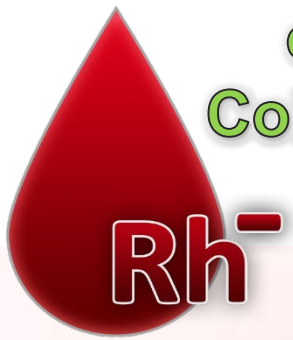
Rh iso-immunization

2025

Assistant prof Dr.Zainab Abdul Ameer Jaafar

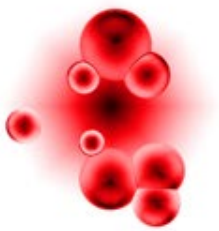
obstetrics and gynecological department

College of medicine al mustansiriya university



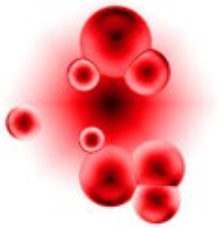
Blood group is defined

- ABO group (O, A, B, AB).
- Rhesus system (C, D, E antigens).



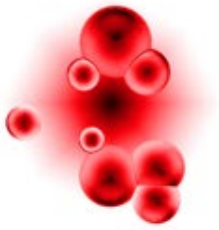
ABO group (O, A, B, AB).

- About 20% of all infants have an ABO maternal blood group incompatibility
- but only 5% are clinically affected.
- Hemolytic disease of the newborn (HDN) due to ABO incompatibility less severe than Rhesus incompatibility.



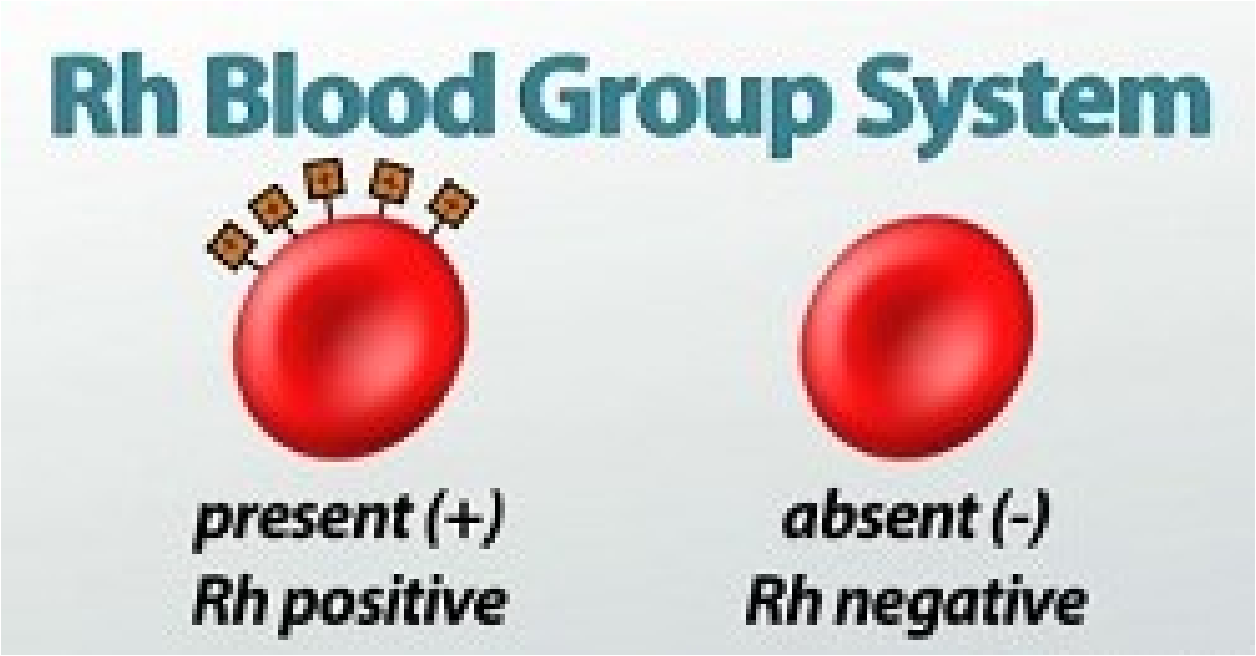
Rhesus system (C, D, E antigens).

- *This system includes five red cell proteins or antigens: c, C, D, e, and E. No “d” antigen.*



