AND HIS MAJOR CONTRIBUTIONS TO HAEMATOLOGY. British Journal of Haematology. 2004
First reference to his discovery in a footnote in 1900 when he stated the following:

“The sera of healthy humans has an agglutinating effect, not only upon animal blood cells, but frequently upon blood cells from other individuals as well; the question is whether this phenomenon is due to inherent individual differences or to the effect of influenced damages, (eg, bacterial nature).”

1 Landsteiner K. Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymph. Centralbl f
2 Figl M and Pelinka LE. Karl Landsteiner, the discoverer of blood groups. Resuscitation. 2004
Published findings in "Agglutination phenomena of normal human blood" in 1901 and defined the blood groups A, B and C (0)

In this paper he states:

"In einer Anzahl von Fällen (Gruppe A) reagiert das Serum auf die Körperchen einer anderen Gruppe (B), nicht aber auf die der Gruppe A, während wieder die Körperchen A vom Serum B in gleicher Weise beeinflusst werden. In der dritten Gruppe (C) agglutiniert das Serum die Körperchen von A und B, während die Körperchen C durch die Sera von A und B nicht beeinflusst werden."

1 Landsteiner K., Ueber Agglutinationserscheinungen normalen menschlichen Blutes. 1901
• Landsteiner’s conclusions:
  – Human blood can be categorized into blood groups referring to the inherent individual physiological differences of the expressed antigens.
  – He thought that his observation might explain the variable clinical consequences of human blood transfusion (antibodies!)
  – The Landsteiner Rule states that the serum of each human contains only iso-haemagglutinins that are not directed against the agglutinable substance of that human's erythrocytes.

2 Figl M et al. Karl Landsteiner, the discoverer of blood groups, Resuscitation, 2004
3 Schwarz HP and Dorner F, KARL LANDSTEINER AND HIS MAJOR CONTRIBUTIONS TO HAEMATOLOGY. British Journal of Haematology. 2004
• One year later Decastelo and Sturli found that there was a fourth group: AB
AB0-antibodies

- Agglutination is caused by antibodies
- It is believed that anti-A and anti-B antibody production is stimulated by agents such as bacteria, pollen or other substances present in the internal or external environment that have molecular configurations similar to the A and B antigen → no sensitization reaction needed

<table>
<thead>
<tr>
<th>Serum of group</th>
<th>Agglutinins in serum</th>
<th>Erythrocytes of group</th>
</tr>
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<tbody>
<tr>
<td>O</td>
<td>αβ</td>
<td>- + + + +</td>
</tr>
<tr>
<td>A</td>
<td>β</td>
<td>- - + + +</td>
</tr>
<tr>
<td>B</td>
<td>α</td>
<td>- + - + +</td>
</tr>
<tr>
<td>AB</td>
<td>-</td>
<td>- - - - -</td>
</tr>
</tbody>
</table>

1 Landsteiner K., *On individual differences in human blood* Nobel Lecture. December 1930
Impact of Landsteiner‘s discovery

- Distinguishing between human blood stains for forensic purposes
- Simple paternity tests: (hereditary transmission)
  - Both parents are group 0 while child is group A → wrong father (5000 investigations, 8% paternity was excluded)
- Transfusions
- Transplantation

1 Landsteiner K., On individual differences in human blood Nobel Lecture. December 1930
Blood Groups

- **Def.**: Specific constitution of erythrocytes’ antigens (glycolipids and glycoproteins) which are characteristic for every individual.

- **33** blood group systems have been described so far

- Most important systems: AB0 and Rhesus
  - Strong agglutinative effect
## Blood group systems

### Table of blood group systems

<table>
<thead>
<tr>
<th>No.</th>
<th>System name</th>
<th>System symbol</th>
<th>Gene name(s)*</th>
<th>Chromosomal location</th>
<th>CD numbers</th>
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<td>ABO</td>
<td>ABO</td>
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<td>GYP A, GYPB, GYPE</td>
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<td>RH0, RHCE</td>
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### Additional systems

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<td>BSG</td>
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<td>CD151</td>
<td>11p15.5</td>
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<td>SEMA7A</td>
<td>15q24.1</td>
<td>CD108</td>
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<tr>
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<td>LAN</td>
<td>LAN</td>
<td>ABCB6</td>
<td>2q36</td>
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</tr>
</tbody>
</table>

1 The International Society of Blood Transfusion
AB0 Blood group system

• Erythrocytes either express antigen A, B, or 0 = Glycoproteins
• Antibodies develop in the first months of life
• Gene, determining blood group is located on Chromosome 9 (9q.34)
• Antigens are also expressed in other cells than erythrocytes

1 Schmidt RF. Et al., Physiologie des Menschen, Springer. 2004
• H-Substance is precursor for different blood groups
Blood group 0

0-Allele encodes for an enzyme with no enzymatic activity. Therefore the H-antigen is not modified and blood group 0 is the result. Terminal fucose reacts as active antigen for blood group 0.

1 Schmidt RF. Et al., Physiologie des Menschen, Springer. 2004
Blood group A

A-Allele on Chromosome 9 encodes for a glycosyltransferase which adds a N-Acetyl-glucosamin to galactose of H-antigen.

