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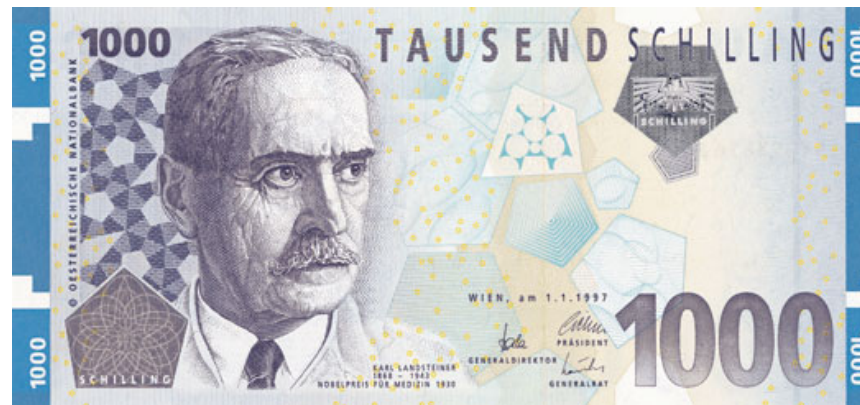
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# ABO-blood group system – Karl Landsteiner

9.12.2013

Philipp Hacker

*“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*

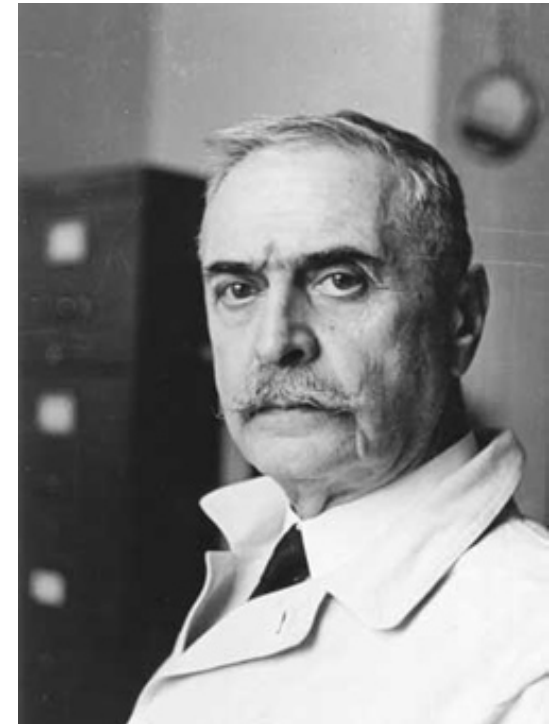


# Structure

- Karl Landsteiner – Biography
- The Discovery of the ABO 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 (ABO blood group system)
- 1923 Landsteiner moves to New York
- 1930 Nobel Price for medicine
- Dies on 26 June 1943 in New York



1 "Karl Landsteiner - Biographical". *Nobelprize.org*. Nobel Media AB 2013. Web. 6 Dec 2013.

[http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1930/landsteiner-bio.html](http://www.nobelprize.org/nobel_prizes/medicine/laureates/1930/landsteiner-bio.html)

2 Karl Landsteiner . Web. 6 Dec 2013. [http://www.pbs.org/wnet/redgold/innovators/bio\\_landsteiner2.html](http://www.pbs.org/wnet/redgold/innovators/bio_landsteiner2.html)

