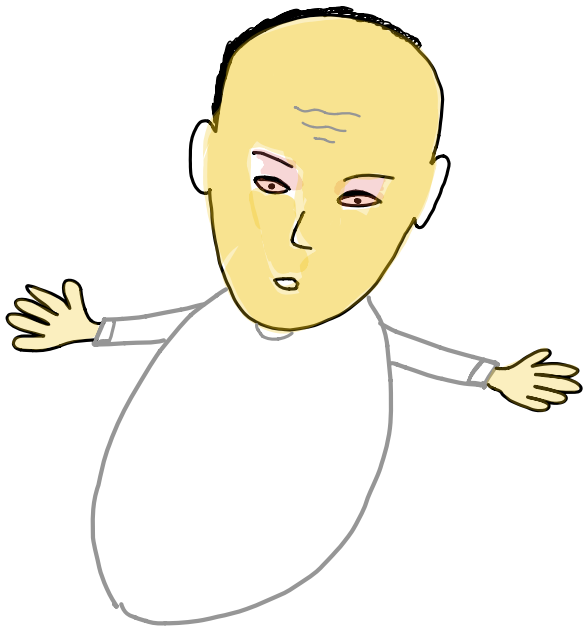
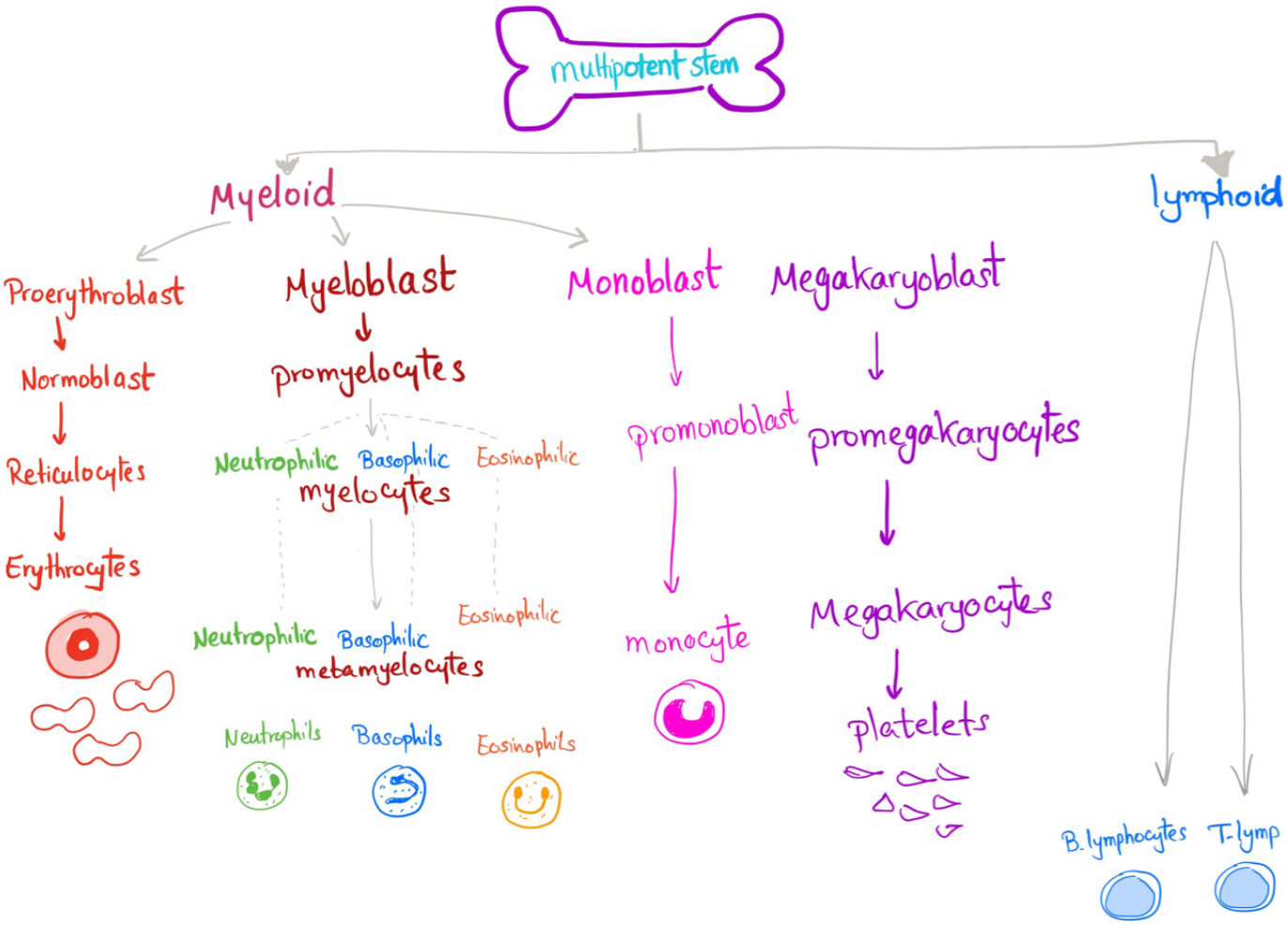
Alloimmune Hemolytic Anemia





What's anemia ?

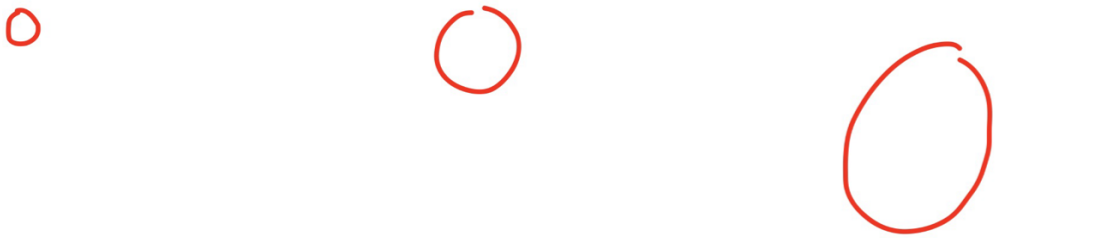
↓ Hb ↓ HCt

↓ RBC Count

MCV

<80 | 80-100 | >100

microcytic | Normocytic | Macrocytic



Anemia MCV 80-100

Acute blood loss
Retic. index < 2.5

External
Internal

Reticulocytic response
1 week later

Normal Saline ?

underproduction
Retic. index < 2.5

- ACD or iron def. [Early]
- Aplastic anemia
- Chronic renal failure
- Malignancy

Overdestruction "Hemolysis"
Retic. index > 2.5

intrinsic
Hb defect
Sickle cell

Membrane defect
Spherocytosis

Enzyme def.
Pyruvate kinase
G6PD

Extrinsic
valve
Aortic Stenosis

Complement
cold agglutinin disease

Antibodies
warm AIHA

Immune Hemolytic Anemia

Classification

1- Autoimmune Hemolytic Anemia (AIHA) — Most Common — Type II Hypersensitivity
- IgG (warm; body Temp. 37°C 98°F)
- IgM (Cold; 4°C → room Temp. 23°C 73°F)

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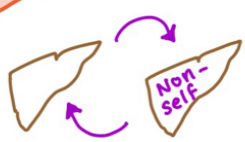