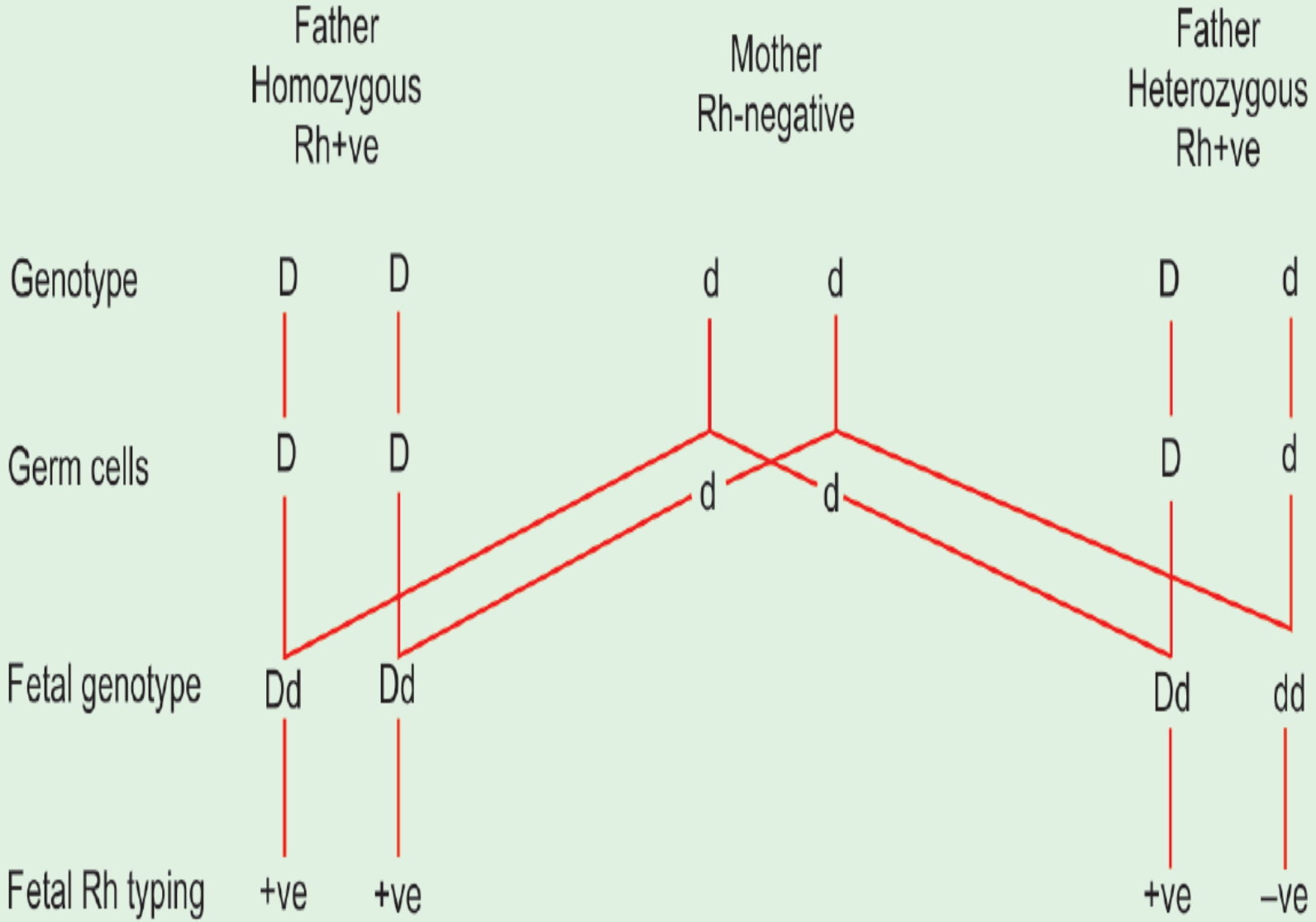
Rhesus system (C, D, E antigens).

- The presence or absence of D antigen site determines whether an individual is Rh positive or Rh negative.