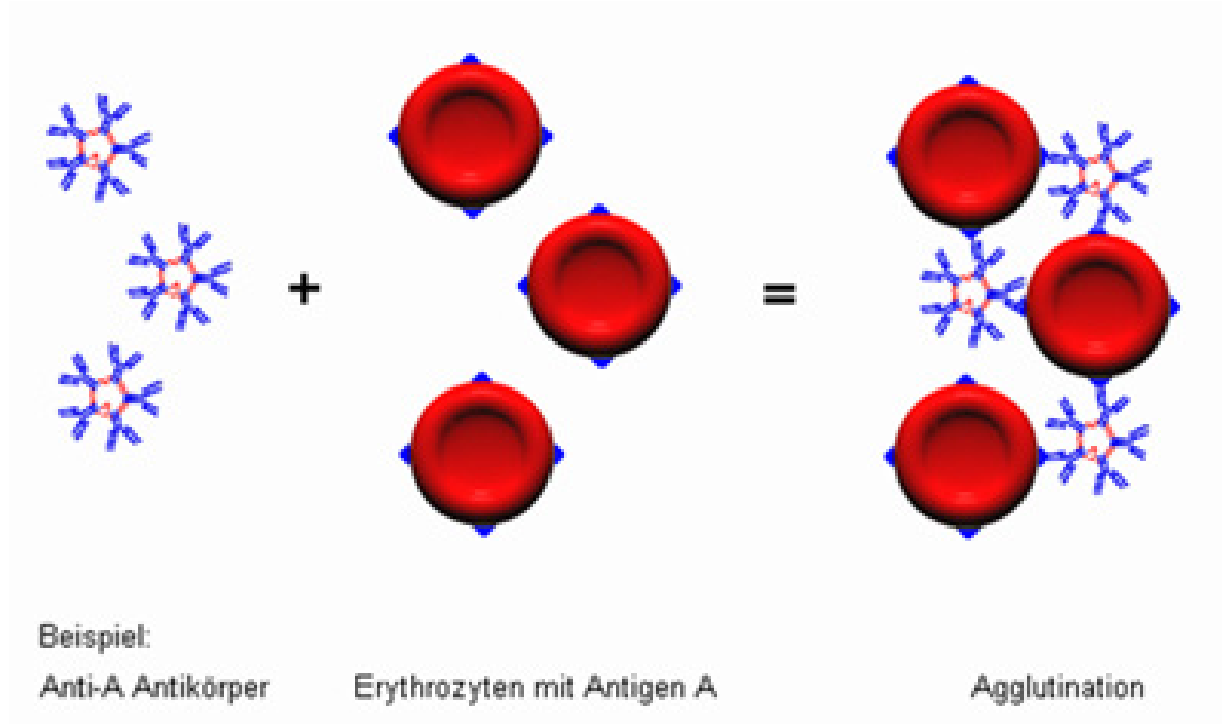
# The Discovery of the ABO Blood groups

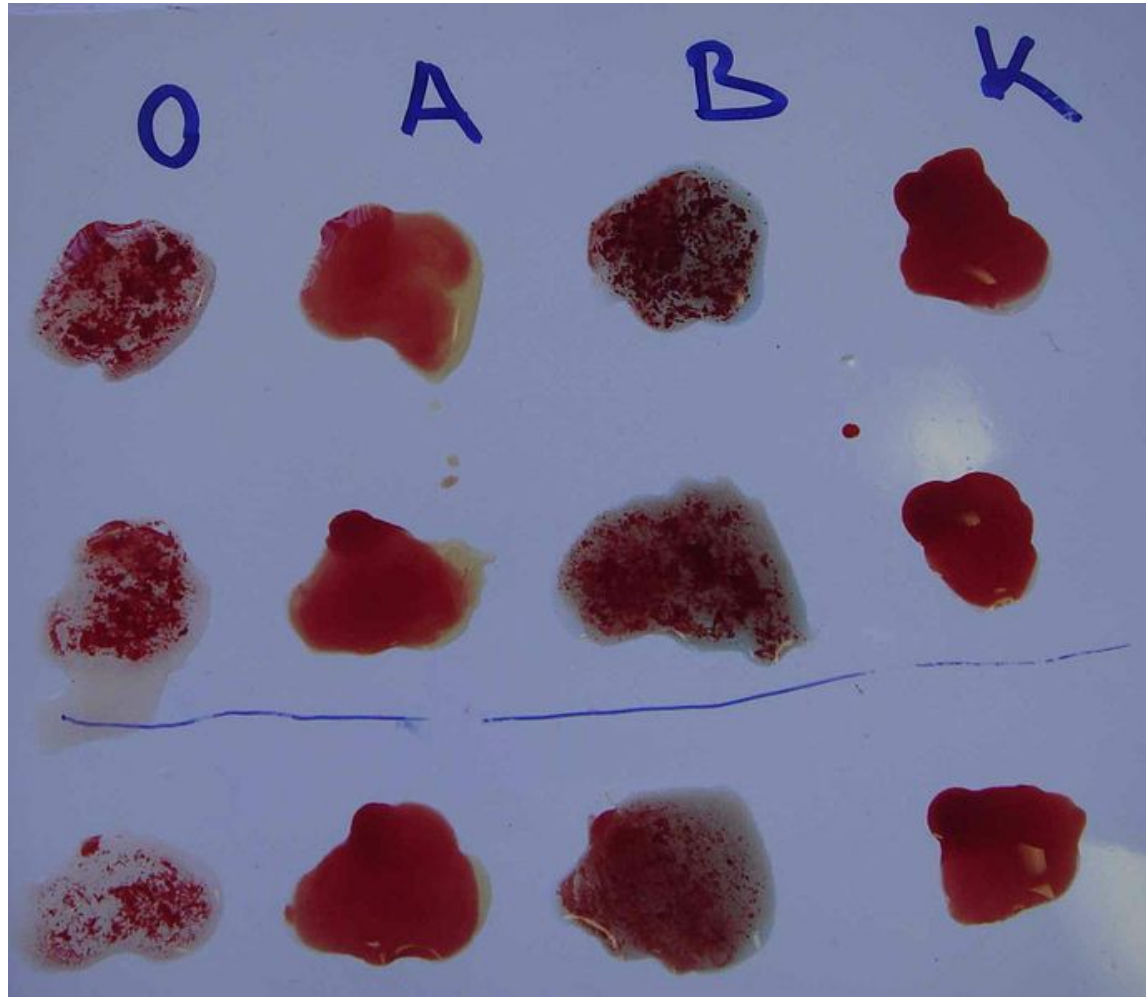
- Before Landsteiner's discovery it was well known that if blood of different animals was mixed **agglutination** would occur
- The idea that blood from two humans would cause the same reaction was novel

