

Abstract from Cardiovascular Physiology Booklet

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StudyAid is a student organization at the Jagiellonian University in Krakow. Throughout the academic year we host seminars in the major theoretical subjects: anatomy, physiology, biochemistry, immunology, pathophysiology, supplementing the lectures provided by the university. We are a group of 25 tutors, who are students at JU, each with their own field of specialty. To make our seminars as useful and relevant as possible, we teach in an interactive manner often using drawings and diagrams to help students remember the concepts. In addition to most seminars we create booklets, on which the seminars are based to aid the students in following the presentations. If you have any questions, do not hesitate to contact StudyAid at www.studyaid.no, we are always happy to answer any questions you may have academically related or not.

Section 7 – Blood

5.0 – Composition

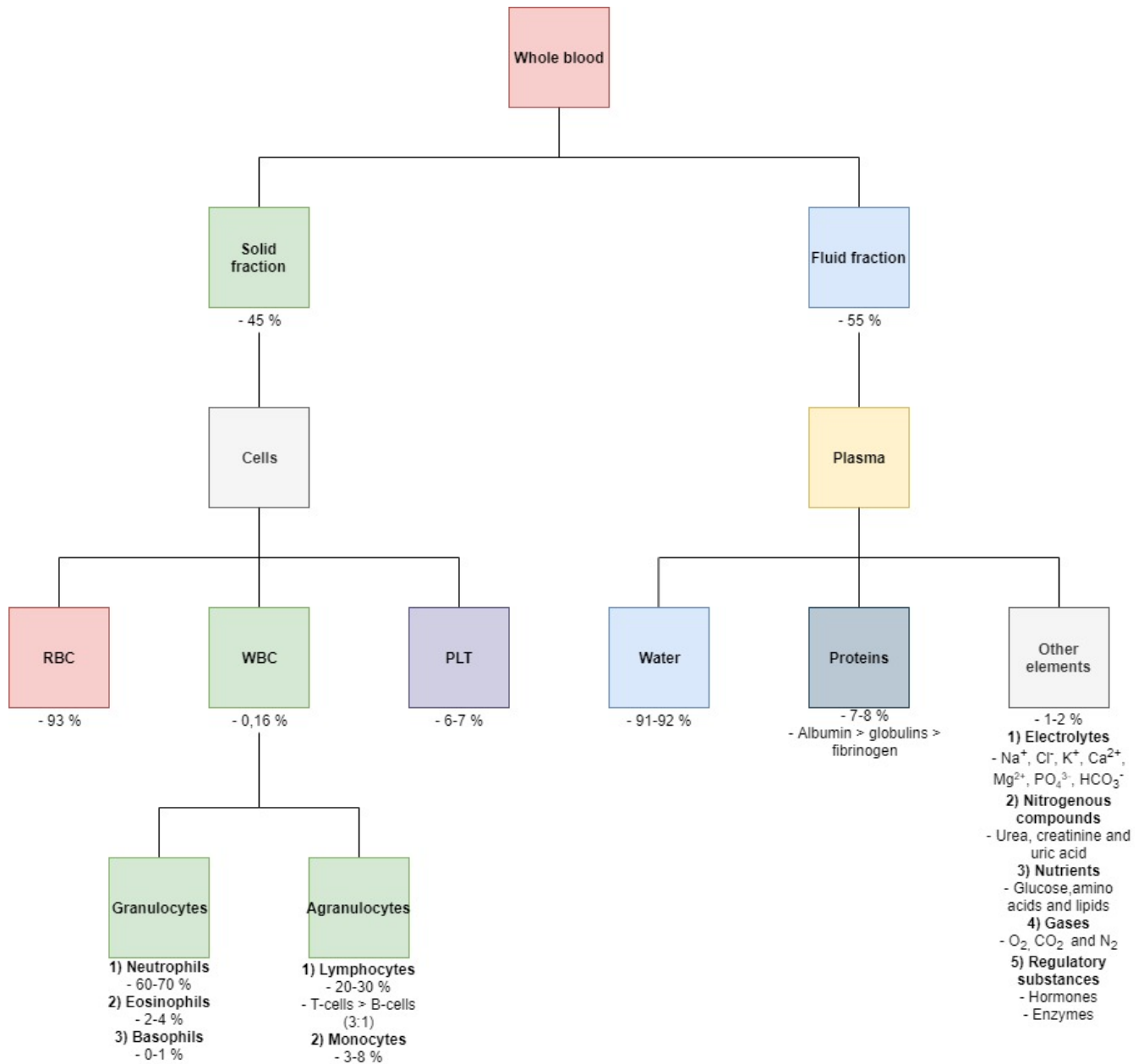
5.1 – Cells

5.2 – Blood Groups

5.4 – Serological Conflicts

5.5 – Test Yourself

5.0 – Composition



MNEUMONIC

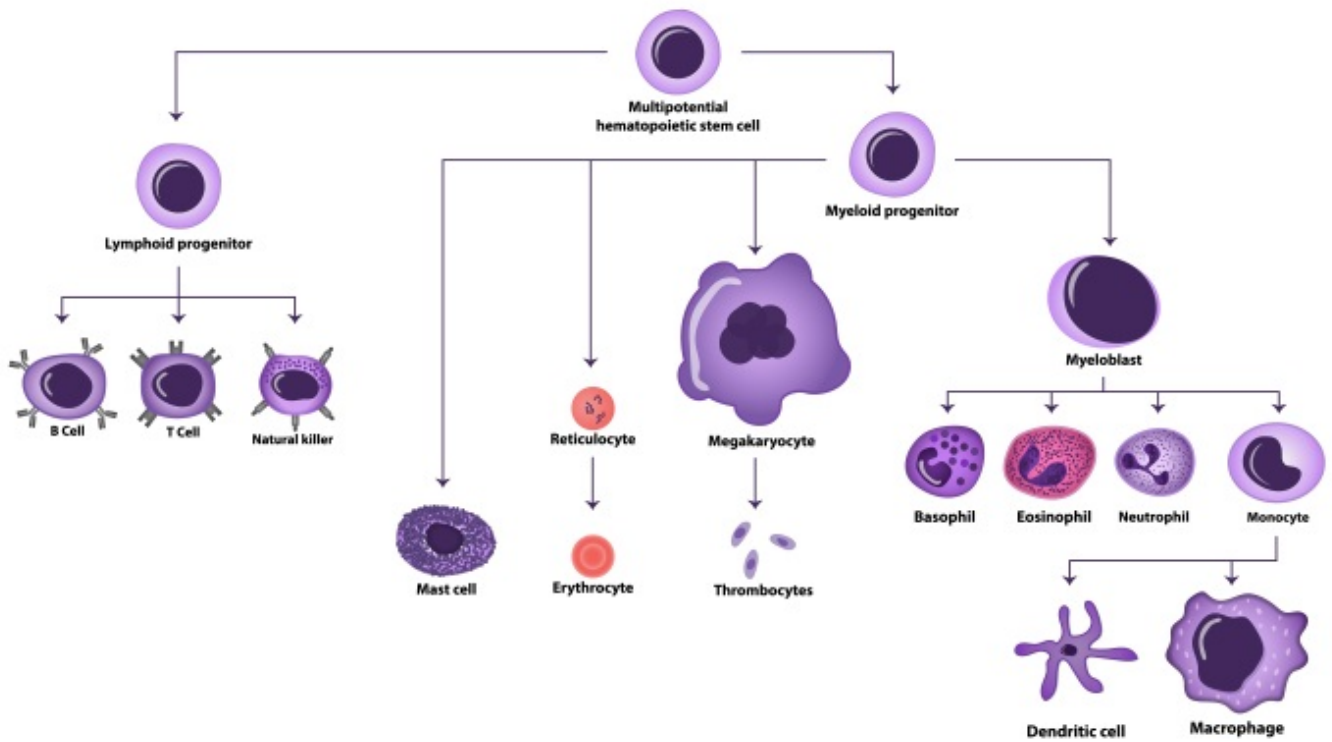
How to remember the order of
WBC based on abundance?

- **N**ever **L**et **M**onkeys **E**at **B**ananas

5.1 – Cells

5.1.1 – Hematopoiesis

- Refers to the process by which blood cells are formed
- Occurs in the bone marrow
- The common progenitor of all blood cells are the CD34⁺ hematopoietic stem cells (HSCs)