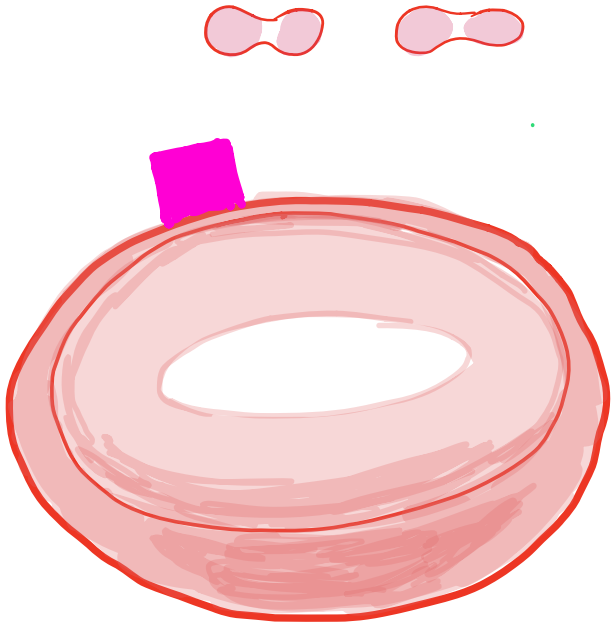
Alloimmune Hemolytic Anemia

Hemolytic Disease of the newborn
- Rh Disease
- ABO incompatibility
- Others:-
  - Anti-kell
  - Rhesus C
  - Rheusus E
  - Kidd
  - Duffy

Alloimmune Hemolytic Transfusion Reactions

ABO

Blood groups



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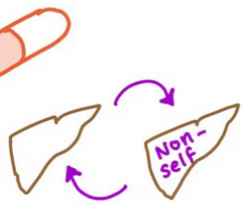

Alloimmune Hemolytic Anemia

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- Rh Disease
- ABO incompatibility "The most common"
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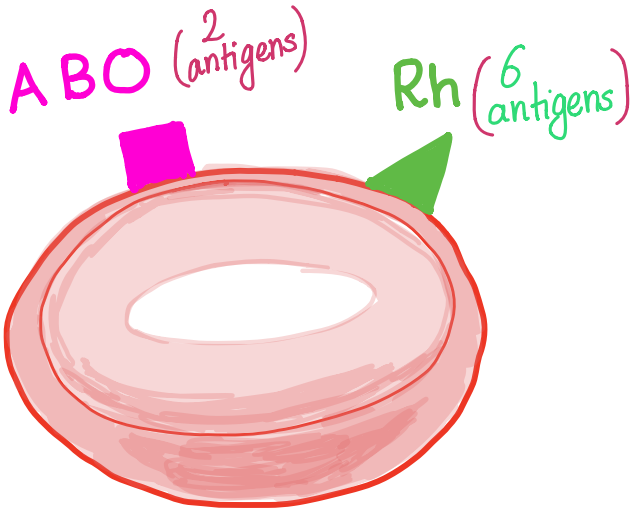
Alloimmune Hemolytic Transfusion Reactions

★ There are hundreds of antigens on RBC surfce

↳ molecule capable of inducing immune response → produce antibodies.



ABO system: antigens (agglutinogen) —triggers→ antibody (agglutinin)

2 antigens "A & B": you can have either, neither or both.

4 blood types: A , B , AB , O (phenotypes)

Genetic locus: 3 alleles: I^A, I^B, I^O ← Immunoglobulin

↳ different gene forms

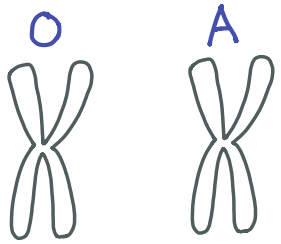
A is dominant, B is dominant, O is recessive

A & B together: Codominance

↳ Both alleles contribute to the phenotype of the heterozygote

2 chromosomes
3 alleles
: 6 possible combinations of alleles (Genotypes)

OA, OO, OB, AA, AB, BB



Genotypes	Blood types	Antigens	Anti-A	Anti-B
OO	O	—	+	+
OA / AA	A	A	−	+
OB / BB	B	B	+	−
AB	AB	A & B	−	−

Prevalence: O 47% , A 41% , B 9% , AB 3%

Agglutinins (Gamma Globulins):

IgM IgG

- At birth: you have ZERO agglutinin.
  - baby is subjected to antigen: finger in mouth, Breastfeeding, food
- 2-8 months later:- agglutinins

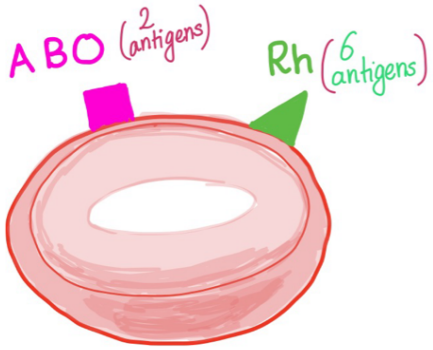
  if baby doesn't have "A" agglutinogen, he/she will produce Anti-A agglutinin
- Antibody concentration in plasma peaks at 10 years of age, then gradually declines.

Antigen + Antibody = Agglutination

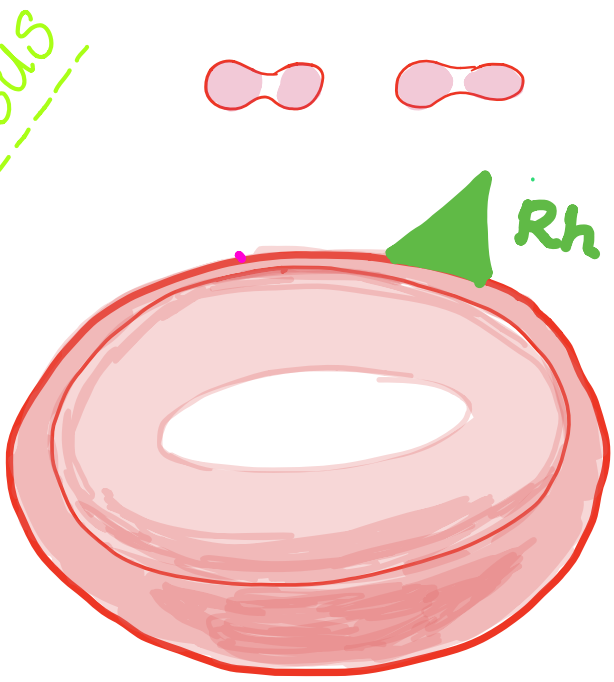
anti-A	anti-B	∴ Blood group
✓	–	A
–	✓	B
✓	✓	AB
–	–	O

Blood Typing

Blood matching



Rh Blood types



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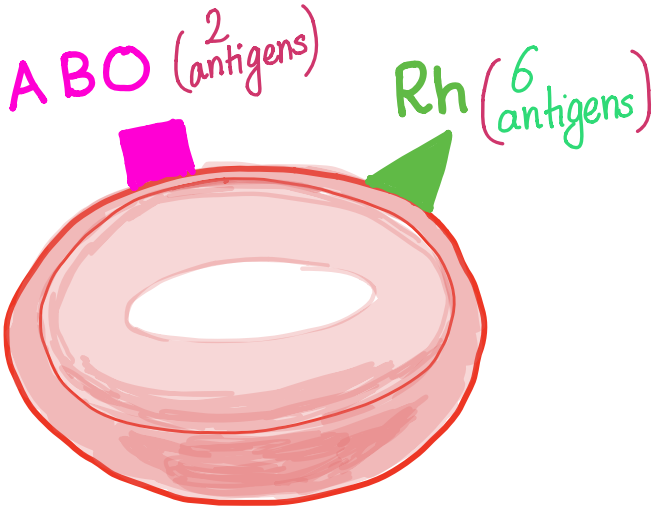