1 Schmidt RF. Et al., Physiologie des Menschen, Springer. 2004
Blood group B

B-allele on long arm of chromosome 9 encodes for a glycosyltransferase which adds Galactose to the preexisting galactose of the H-antigen generating the B blood group.

1 Schmidt RF. Et al., Physiologie des Menschen, Springer. 2004
Blood group AB

A and B antigen is generated and expressed on erythrocyte's membrane.

1 Schmidt RF. Et al., Physiologie des Menschen, Springer. 2004
Rhesus-Factor

- Discovered by Landsteiner and Wiener in 1940 in Rhesus monkeys
- Consists of 49 antigens based on a complex genetic basis (RhD and RhCE)
- The RhD protein determining the rhesus factor is either absent or present (RhD –/+)
- Unlike proteins of other blood groups, Rhesus proteins are only expressed in the membranes of red blood cells

1 Flegel WA., *The genetics of the Rhesus blood group system*, Blood Transfusion. 2007
Rhesus-Factor

- Clinical Importance:
  - Morbus haemolyticus neonatorum:
    - Mother Rhesus – while child is Rhesus +
    - At birth fetal blood intrigues the mother’s cardiovascular system and anti-D antibodies are built
    - IgG antibodies pass through placenta binding fetal red blood cells causing haemolysis
    - The result is anaemia and kernicterus
  - Blood transfusion had a higher success rate

1 Flegel WA., *The genetics of the Rhesus blood group system*, Blood Transfusion. 2007
### Blood groups frequency

<table>
<thead>
<tr>
<th>Blutgruppe</th>
<th>Häufigkeit weltweit</th>
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<tbody>
<tr>
<td>0+</td>
<td>38%</td>
</tr>
<tr>
<td>A+</td>
<td>34%</td>
</tr>
<tr>
<td>B+</td>
<td>9%</td>
</tr>
<tr>
<td>0−</td>
<td>7%</td>
</tr>
<tr>
<td>A−</td>
<td>6%</td>
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<td>AB+</td>
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<tr>
<td>B−</td>
<td>2%</td>
</tr>
<tr>
<td>AB−</td>
<td>1%</td>
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<table>
<thead>
<tr>
<th>Blutgruppenmerkmal</th>
<th>Deutschland</th>
<th>Österreich</th>
<th>Schweiz</th>
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<td>A</td>
<td>43%</td>
<td>41%</td>
<td>47%</td>
</tr>
<tr>
<td>O</td>
<td>41%</td>
<td>37%</td>
<td>41%</td>
</tr>
<tr>
<td>B</td>
<td>11%</td>
<td>15%</td>
<td>8%</td>
</tr>
<tr>
<td>AB</td>
<td>5%</td>
<td>7%</td>
<td>4%</td>
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<tr>
<td>Rhesus positiv</td>
<td>85%</td>
<td>85,5%</td>
<td>85%</td>
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<tr>
<td>Rhesus negativ</td>
<td>15%</td>
<td>14,5%</td>
<td>15%</td>
</tr>
<tr>
<td>Kell negativ</td>
<td>91%</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>Kell positiv</td>
<td>9%</td>
<td>9%</td>
<td></td>
</tr>
</tbody>
</table>

Blood transfusion

- Blood circulation discovered in 1616 by William Harvey
- First blood transfusion into human in 1667 done by Denis and Emmerez
- First transfusion with human blood carried out by Blundell during first half of 19th century

1. Landsteiner K., *On individual differences in human blood* Nobel Lecture, December 1930
Blood transfusion

- Reactions to transfusion were unpredictable (haemolysis and agglutination occurred and caused severe symptoms and even death)
- Landsteiner’s discovery in 1901, however, explained the severe effects of blood group incompatibility. In the last sentence of his paper he stated:

  — „Endlich sei noch erwähnt, dass die angeführten Beobachtungen die wechselnden Folgen therapeutischer Menschenbluttransfusionen zu erklären gestatten.“

1 Landsteiner K., On individual differences in human blood Nobel Lecture. December 1930
2 Watkins WM, The ABO blood group system: historical background. Transfusion Medicine, 2001
• ABO blood grouping test for selecting donors made safe transfusion possible
• Reuben Ottenberg carried out successful transfusions guided by Landsteiner’s work.
• Blood transfusions were then widely used in World War I/II in order to save many soldiers’ lives.

1 http://bloodcenter.stanford.edu/blog/archives/blood-donation/ Web. 8 Dec 2013
2 Kaadan et al., Blood transfusion in history.
• Cross-Test

0 - = universal donor → no antigens
AB + = universal recipient → no antibodies
Bedside-test

Serafol® ABO+D

Anti-A  Anti-B  Anti-D

Name (Name/Nom)  Kons.-Nr. (Unit No./No.Poche)

Geb.Dat. (Date of Birth/Date de Naissance)  Blutgruppe: A POS

Datum (Date)  Blut (Blood/Sang)

Unterschrift (Signature)  Datum

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