1Tan SY et al., *Karl Landsteiner (1868–1943): Originator of ABO blood classification*. Singapore Med J. 2013

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





# Landsteiner's Experiment

- In 1900 Landsteiner crosstested six sera and erythrocytes of his own blood and five coworkers and “accidentally” discovered human blood groups
- Landsteiners **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

1Tan SY et al., *Karl Landsteiner (1868–1943): Originator of ABO blood classification*. Singapore Med J. 2013

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- 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).”*

- 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) agglutinirt das Serum die Körperchen von A und B, während die Körperchen C durch die Sera von A und B nicht beeinflusst werden.“*

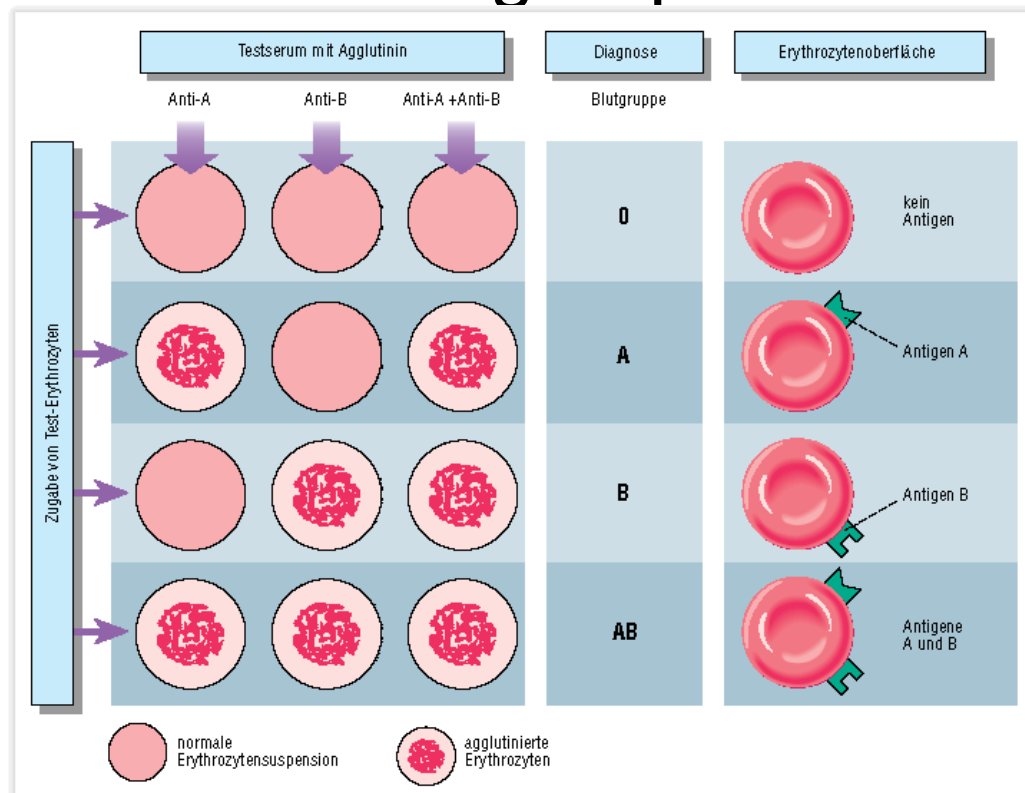
- **Landsteiner's conclusions:**
  - Human blood can be categorized into blood groups referring to the inherent individual physiological differences of the expressed antigens
  - He thought that his observation might explain the variable clinical consequences of human blood transfusion (antibodies!)
  - 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