C D E c d e

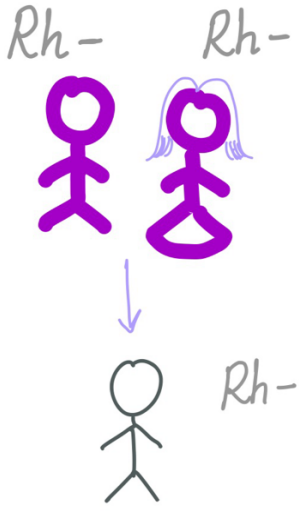
you have 1 of each of the 3 pairs of Rh antigens

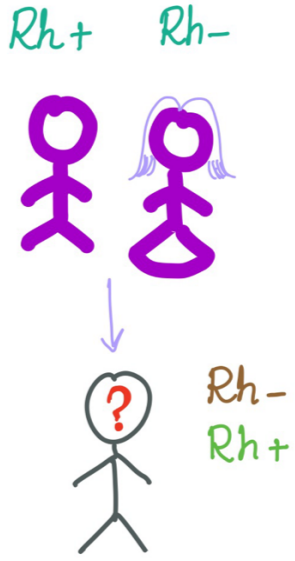
if you have D antigen → you're Rh-positive

if you do not → Rh-negative

prevalence among ethnicities

	Whites	American Blacks	African Blacks
Rh (+ve)	85% of whites	95%	≈ 100%
Rh (-ve)	15%	5%	—





ABO system

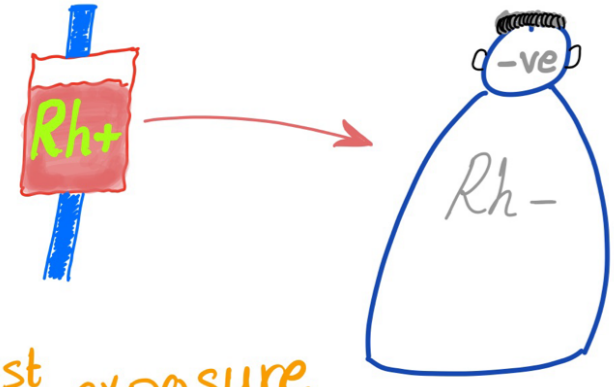
- Spontaneous agglutinins
- Not require previous exposure

Rh system

- No spontaneous agglutinins
- Requires previous exposure

SENSITIZED

2nd response will be faster and stronger

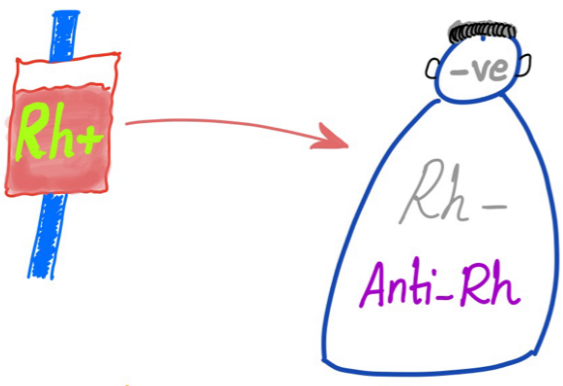


1st exposure

- No immediate reaction
- Anti-Rh antibodies will gradually form in ≃ 3 weeks.

if blood is still there → hemolysis by tissue macrophages

∵ few → mild or no hemolysis



2nd exposure

- immediate & severe reaction

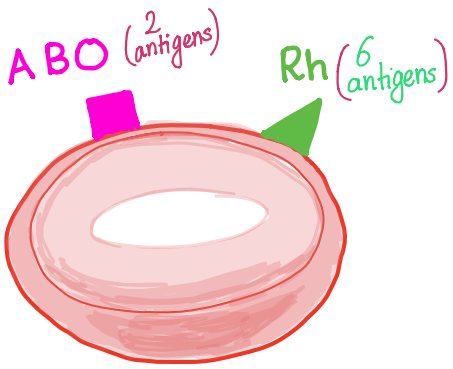
faster & stronger

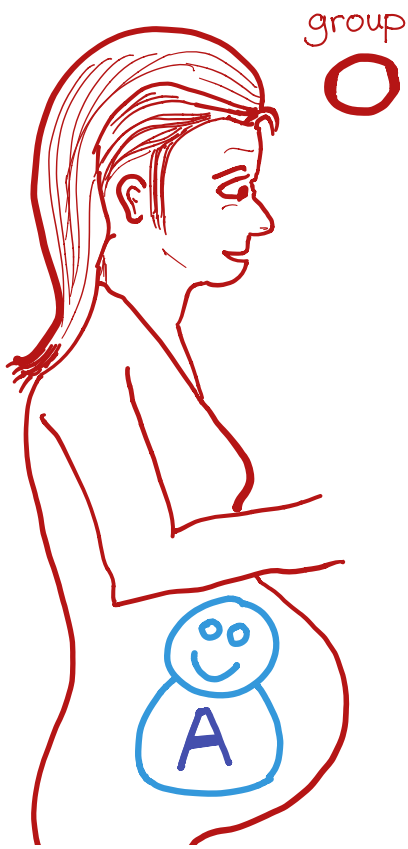
↳ severe extravascular hemolysis

Jaundice ←

ABO Hemolytic Disease of the Newborn

INCOMPATIBILITY





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Alloimmune Hemolytic Anemia

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  - ABO incompatibility "more common, less severe"
  - Rh Disease "less common, more severe"
  - Others:-
    - Anti-kell
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ABO incompatibility "more common, less severe" → can trigger DIC

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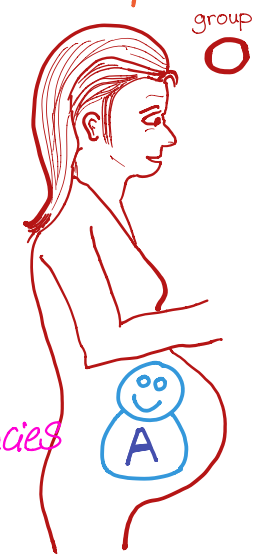