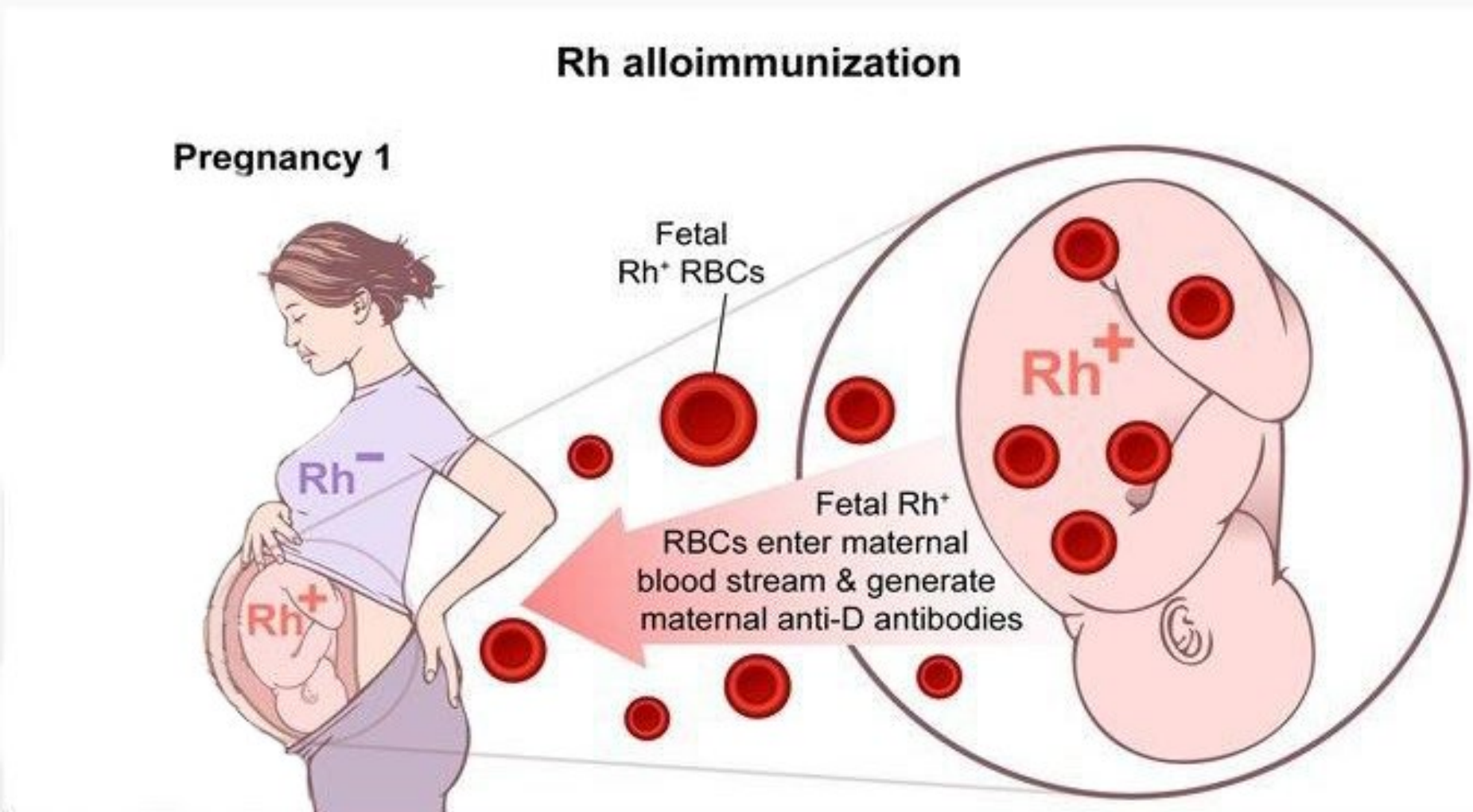
- *The incidence of Rh-negative genotype is **15%** in UK.*

Mating of Rh-positive Male with Rh-negative Female and the Resultant Possible Rh-group of the Baby