5.1.2 – Red Blood Cells, White Blood Cells and Platelets

	Red blood cells	White blood cells	Platelets
Scientific name	- Erythrocytes	- Leukocytes	- Thrombocytes
Origin	- Bone marrow	- Bone marrow	- Bone marrow
Removed by	- Spleen	- Spleen	- Spleen
Stimulated by	- Erythropoietin (EPO)	- Cytokines - Colony-stimulating factors (CSF)	- Thrombopoietin (TPO)
Percentage distribution¹	- 93 %	- 0, 16 %	- 6-7 %
Normal range	- 4,000,000-6,000,000 ² cells/mm ³	- 4,000-10,000 cells/mm ³	- 150,000-400,000 cells/mm ³
Relative size	- Medium	- Large	- Small
Function	- Transport of O ₂ and CO ₂	- Immunological defense	- Hemostasis
Division in peripheral blood	- No ³	- Yes ⁴ and no ⁵	- No ⁶
Life span	- 90-120 days	- Depends ⁷	- 3-5 days
Appearance		- See section 5.2.2	

¹ Percentage distribution in the cellular fraction of whole blood

² The normal range of RBC depends on gender - 4,000,000 represents the lower limit of the normal range in females, while 6,000,000 represents the upper limit of the normal range in males

³ Absence of nucleus

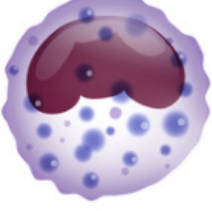
⁴ Lymphocytes divide after entering peripheral blood, because they have a nucleus

⁵ Granulocytes do not divide after entering peripheral blood, because their DNA is partly euchromatin and heterochromatin

⁶ Absence of nucleus

⁷ Granulocytes have a lifespan of 12-16 hours, while lymphocytes may live for days-months-years (*depending on the specific subtype*)