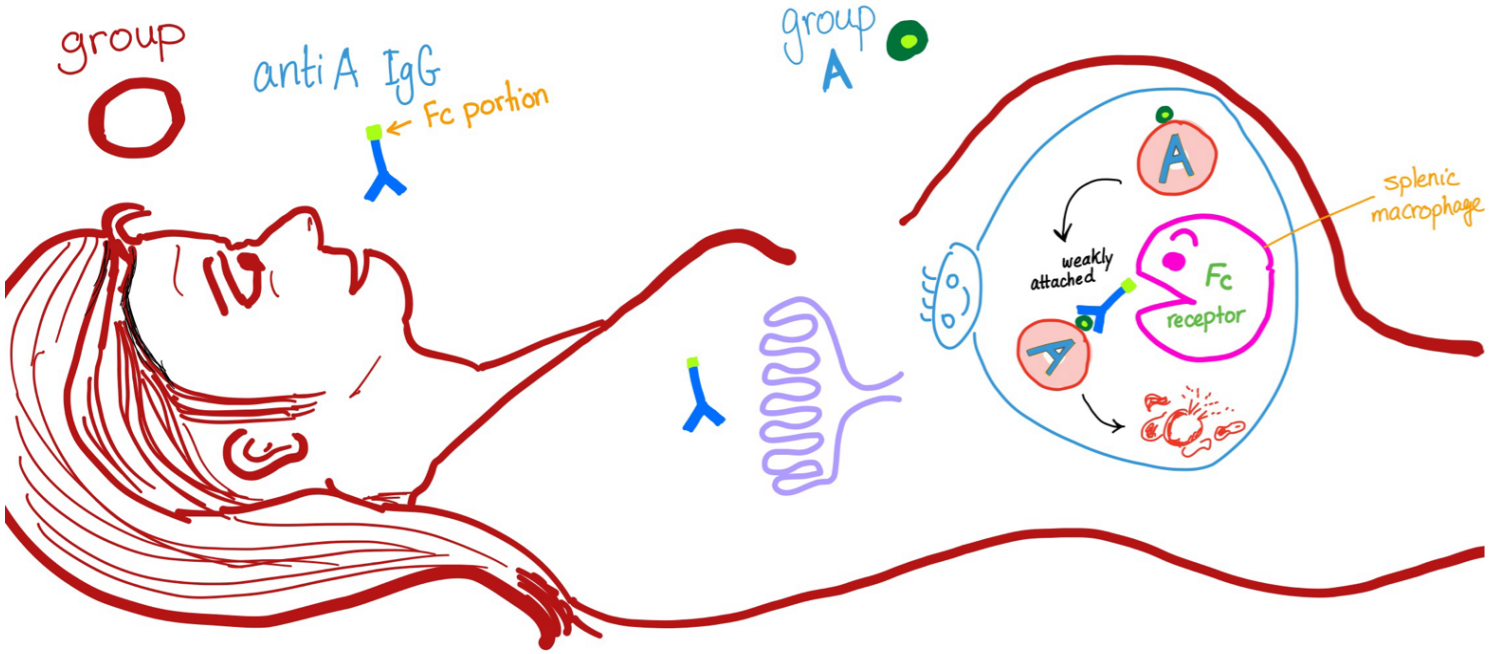
mother
O
IgG anti A & Anti B

baby
A or B
anti B anti A

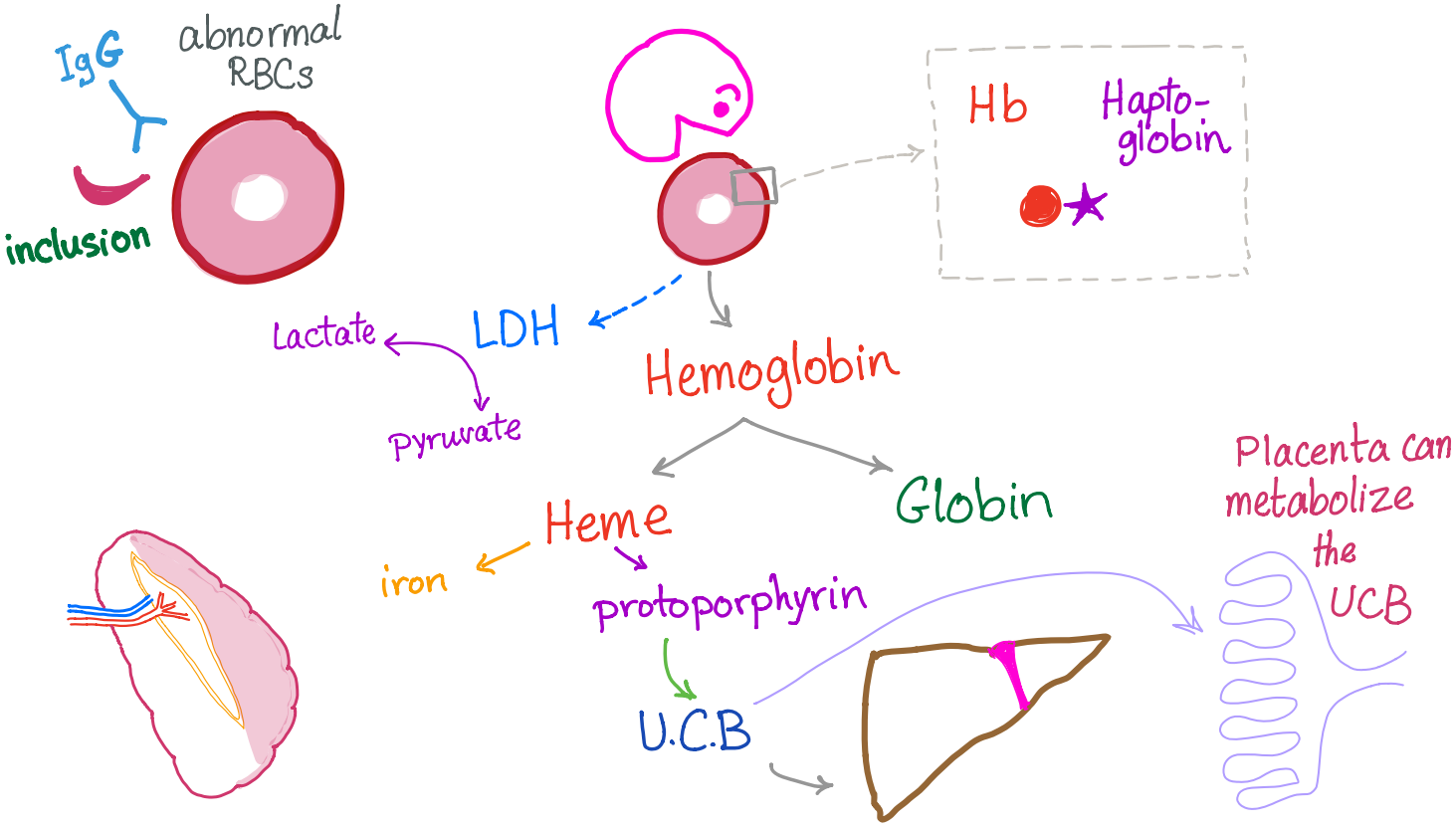
- Antigen – Antibody reaction → agglutination

∵ No need for previous exposure "sensitization"

∴ (1) ABO HDN can occur during first pregnancy & subsequent pregnancies
(2) you cannot prevent it.

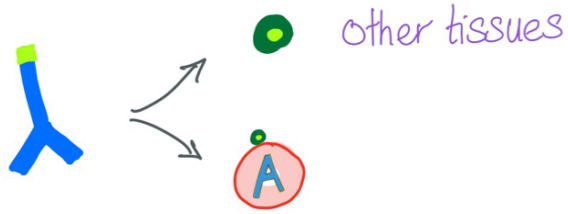


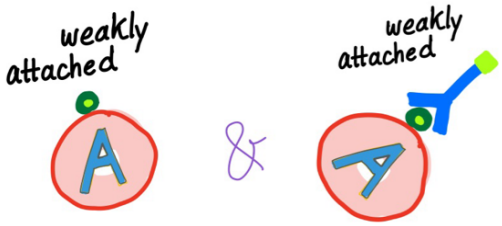
Extravascular Hemolysis



In ABO incompatibility, anemia is mild or non-existent.

Why?