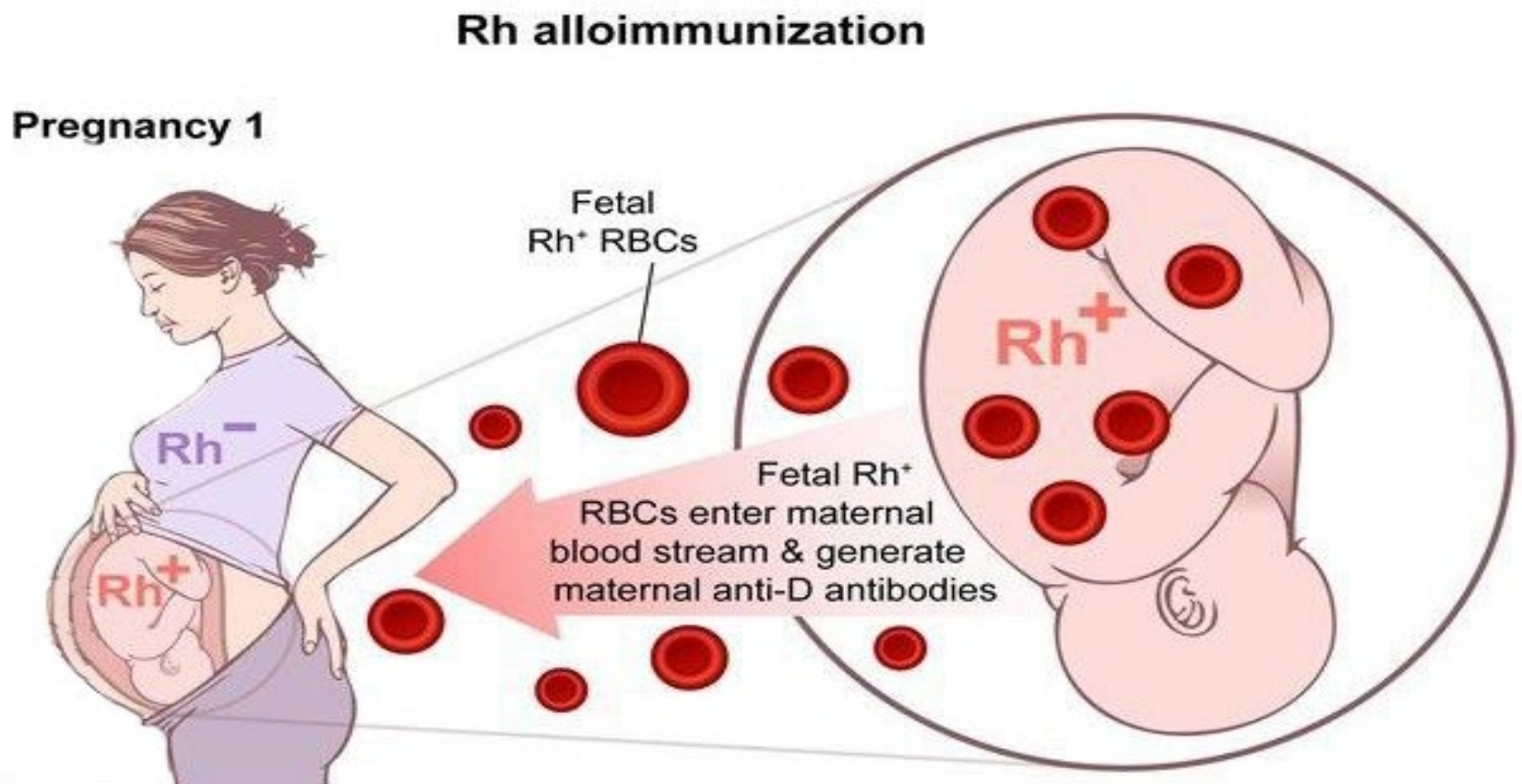
Pathology of rhesus isoimmunization

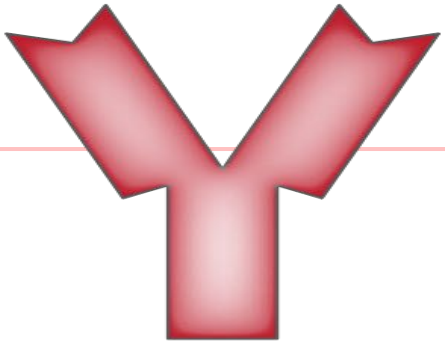
- *Rh-positive red cells of the fetus enter into the maternal circulation*



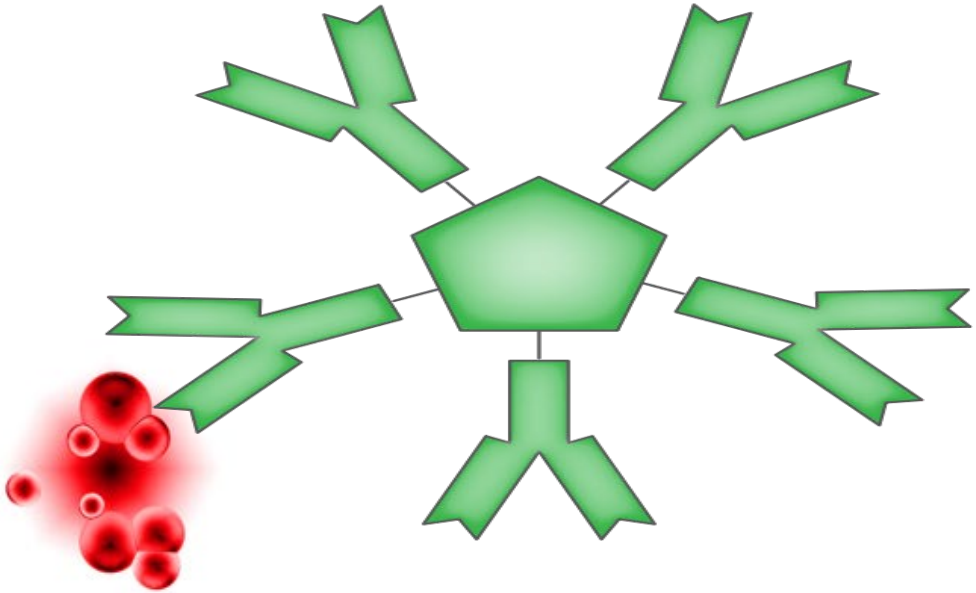
Pathology of rhesus isoimmunization

- the first immune response in the mother is the formation of IgM antibodies (they do not cross the placenta) and so the first baby is usually unaffected.