<sup>1</sup>Tan SY et al., *Karl Landsteiner (1868–1943): Originator of ABO blood classification*. Singapore Med J. 2013

<sup>2</sup> Figl M et al. *Karl Landsteiner, the discoverer of blood groups*, Resuscitation, 2004

<sup>3</sup> 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



# ABO-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

Serum of group	Agglutinins in serum	Erythrocytes of group			
		O	A	B	AB
O	$\alpha\beta$	-	+	+	+
A	$\beta$	-	-	+	+
B	$\alpha$	-	+	-	+
AB	-	-	-	-	-

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

2 *ABO and H Blood Groups*. <http://www.austincc.edu/kotrla/bblec6ABOSPG05.pdf> . Web. 7 Dec 13

# 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

2 *ABO and H Blood Groups*. <http://www.austincc.edu/kotrla/bblec6ABOSPG05.pdf> . Web. 7 Dec 13

# 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**

No.	System name	System symbol	Gene name(s)*	Chromosomal location	CD numbers
001	ABO	ABO	<i>ABO</i>	9q34.2	
002	MNS	MNS	<i>GYPA, GYPB, GYPE</i>	4q31.21	CD235
003	P1PK	P1PK	<i>A4GALT</i>	22q13.2	
004	Rh	RH	<i>RHD, RHCE</i>	1p36.11	CD240
005	Lutheran	LU	<i>LU</i>	19q13.32	CD239
006	Kell	KEL	<i>KEL</i>	7q34	CD238
007	Lewis	LE	<i>FUT3</i>	19p13.3	
008	Duffy	FY	<i>DARC</i>	1q23.2	CD234
009	Kidd	JK	<i>SLC14A1</i>	18q12.3	
010	Diego	DI	<i>SLC4A1</i>	17q21.31	CD233
011	Yt	YT	<i>ACHE</i>	7q22.1	
012	Xg	XG	<i>XG, MIC2</i>	Xp22.33	CD99+
013	Scianna	SC	<i>ERMAP</i>	1p34.2	
014	Dombrock	DO	<i>ART4</i>	12p12.3	CD297
015	Colton	CO	<i>AQP1</i>	7p14.3	
016	Landsteiner-Wiener	LW	<i>ICAM4</i>	19p13.2	CD242
017	Chido/Rodgers	CH/RG	<i>C4A, C4B</i>	6p21.3	
018	H	H	<i>FUT1</i>	19q13.33	CD173
019	Kx	XK	<i>XK</i>	Xp21.1	
020	Gerbich	GE	<i>GYPE</i>	2q14.3	CD236

No.	System name	System symbol	Gene name(s)*	Chromosomal location	CD numbers
021	Cromer	CROM	<i>CD55</i>	1q32.2	CD55
022	Knops	KN	<i>CR1</i>	1q32.2	CD35
023	Indian	IN	<i>CD44</i>	11p13	CD44
024	Ok	OK	<i>BSG</i>	19p13.3	CD147
025	Raph	RAPH	<i>CD151</i>	11p15.5	CD151
026	John Milton Hagen	JMH	<i>SEMA7A</i>	15q24.1	CD108
027	I	I	<i>GCNT2</i>	6p24.2	
028	Globoside	GLOB	<i>B3GALT3</i>	3q26.1	
029	Gill	GIL	<i>AQP3</i>	9p13.3	
030	Rh-associated glycoprotein	RHAG	<i>RHAG</i>	6p21-qter	CD241
031	FORS	FORS	<i>GBGT1</i>	9q34.13	
032	JR	JR	<i>ABCG2</i>	4q22	
033	LAN	LAN	<i>ABCB6</i>	2q36	