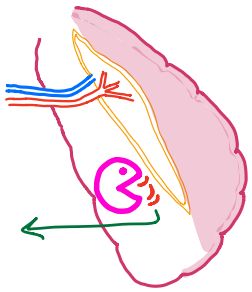




Clinically Mild

∵ HA → ∴ Normocytic

Extravascular Hemolytic anemia



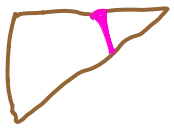
signs & Symptoms of anemia

+

Jaundice UCB

Hemoglobin → Heme + Globin

Heme → iron + Uprotoporphyrin → .C.B



Splenomegaly

Hepatomegaly

Diagnosis clinically + investigation

Blood film "Spherocytes" [in the cord blood]

CBC

Hb HCt MCV

Retic. count

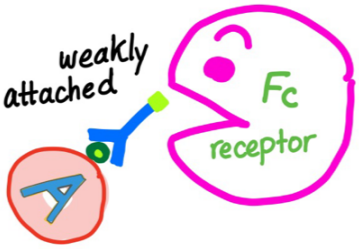
LDH

UCB

Haptoglobin

Direct Coombs test weakly Positive

(Direct Antiglobulin test)

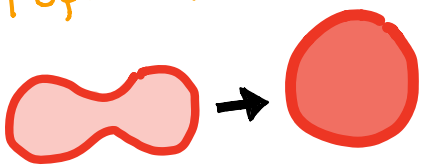


↑MCHC

Hereditary

Hereditary spherocytosis

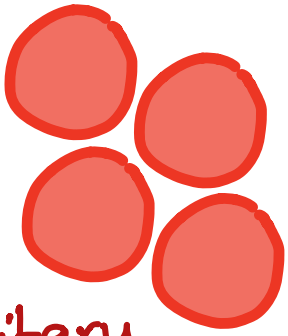
loss of spectrin, ankyrin, band 3.1



Coombs test

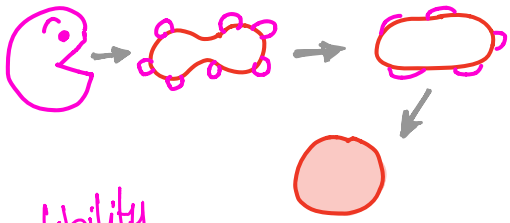
Splenectomy

Spherocytosis



Non-Hereditary

- Hemolytic Anemia -

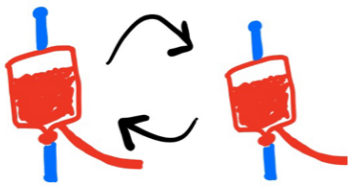


spherocytes in umbilical cord ↘ ABO incompatibility

"not Rh"

TREATMENT

- No anemia or Jaundice → No ttt
- Anemia :- exchange transfusion

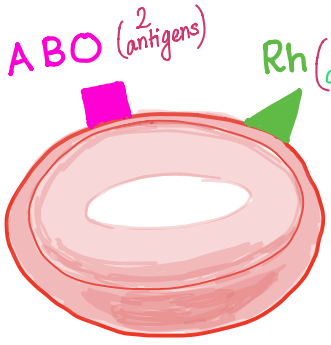


- Jaundice :- phototherapy

UCB → lumirubin

ABO Hemolytic Disease of the Newborn

INCOMPATIBILITY



Mnemonic

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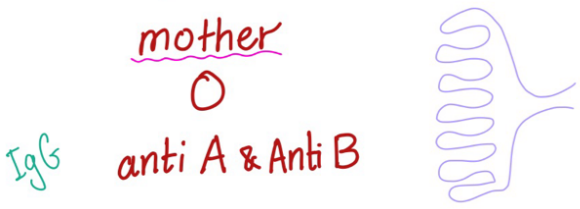


- Antigen – Antibody reaction → agglutination

∵ No need for previous exposure "sensitization"

∴ (1) ABO HDN can occur during first pregnancy & subsequent pregnancies

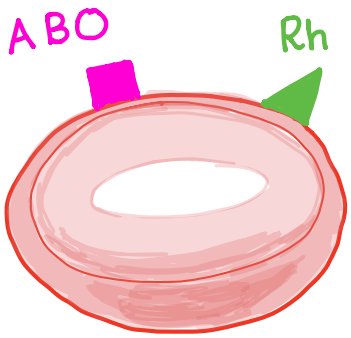
(2) you cannot prevent it.

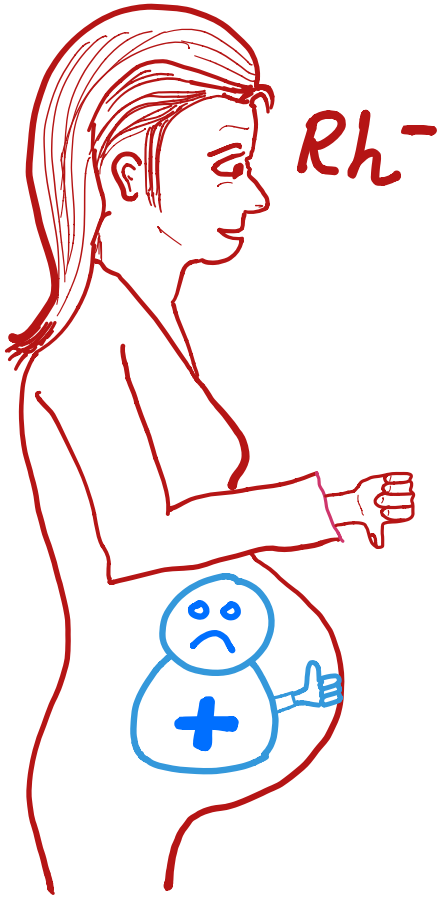
mOther

bA-By

Rh Hemolytic Disease of the Newborn

INCOMPATIBILITY





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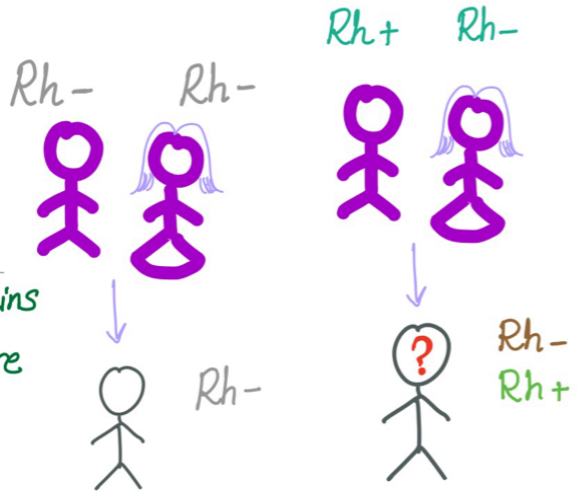
Alloimmune Hemolytic Transfusion Reactions

if you have D antigen → you're Rh-positive

if you do not → Rh-negative



ABO system	Rh system
• Spontaneous agglutinins	• No spontaneous agglutinins
• Not require previous exposure	• Requires previous exposure
	↓
	SENSITIZED
	↓
	2nd response will be faster and stronger

Rh Disease "less common, more severe"

- mother: Rh "-ve" baby: Rh "+ve"