IgG



Pentamer
IgM

Pathology of rhesus isoimmunization

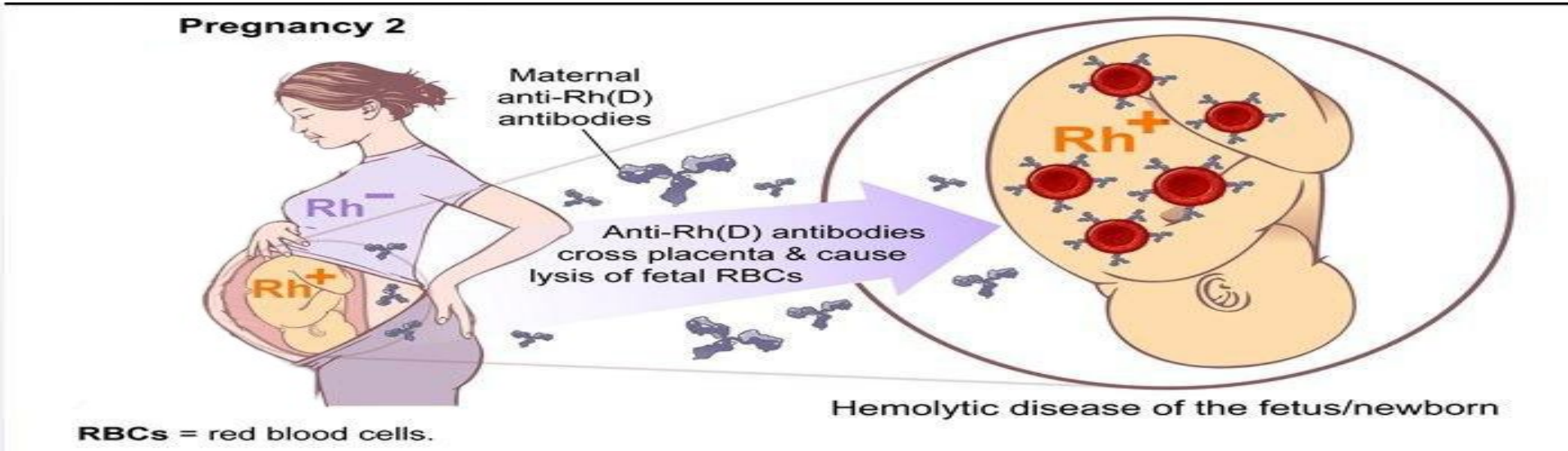
- *In Subsequent pregnancy IgG formation in the mother, which cross the placenta and destroy the fetal red blood cells (RBC) leading to :*

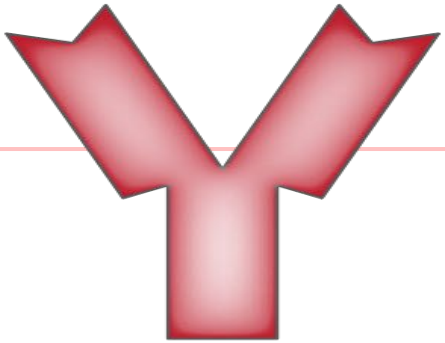
Reticulocytosis

anemia

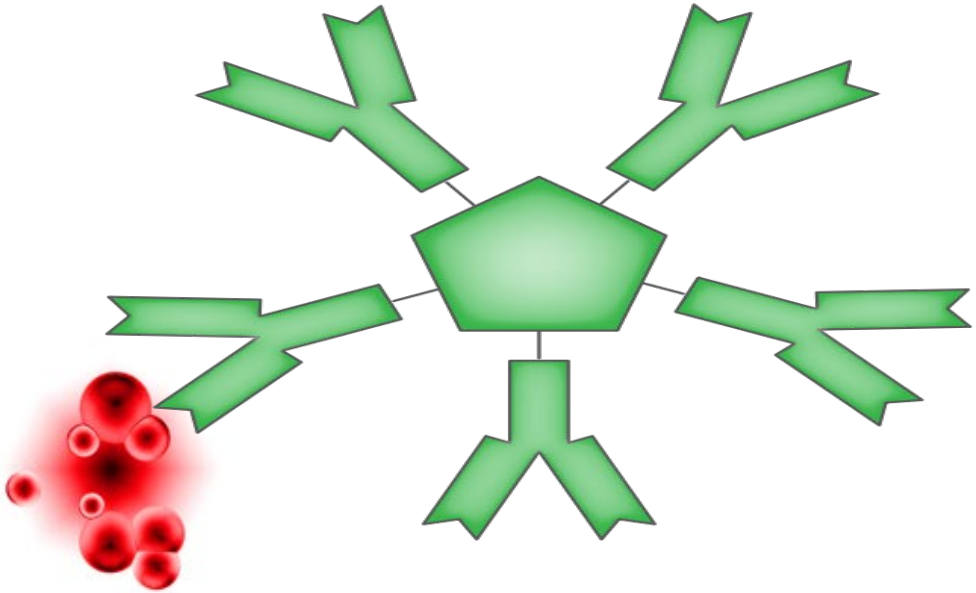
heart failure

hydrops.