5.1.3 – Granulocytes and Macrophages

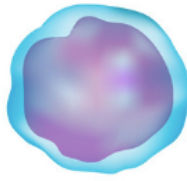
	Neutrophils	Macrophages	Eosinophils	Basophils
Origin	- Bone marrow	- Bone marrow ¹	- Bone marrow	- Bone marrow
Localization	- Blood	- Tissues ²	- Blood	- Blood
Protects against	- Extracellular bacteria	- Intracellular bacteria	- Parasites - Worms	- Parasites ³
Appearance		Monocyte  Macrophage 		

¹ Produced as monocytes

² Monocytes typically circulate in the blood for 1-3 days, before they migrate to the tissue and convert into macrophages

³ The role of basophils in the defense against parasites is somewhat unclear

5.1.4 – B – and T-lymphocytes

	B-cells	T-cells
Origin	- Bone marrow	- Bone marrow
Maturation	- Bone marrow	- Thymus
Immunological response	- Humoral ¹	- Cellular ²
Function	- Production of antibodies	- Kill cells infected with virus, fungi or cancer
Appearance		

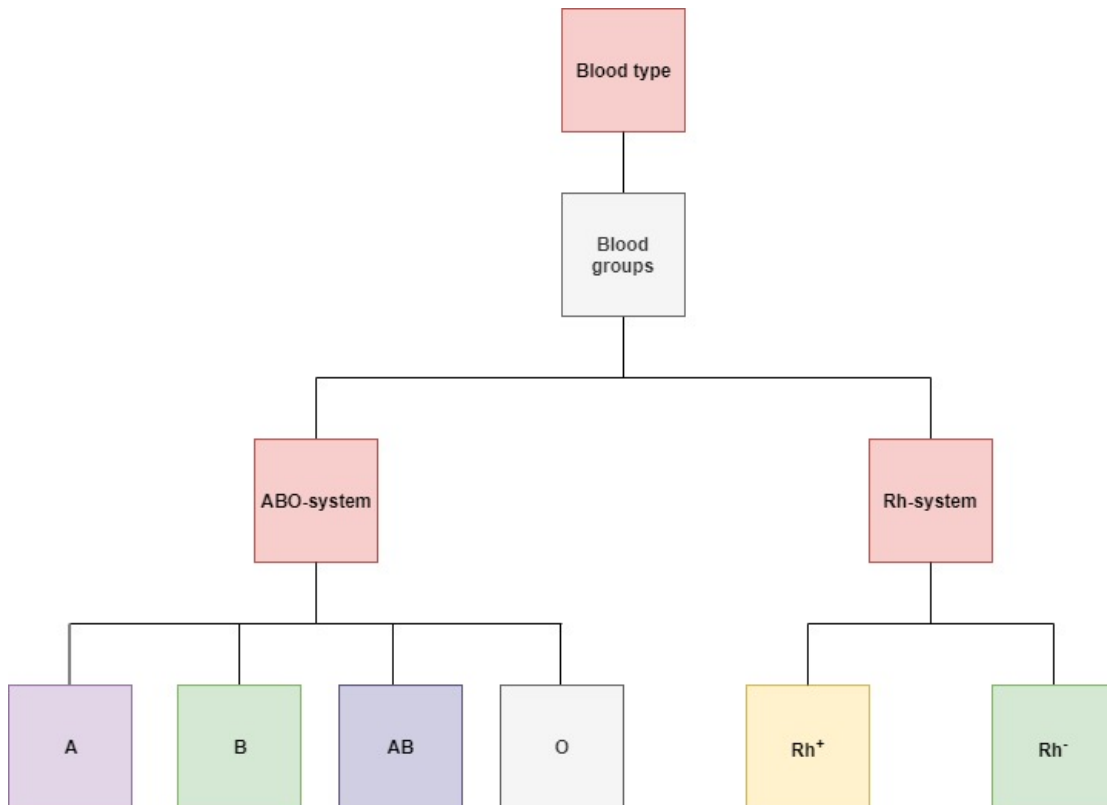
¹ Antibody-mediated immunological response

² Cellular-mediated immunological response

5.2 - Blood Groups

5.2.1 – Overview

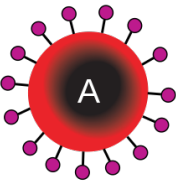
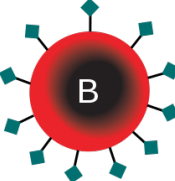
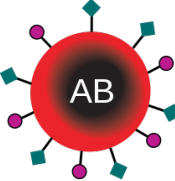
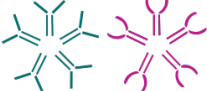
- There are 35 known human blood groups
- The ABO – and Rh-system are the most important



5.2.2 - ABO System

I. Overview

- Antigens determine the ABO-status
- Antibodies are present against the antigen you do not have
- Sensitization does not have to occur

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

II. Compatibility

DONOR	RECIPIENT			
		AB	A	B
	AB	Yes	No	No
	A	Yes	Yes	No
	B	Yes	No	Yes
	O	Yes	Yes	Yes

STEPWISE APPROACH TO FILLING IN THE COMPATIBILITY CHARTS

1) General rules

- Determine the axis (*recipient, donor*)
- Fill in the universal recipient and the universal donor