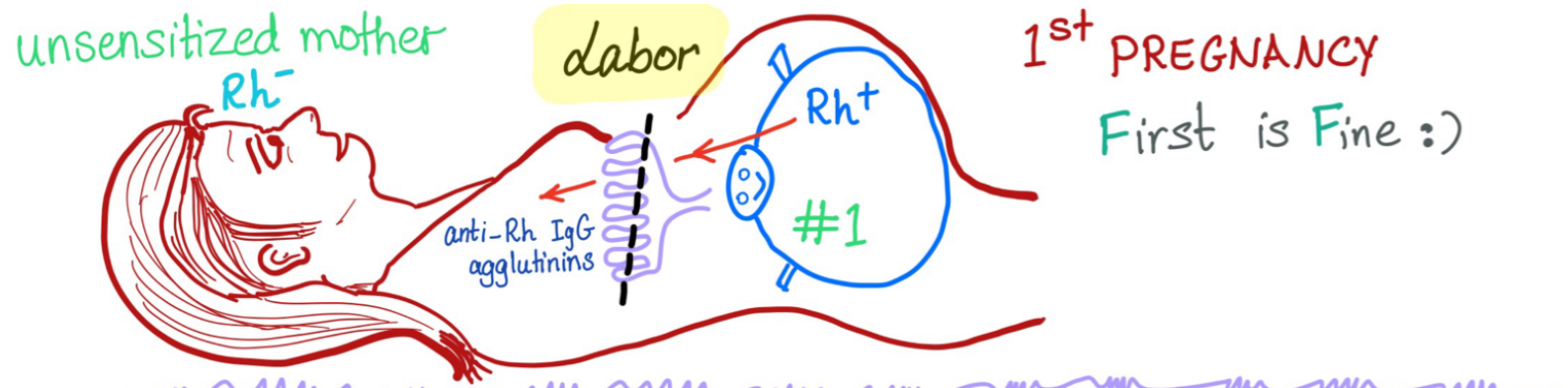
Like father, Like son.

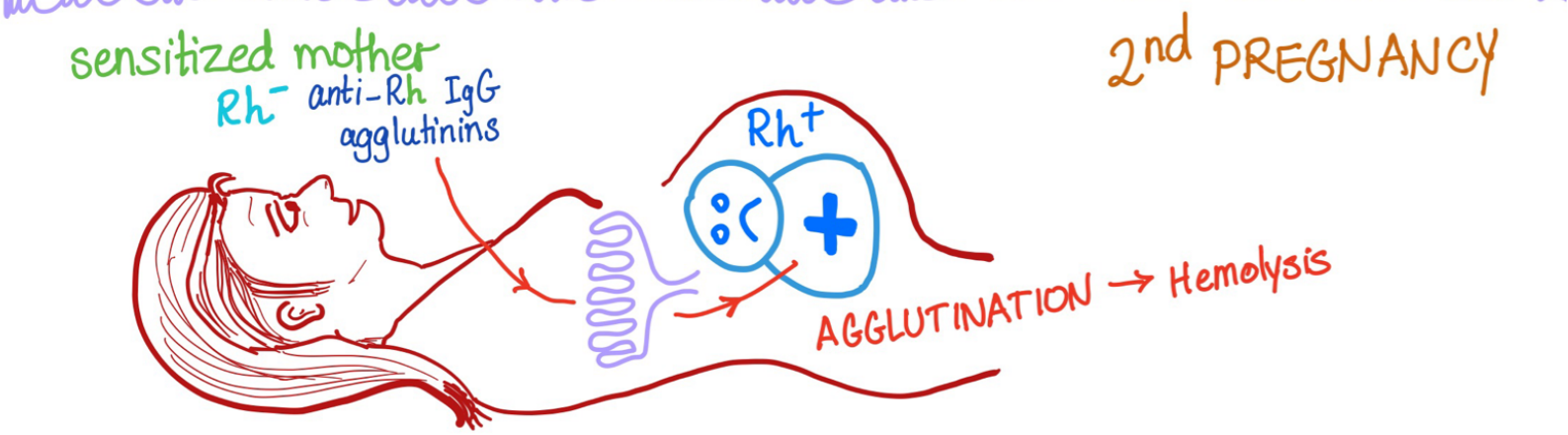
During fetomaternal hemorrhage:-

- Labor/delivery
- Rh+ blood being transfused to mum
- Ruptured ectopic pregnancy
- Placental abruption
- Abortion (spontaneous or elective)
- During 3rd trimester: absent cytotrophoblast of placenta

#1 is fine Rh+ "D" → Broken → SENSITIZED → anti-Rh IgG agglutinins "anti-D"

(1) Requires sensitization (2) Can be prevented





What's the incidence ?

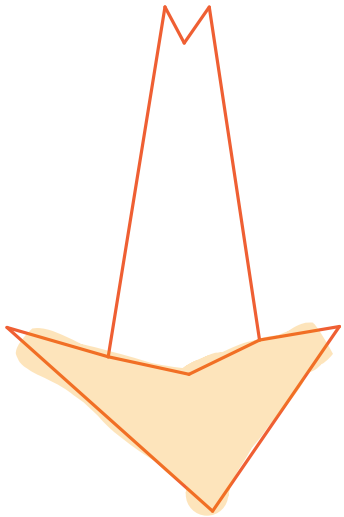
First is Fine :)

1st PREGNANCY : Zero

provided that -----

2nd PREGNANCY 3% HDN

3rd PREGNANCY 10% HDN



INCIDENCE INCREASES WITH SUBSEQUENT PREGNANCIES

PATHOGENESIS

(1) Diffusion

(2) Attachment

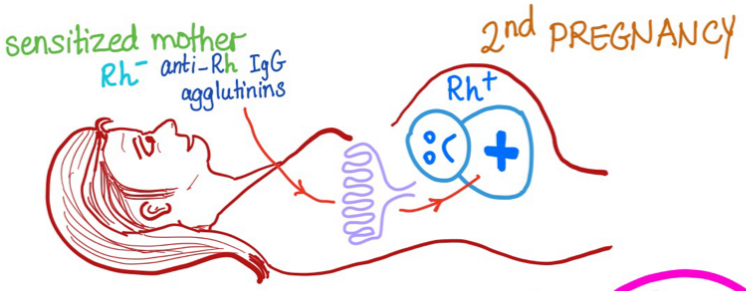
(3) Agglutination

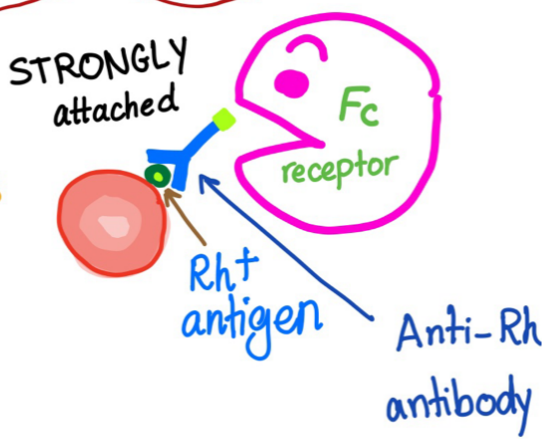
(4) Lysis

(5) Phagocytosis : whole RBC → No spherocytes

(6) UCB → CB

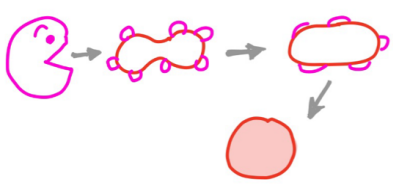
(7) Extramedullary Hematopoiesis





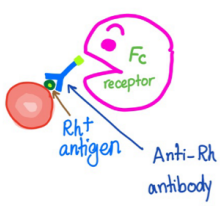
ABO incompatibility

spherocytes



Rh incompatibility

No spherocytes



SEVERE ANEMIA

Hydrops fetalis ←

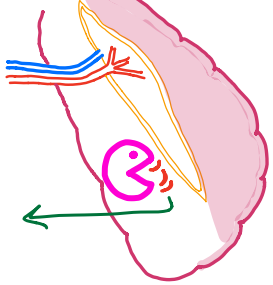
Clinically

All signs & Symptoms of anemia

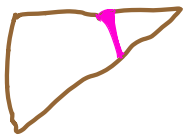
+

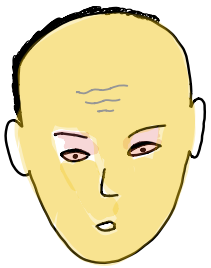
pathological → **Jaundice** UCB

- Urine discoloration (CocaCola-like)