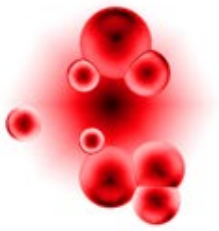
IgG



Pentamer
IgM

Pathology of rhesus isoimmunization

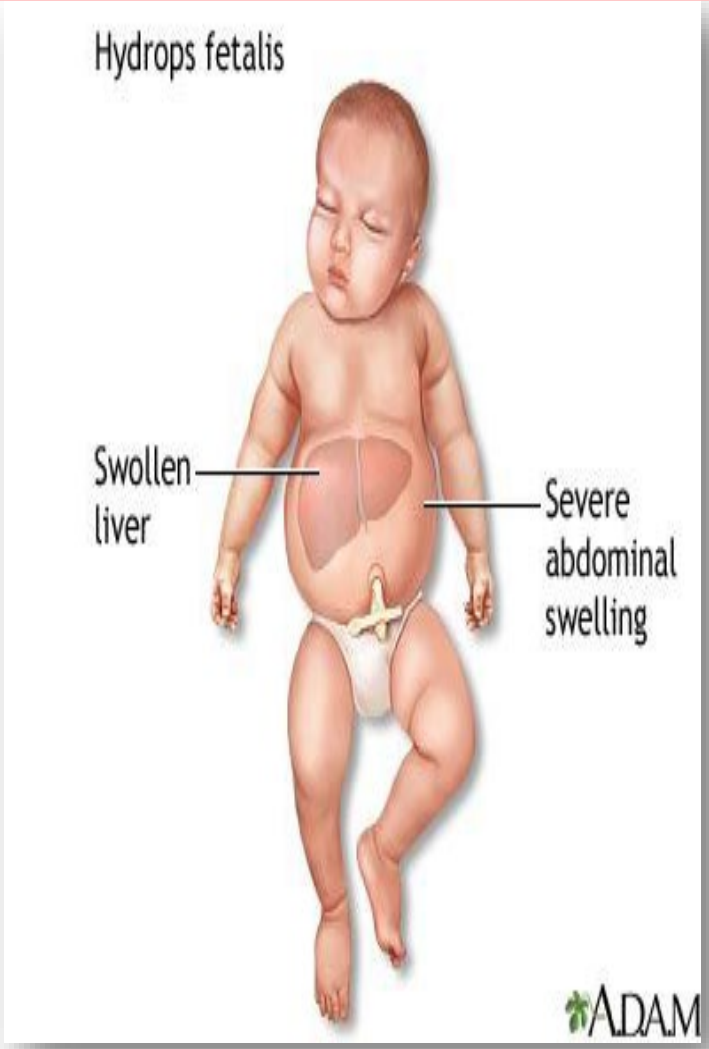
- **Isoimmunization depends on the volume of fetal blood entering the maternal circulation and usually occurs when at least 0.1 ml of fetal blood enters the maternal circulation.**



What are the fetal and neonatal complications that may occur when mother iso immunized?

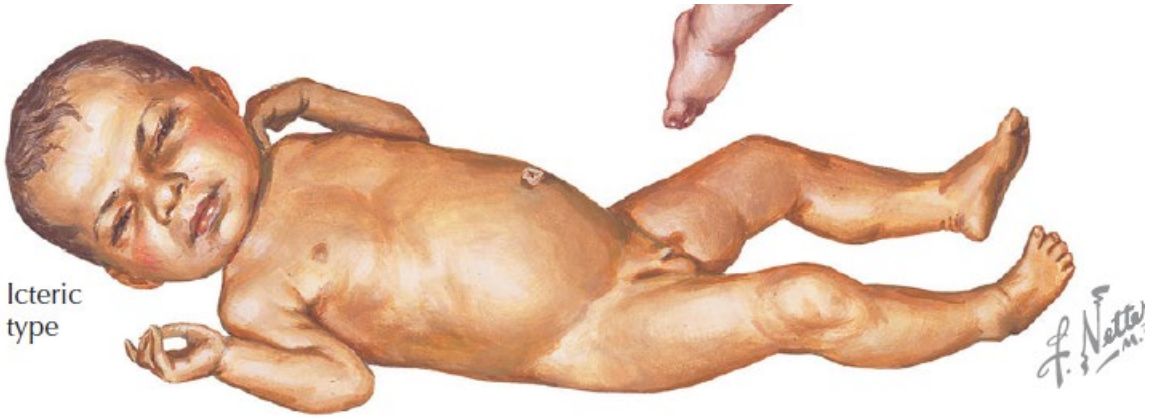
1-Hydrops fetalis.

2-Intrauterine fetal death or early neonatal death due to cardiac failure.



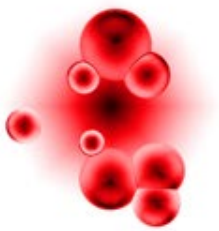
3-Congenital anemia of the newborn

4-Jaundice



sensitization events causing fetal-maternal hemorrhage

Indication for administration of anti-D immunoglobulin



I. antepartum

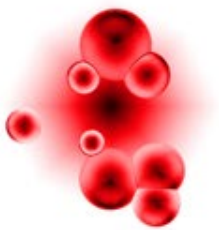
1. **Threatened abortion**: **(if)**repeated or with pain **or** after 12 weeks of gestation
2. **spontaneous abortions** if after 12 weeks of gestation
3. **Therapeutic termination of pregnancy (whether medically or surgically) whatever gestation age.**
4. **ectopic pregnancy**
5. **Evacuation of molar pregnancy**
6. **Invasive prenatal testing (amniocentesis, chorion villus biopsy& cordocentesis)**
7. **In-utero interventions (transfusion, surgery, insertion of shunts, laser)**
8. **Antepartum haemohage (APH)**
9. **Antepartum trauma to abdominal: (sharp/blunt, open/closed)**
10. **Intrauterine death**
11. **External cephalic version**