## 1 The International Society of Blood Transfusion

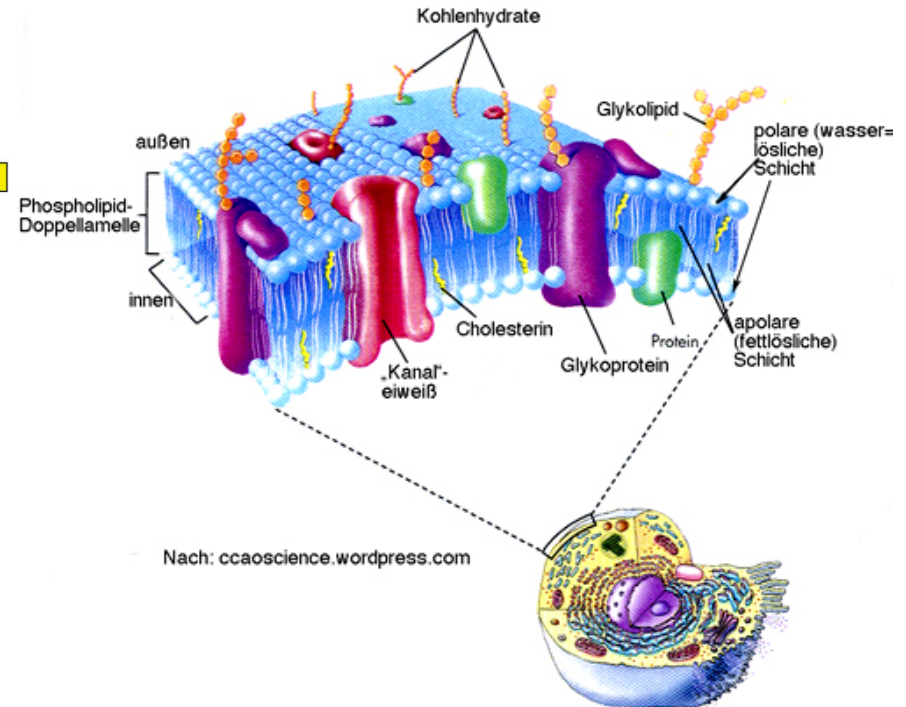
[http://www.isbtweb.org/fileadmin/user\\_upload/WP\\_on\\_Red\\_Cell\\_Immunogenetics\\_and/Table\\_of\\_blood\\_group\\_systems\\_v3.0\\_121028.pdf](http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/Table_of_blood_group_systems_v3.0_121028.pdf) . Web. 7 Dec. 13