Hemoglobin → Heme + Globin

iron ← Heme → protoporphyrin → U.C.B → 



Splenomegaly

Hepatomegaly

Kernicterus

Diagnosis

clinically + investigation

- Blood film
  - NO "Spherocytes" [in the cord blood]
  - Nucleated RBCs
- CBC
  - Hb HCt MCV
  - Retic. Count
  - LDH
  - UCB
  - Haptoglobin
  - ↓↓ Albumin
- Direct & Indirect Coombs test (Direct Antiglobulin test) — strongly Positive

cord bilirubin: 3-5 mg/dL

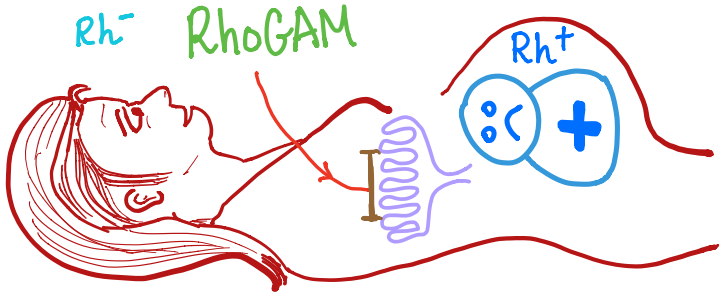
PREVENTION :- "in the unsensitized mother"

- Do Atypical Antibody Test at 28 weeks

Rho(D)immunoglobulin [RhoGAM] — 28-30 weeks of gestation

Rho(D)immunoglobulin [RhoGAM] — when mum delivers an Rh+ baby. #prevent_sensitization

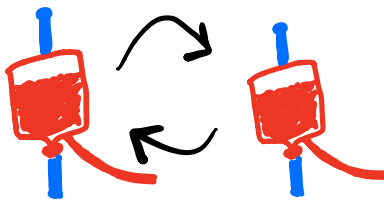
We give her the antibody, so she doesn't have to make it :) #analogy



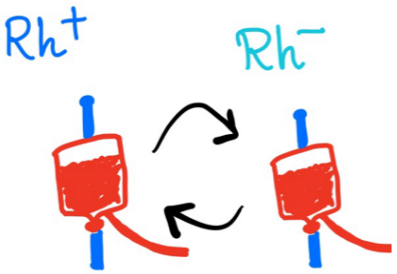
- What if the mother is already sensitized
  - DO NOT give RhoGAM
  - Repeated titers & amniocentesis
  - Spectrophotometric analysis of amniotic fluid

Why?

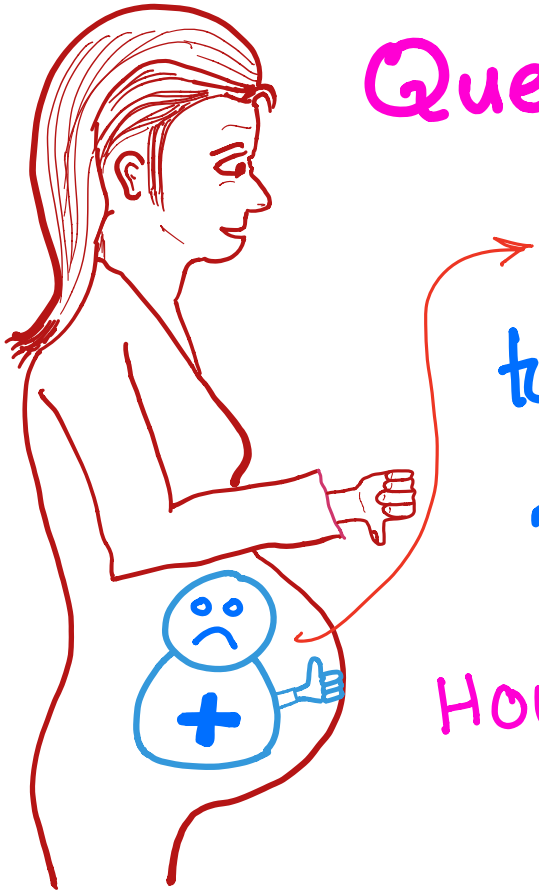
in utero exchange transfusion



TREATMENT



- Anemia :- exchange transfusion
- Jaundice:- phototherapy



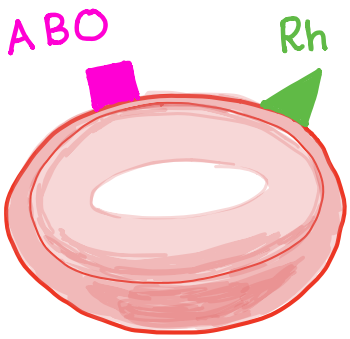
Question of the day ?

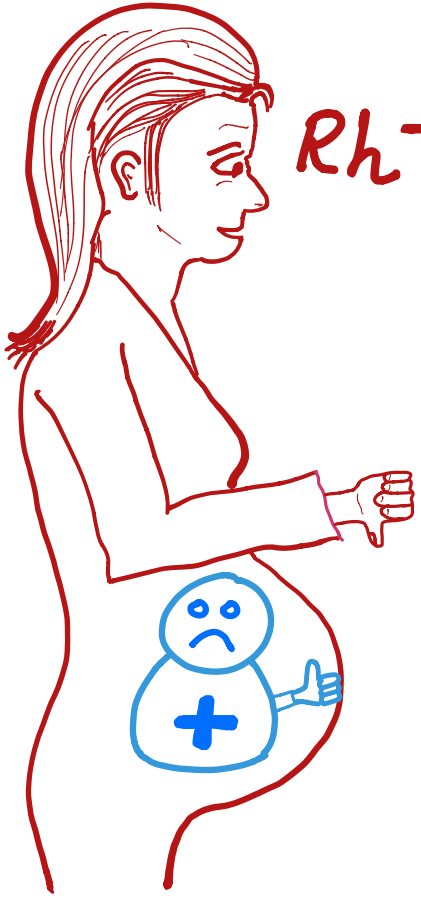
I am the first newborn to this mother, yet, I had Rh HDN "erythroblastosis fetalis"

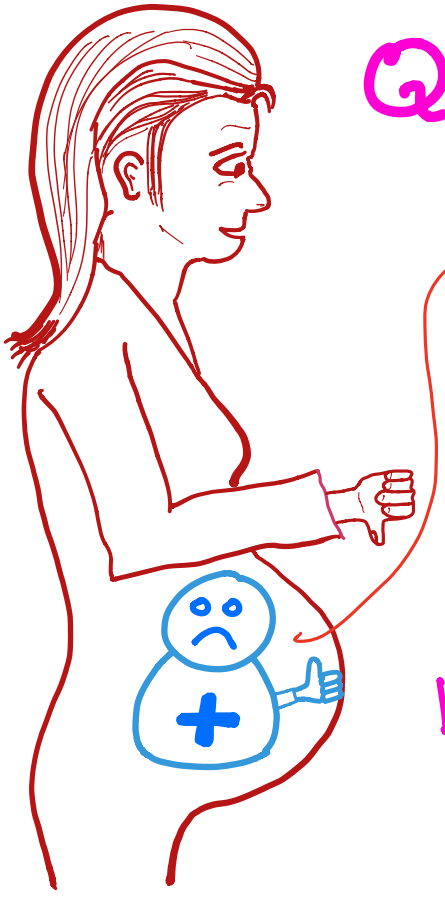
How can this be?!!!