II. intrapartum

1-Delivery –

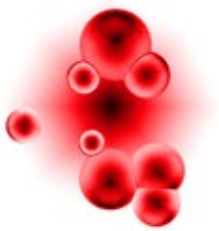
- ✓ Normal
- ✓ instrumental
- ✓ Caesarean section

2-Manual placental extraction



III. Any time

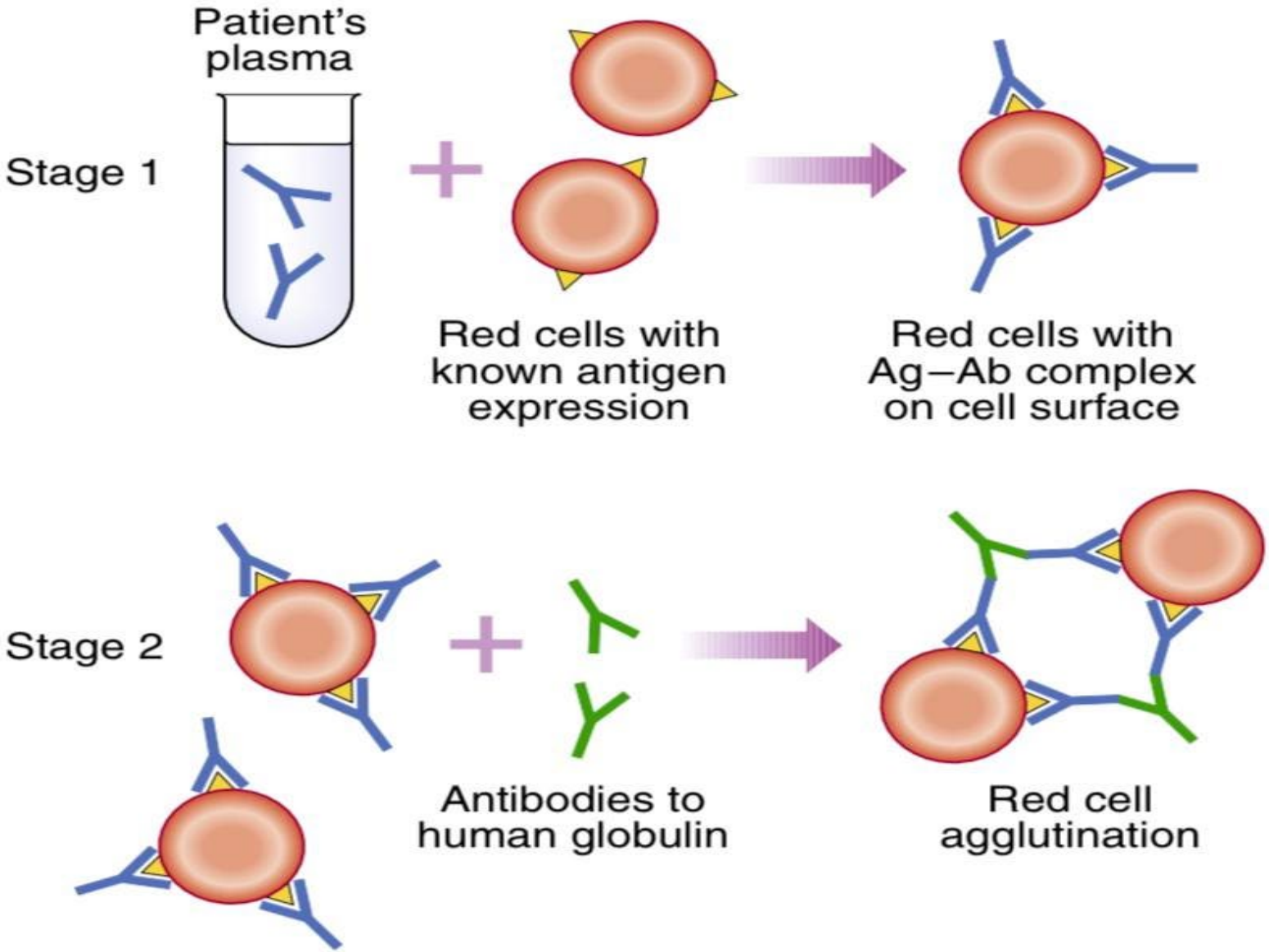
- **Administration of (Rh-+ve) blood components to (Rh-ve) female**