2) ABO-system

- Antibodies are present against the antigen you do not have

5.2.3 – Rh-System

I. Overview

- The presence or absence of expression of the Rh-D antigen determine the Rh-status
- Majority of individuals are Rh⁺
- Sensitization has to occur

II. Mode of inheritance

- Autosomal dominant

		father				father	
		D	D			D	d
mother	d	Dd	Dd	mother	d	Dd	dd
	d	Dd	Dd		d	Dd	dd
100% Rh+ children				50% Rh+ children			

III. Compatibility

DONOR	RECIPIENT								
		AB ⁺ 2	AB ⁻	A ⁺	A ⁻	B ⁺	B ⁻	O ⁺	O ⁻
	AB ⁺	Yes	No	No	No	No	No	No	No
	AB ⁻	Yes	Yes	No	No	No	No	No	No
	A ⁺	Yes	No	Yes	No	No	No	No	No
	A ⁻	Yes	Yes	Yes	Yes	No	No	No	No
	B ⁺	Yes	No	No	No	Yes	No	No	No
	B ⁻	Yes	Yes	No	No	Yes	Yes	No	No
	O ⁺	Yes	No	Yes	No	Yes	No	Yes	No
	O ⁻ 1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

¹ Universal donor (no antigens → not recognized by the immune system of the recipient)

² Universal recipient (no antibodies → the immune system of the recipient has nothing to react with)

STEPWISE APPROACH TO FILLING IN THE COMPATIBILITY CHARTS

1) General rules

- Determine the axis (recipient, donor)
- Fill in the universal recipient and the universal donor

2) ABO-system

- Antibodies are present against the antigen you do not have

3) Rh-system

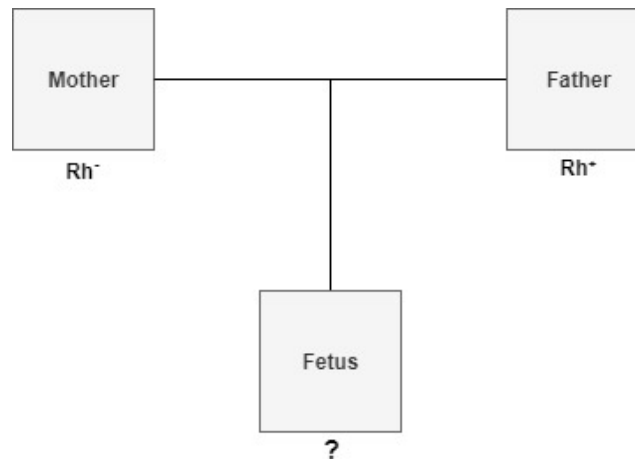
- Rh⁺ may receive blood from Rh⁺ and Rh⁻
- Rh⁻ may only receive blood from Rh⁻

5.3 – Serological Conflicts

5.3.1 – Maternal-Fetal Rh Incompatibility

I. “A Rh⁻ woman wants to have a child with a Rh⁺ man. She has never been pregnant before. What is the probability that the fetus will be Rh⁺?”

- Based on the facts that the phenotype of the man is Rh⁺ and the mode of inheritance is autosomal dominant, we can safely assume that the genotype of the man is either heterozygous or homozygous dominant



	D	d
d	Dd	dd
d	Dd	dd

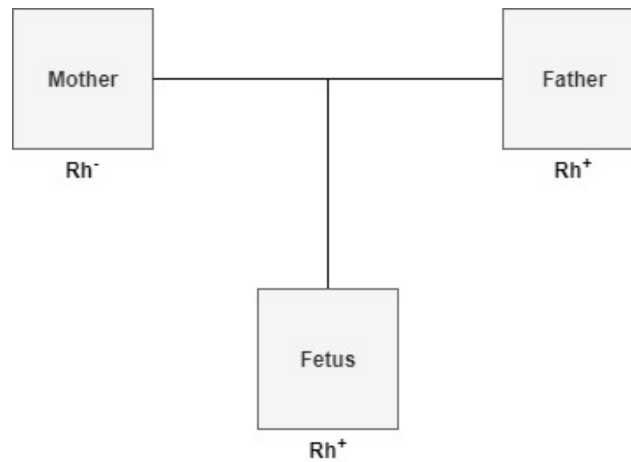
- **Male genotype:** Heterozygous
- **Female genotype:** Homozygous recessive
- **Probability:** 50 % probability that the fetus will be Rh⁺