# ABO 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

- H-Substance is precursor for different blood groups

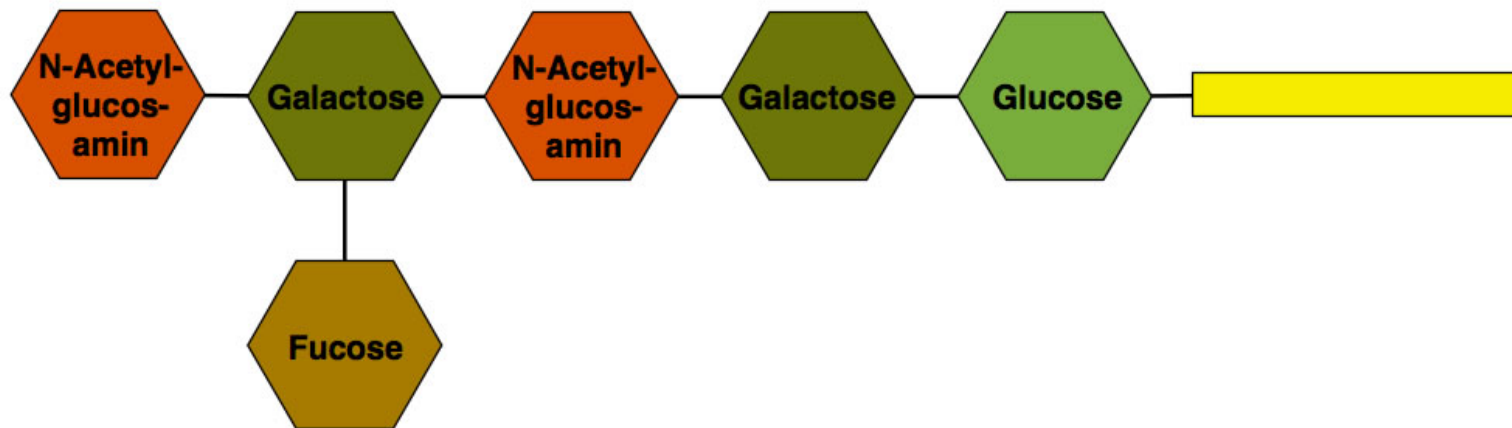


# Blood group 0



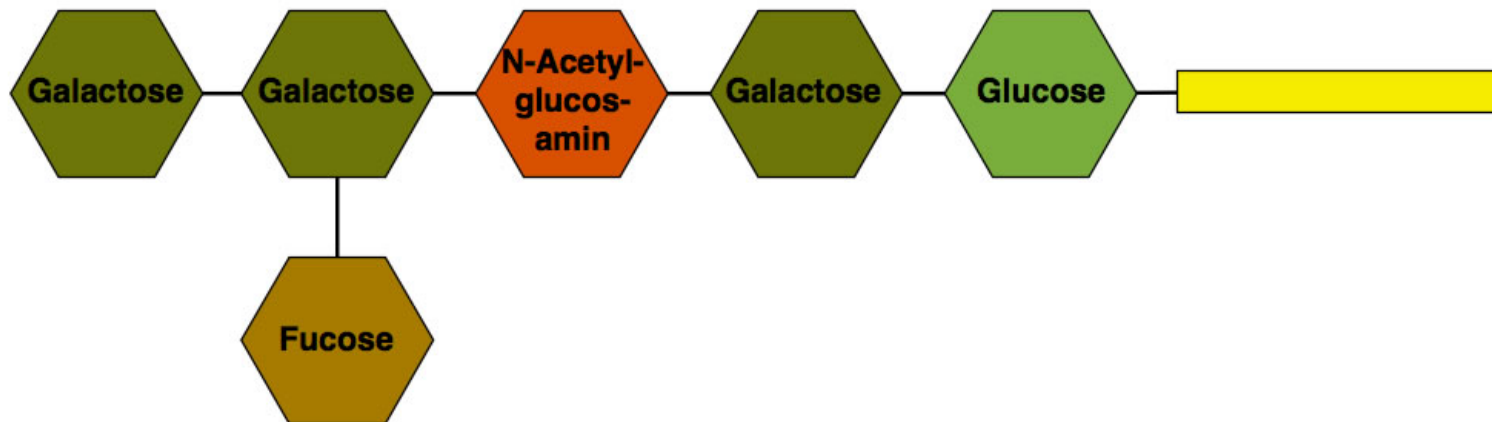
0-Allel encodes for an enzyme with no enzymatic activity.  
Therefore the H-antigen is not modified and blood group 0 is the result.  
Terminal fucose reacts as active antigen for blood group 0.