Rh INCOMPATIBILITY

Hemolytic Disease of the Newborn







Question of the day ?

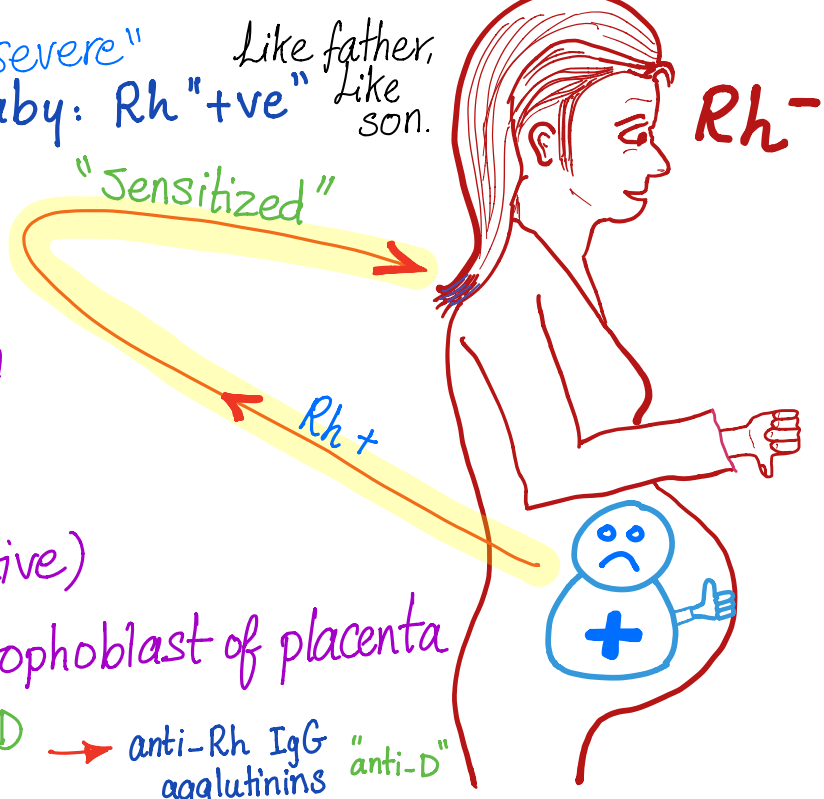
I am the first newborn to this mother, yet, I had Rh HDN "erythroblastosis fetalis"

How can this be ?!!!

Rh Disease "less common, more severe"

- mother: Rh "-ve" baby: Rh "+ve"

Like father, Like son.

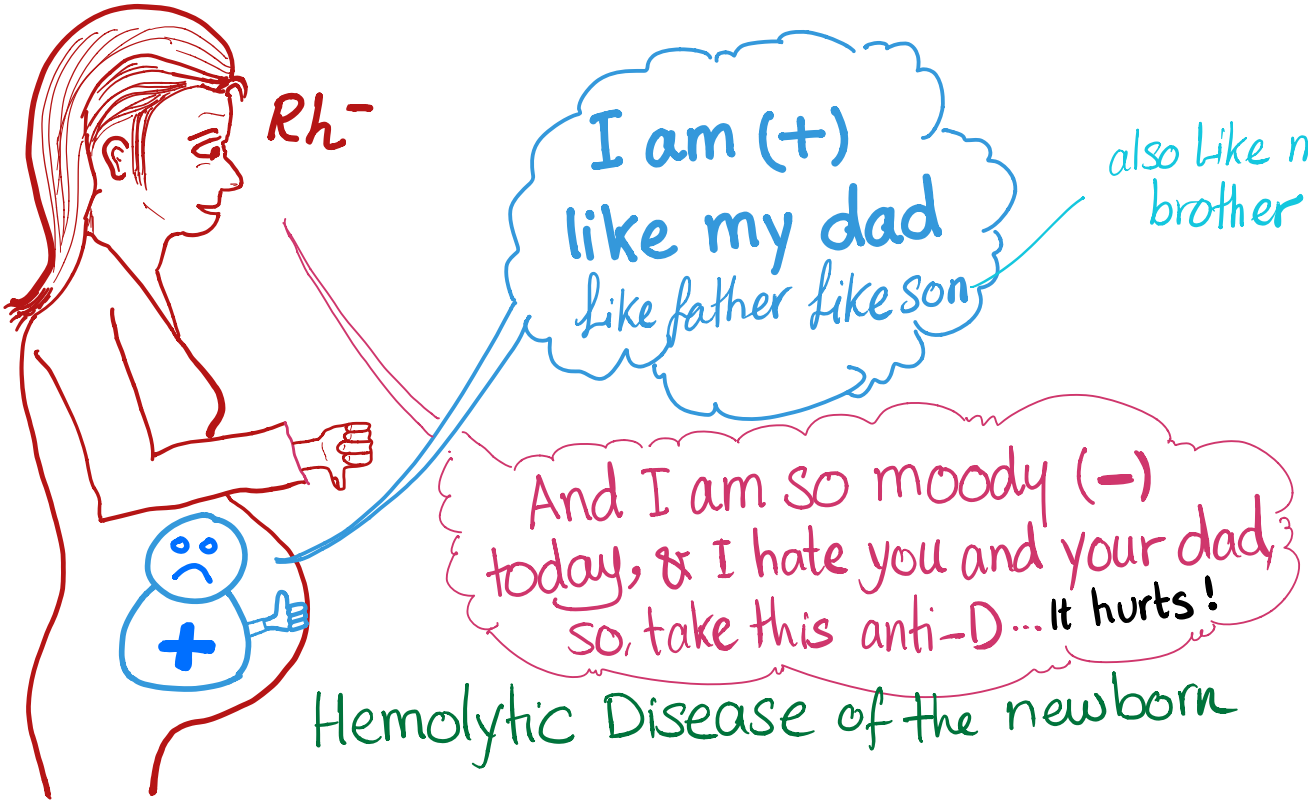


During fetomaternal hemorrhage:-

- Labor/delivery
- Rh+ blood being transfused to mum
- Ruptured ectopic pregnancy
- Placental abruption
- Abortion (spontaneous or elective)
- During 3rd trimester: absent cytotrophoblast of placenta

#1 is fine

Rh+ "D" → Broken → SENSITIZED → anti-Rh IgG agglutinins "anti-D"



Hemolytic Disease of the newborn

ABO incompatibility

Rh incompatibility

ABO incompatibility

- More common, less severe
- Mother: group O fetus: A or B
- 1st pregnancy can be affected (No sensitization)
- Hepatosplenomegaly is less common
  - ↑↑ UCB Jaundice HA kernicterus Retic. Nucleated
- Weakly positive direct Coombs "fetal RBCs"
- Spherocytes

Rh incompatibility

- less common, more severe
- Mother can be of any blood group
  - mother: Rh⁻, fetus: Rh⁺
- 1st pregnancy is safe [sensitization]
- Hepatosplenomegaly is more common
  - ↑↑ UCB Jaundice HA kernicterus Retic.
- Both Direct & Indirect Coombs: strongly ⊕
- No spherocytes