	D	D
d	Dd	Dd
d	Dd	Dd

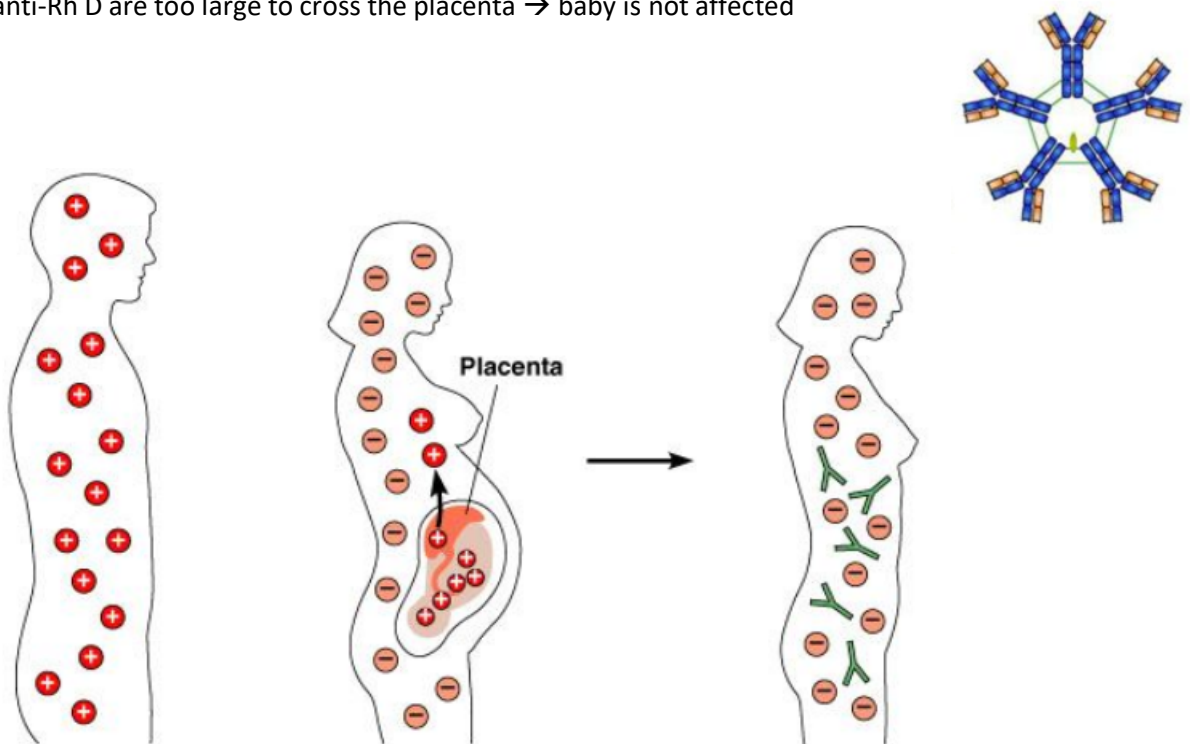
- **Male genotype:** Homozygous dominant
- **Female genotype:** Homozygous recessive
- **Probability:** 100 % probability that the fetus will be Rh⁺

II. "If the fetus ends up being Rh⁺. What will the effect be on the first pregnancy?"

- The illustration shows the setup of the 1st pregnancy



- 1st pregnancy with Rh⁺ fetus → leakage of Rh⁺ fetal RBC into the maternal circulation before, during or after delivery → sensitization → production of IgM anti-Rh D → IgM anti-Rh D are too large to cross the placenta → baby is not affected



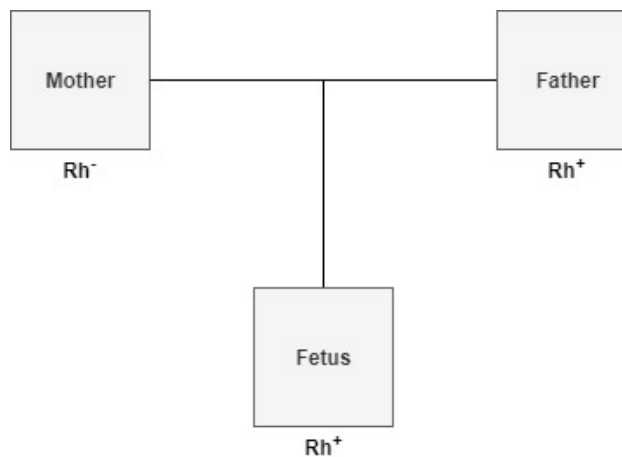
- III. During delivery of the baby, the mother starts to lose a lot of blood. Her blood pressure falls dramatically, and you consider giving her a blood transfusion. You ask the nurse to check the blood type of the patient. The nurse checks the papers and tells you that the blood type is A⁺. What type of blood can you give to the patient?

DONOR	RECIPIENT								
		AB ⁺	AB ⁻	A ⁺	A ⁻	B ⁺	B ⁻	O ⁺	O ⁻
	AB ⁺	Yes	No	No	No	No	No	No	No
	AB ⁻	Yes	Yes	No	No	No	No	No	No
	A ⁺	Yes	No	Yes	No	No	No	No	No
	A ⁻	Yes	Yes	Yes	Yes	No	No	No	No
	B ⁺	Yes	No	No	No	Yes	No	No	No
	B ⁻	Yes	Yes	No	No	Yes	Yes	No	No
	O ⁺	Yes	No	Yes	No	Yes	No	Yes	No
	O ⁻	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