# Blood group A



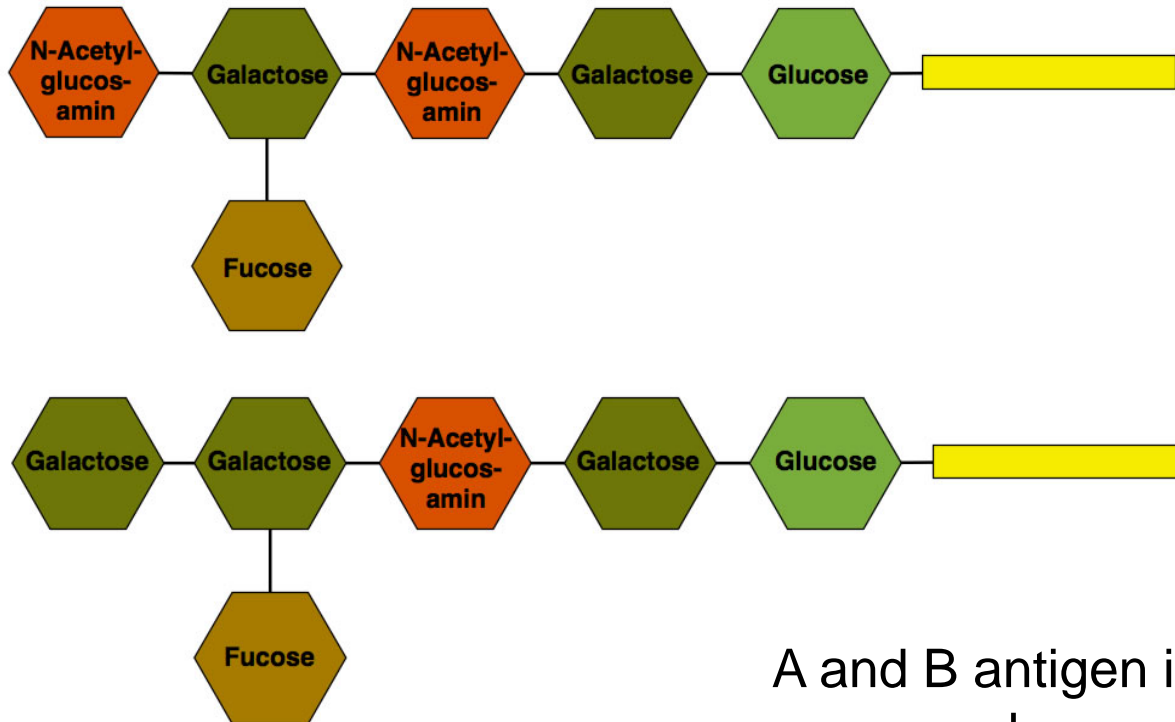
A-Allel on Chromosome 9 encodes for a glycosyltransferase which adds a N-Acetyl-glucosamin to galactose of H-antigen.

# 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.

# Blood group AB



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

# 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

# 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 kern icterus
  - Blood transfusion had a higher success rate



# Blood groups frequency

Blutgruppe	Häufigkeit weltweit
<b>0+</b>	38%
<b>A+</b>	34%
<b>B+</b>	9%
<b>0-</b>	7%
<b>A-</b>	6%
<b>AB+</b>	3%
<b>B-</b>	2%
<b>AB-</b>	1%

Blutgruppenmerkmal	Häufigkeit		
	Deutschland	Österreich	Schweiz
A	43%	41%	47%
0	41%	37%	41%
B	11%	15%	8%
AB	5%	7%	4%
Rhesus positiv	85%	85,5%	85%
Rhesus negativ	15%	14,5%	15%
Kell negativ	91%	91%	
Kell positiv	9%	9%	

# 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

2 Watkins WM, *The ABO blood group system: historical background*. Transfusion Medicine, 2001

# 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

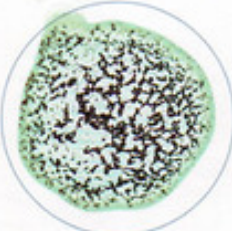
- Cross-Test

		YOU CAN RECEIVE TYPE							
		O+	O-	A+	A-	B+	B-	AB+	AB-
I F  Y O U  A R E  T Y P E	O+	*	*						
	O-		*						
	A+	*	*	*	*				
	A-		*		*				
	B+	*	*			*	*		
	B-		*				*		
	AB+	*	*	*	*	*	*	*	*
	AB-		*		*		*		*


O - = universal donor → no antigens  
 AB + = universal recipient → no antibodies

# Bedside-test


**Serafol® ABO+D**



**Anti-A**



**Anti-B**



**Anti-D**

Ch.-B./Lot No. **080601** Expiry date **31.12.01**


Blut (Blood/Sang)

Name (Name/ Nom) \_\_\_\_\_

Geb.Dat. (Date of Birth/ Date de Naissance) \_\_\_\_\_ Kons.-Nr. (Unit No./ No.Poche) \_\_\_\_\_


Datum (Date) 1/1/02 Blutgruppe (Blood Group/ Groupe Sanguin) A POS

Unterschrift (Signature) \_\_\_\_\_



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