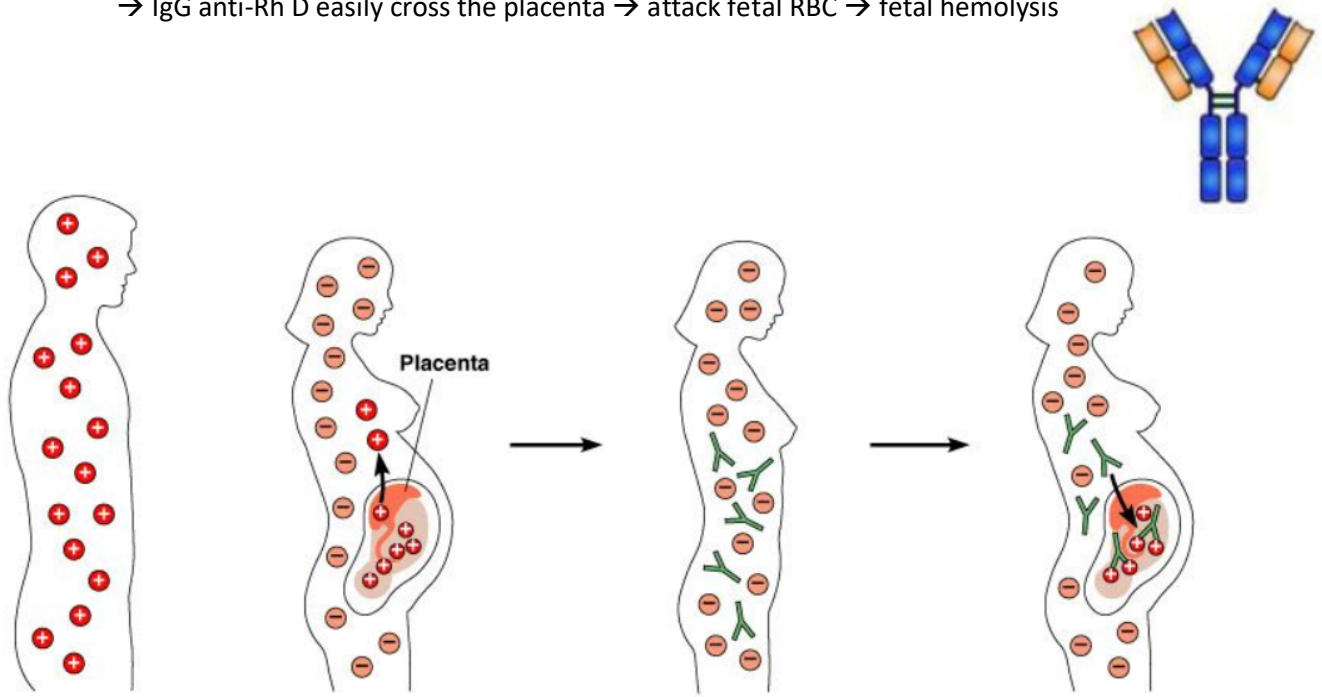
- You may give A⁺, A⁻, O⁺ and O⁻

- IV. Serological testing of the newborn reveals that the baby was in fact Rh⁺. If we assume that the same couple will have a Rh⁺ baby in the next pregnancy - what will be the effect and how can you prevent it?"

- The illustration shows the setup of the 2nd pregnancy

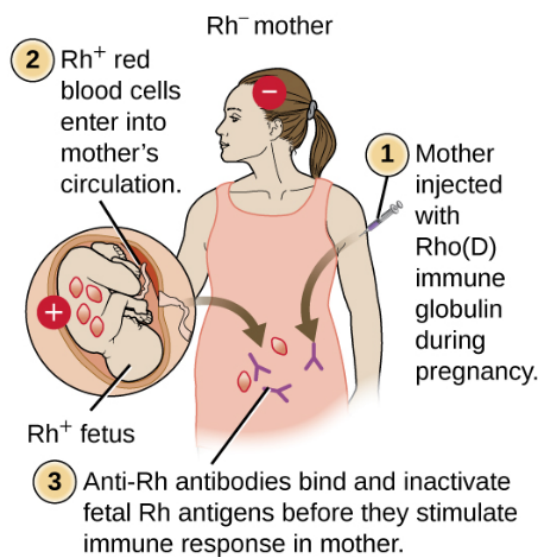


- 2nd pregnancy with Rh⁺ fetus → the antibody class is switched from IgM to IgG anti-Rh D
→ IgG anti-Rh D easily cross the placenta → attack fetal RBC → fetal hemolysis



- Injection of anti-Rh D Ig (*Rhogam*) into the Rh⁻ mother during the 1st pregnancy → anti-Rh D Ig attaches to the Rh-D antigen on leaked Rh⁺ fetal RBC
- The attachment has two major effects
- Firstly, it will “hide” the Rh-D antigen on the fetal RBC, thereby preventing sensitization in the mother
- Secondly, it will mark the fetal RBC for destruction by the spleen

First pregnancy with Rh⁺ fetus and anti-Rh antibody treatment



Section 8 – Hemostasis

8.0 – Hemostasis

8.1 – Secondary Hemostasis

8.2 – The Coagulation Cascade

8.3 – The Fibrinolytic System

8.0 – Hemostasis

I. Function

- Prevention of blood loss

II. Stages of hemostasis

1. Vasoconstriction
2. Primary hemostasis
 - Formation of a platelet plug
3. Secondary hemostasis
 - Production of fibrin, which stabilizes the platelet plug

	Primary	Secondary
Goal	- Platelet plug	- Fibrin
Mechanism	- Platelets	- Coagulation cascade
Characteristics of the clot	- Unstable	- Stable

8.1 – Secondary Hemostasis

I. Goal

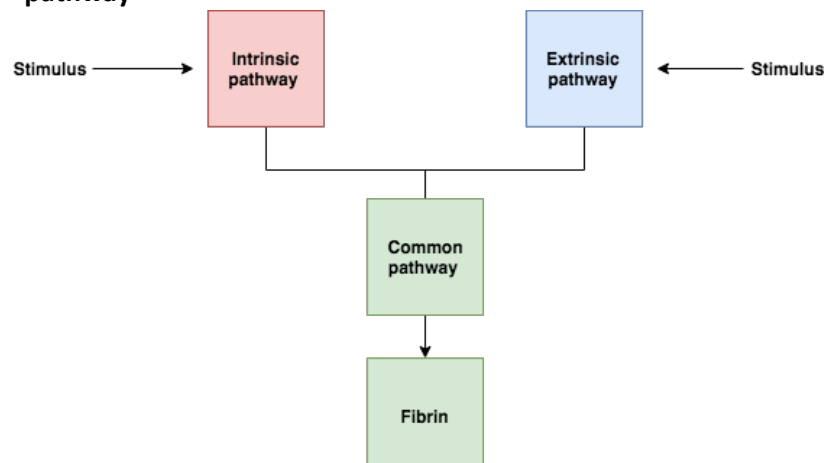
- Production of **fibrin** (*cross-linked*) by the **coagulation cascade**

II. Coagulation factors

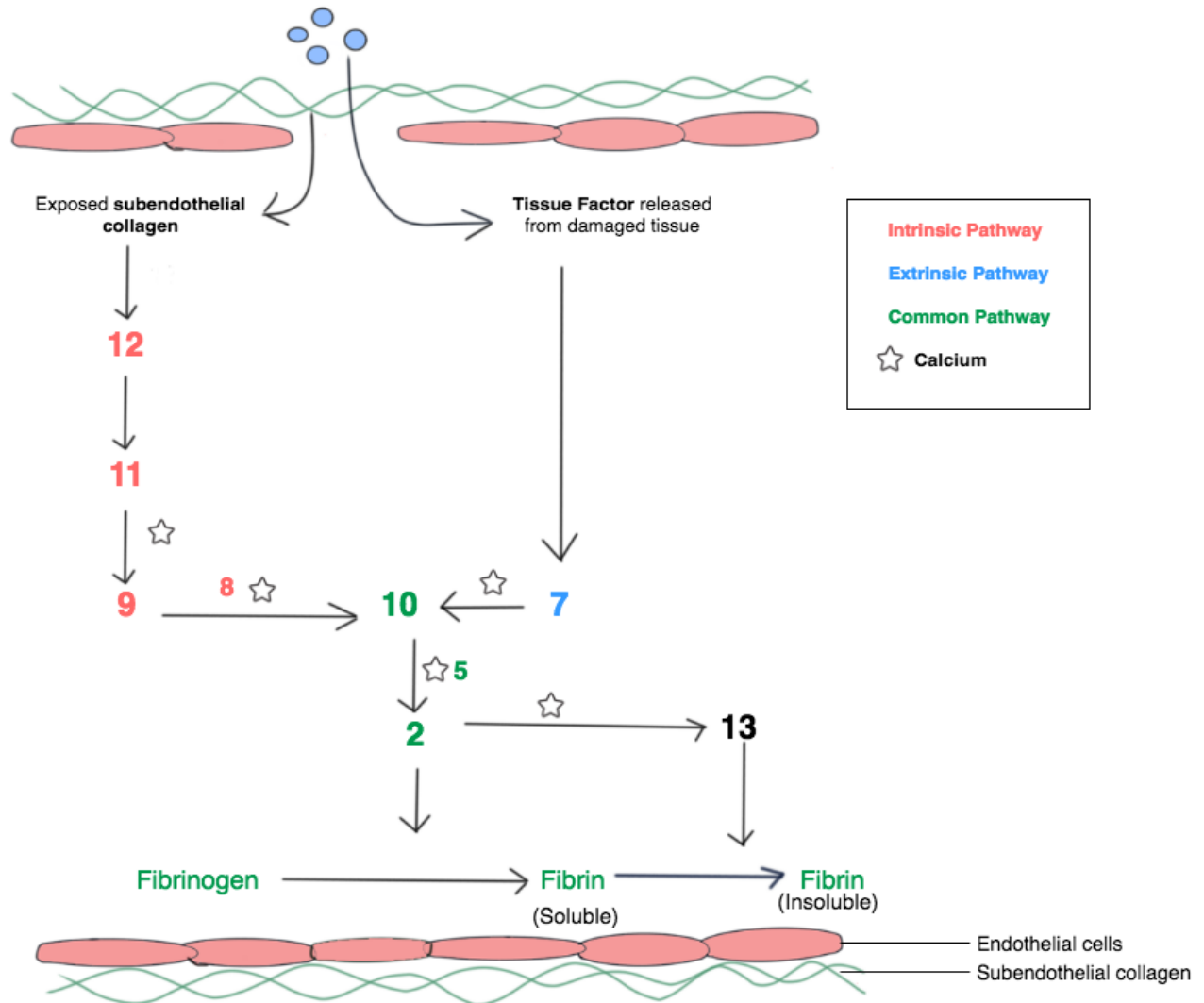
- The coagulation cascade consists of coagulation factors, which are plasma proteins produced by the liver
- Circulate in an inactive form and is activated by vascular damage through enzymatic reactions

III. Pathways

- Divided into the **intrinsic** and **extrinsic pathway**, which both activate a **common pathway**



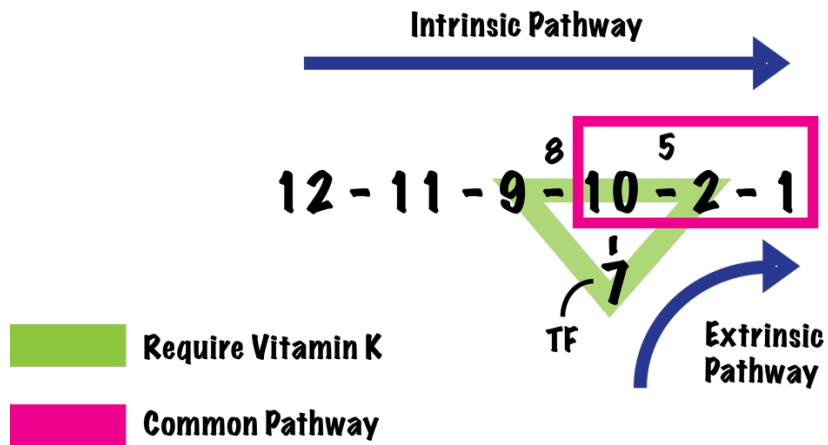
8.2 – The Coagulation Cascade



	Intrinsic	Extrinsic	Common
Activated by	- Subendothelial collagen	- Tissue factor	- Intrinsic pathway - Extrinsic pathway
Factors	- 12,11,9,8	- 7	- 10,5,2,1
Goal	- Continuing coagulation	- Initiating coagulation	- Production of thrombin - Fibrinogen → fibrin - Activation of factor 13 → cross-linked fibrin
Vitamin K - dependent¹	- 9	- 7	- 10,2
Inhibited by	- Heparin ²	- Warfarin ²	

¹ Vitamin K is stored in the liver

² Heparin and warfarin are pharmacological anticoagulants given to patients with an increased risk for clot formation

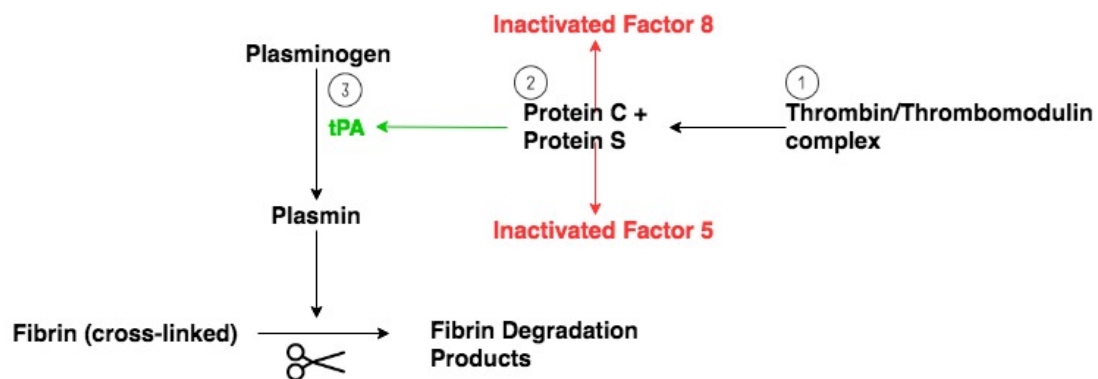


Clotting Factors		Mnemonic
I	Fibrinogen	Foolish
II	Prothrombin	People
III	Tissue Factor	Try
IV	Calcium	Climbing
V	Labile Factor	Long
VII	Stabile Factor	Slopes
VIII	Antihæmophilic factor	After
IX	Christmas Factor	Christmas
X	Stuart-Prower Factor	Some
XI	Plasma Thromboplastin Antecedent (PTA)	People
XII	Hageman Factor	Have
XIII	Fibrin Stabilizing Factor	Fallen

8.3 – The Fibrinolytic System

- Anticlotting mechanisms which function to **degrade cross-linked fibrin**
- Prevent uncontrolled clotting and remove the clot once the vessel has healed
- The result is fibrin degradation products (FDPs)

Antithrombin III is an inhibitor of the coagulation cascade. It blocks the activity of factor 2,7,9,10,11 and 12.



Event	Mechanism
1	Thrombin (activated factor 2), made during the coagulation cascade, forms a complex with thrombomodulin. This complex enables activation of Protein C and Protein S
2	Activated protein S and C will inactivate factor 8 and 5 of the coagulation cascade and activate tPA (tissue-plasminogen activator)
3	tPA converts plasminogen into plasmin, which will degrade fibrin and form fibrin degradation products