At the beginning 3 important test should you know

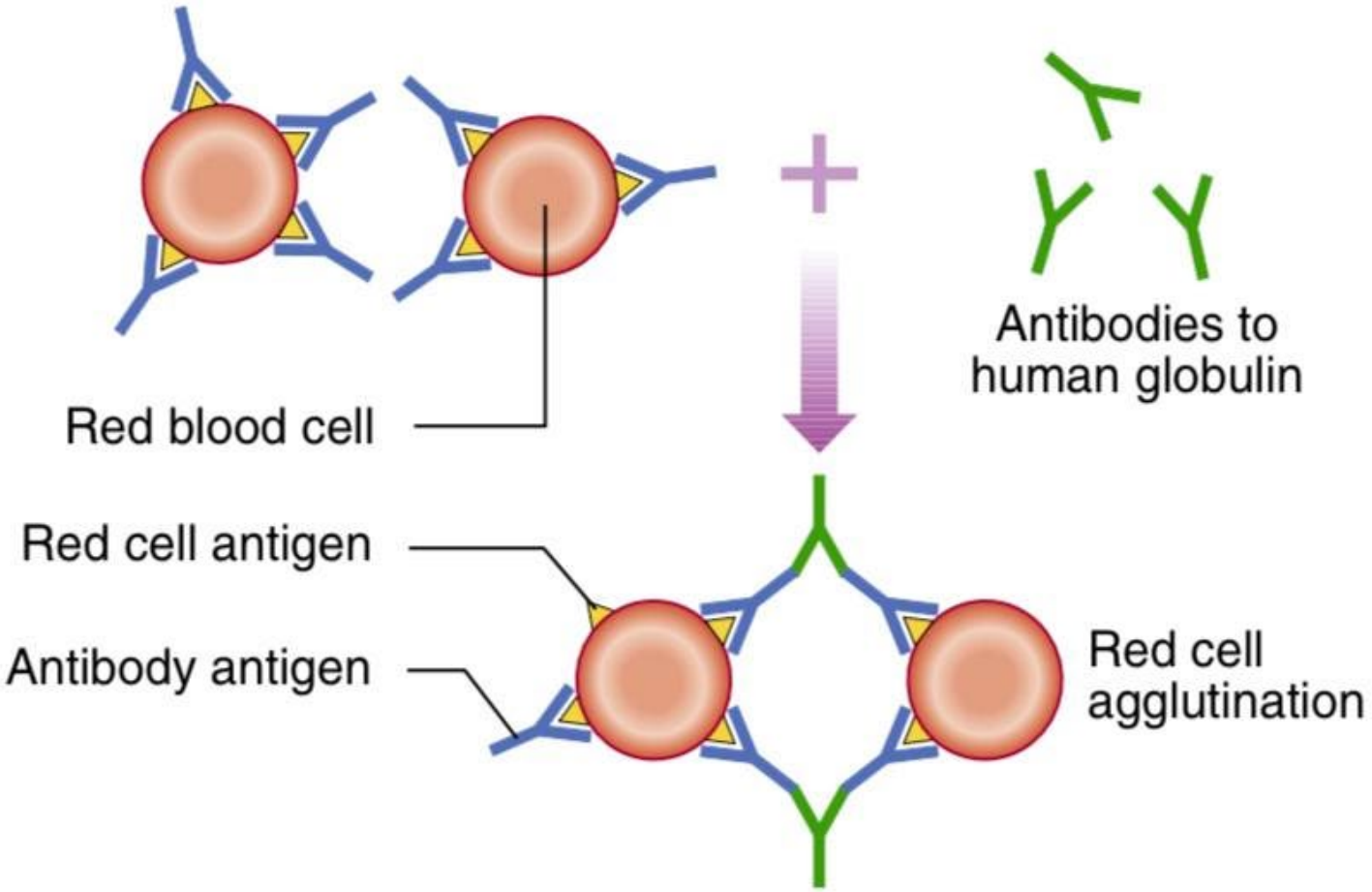
Indirect antiglobulin test (IAT) (indirect Coombs test)

Detects antibodies in the plasma, e.g., antibody screen in pre-transfusion testing



Direct antiglobulin test (DAT) (Coombs test)

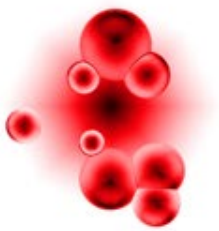
Detects the presence of antibody bound to the red cell surface, e.g.,
1. autoimmune haemolytic anaemia
2. haemolytic disease of newborn (HDN)
3. transfusion reactions

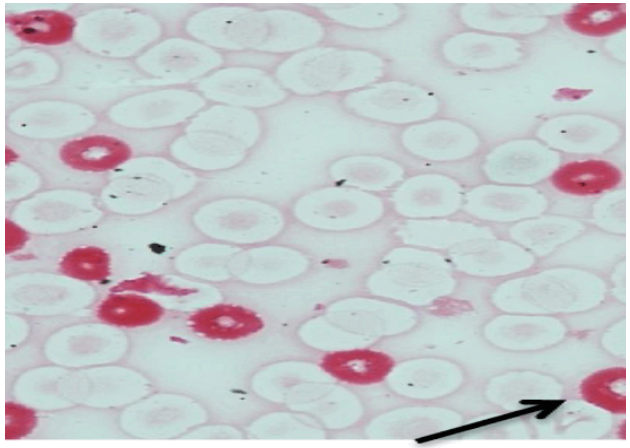


Kleihauer–Betke test:

- performed within 2 hours of delivery
- to assess whether more than one vial of anti D needs to be given if large volumes of fetal–maternal bleed may occur (e.g., abruptio placentae).

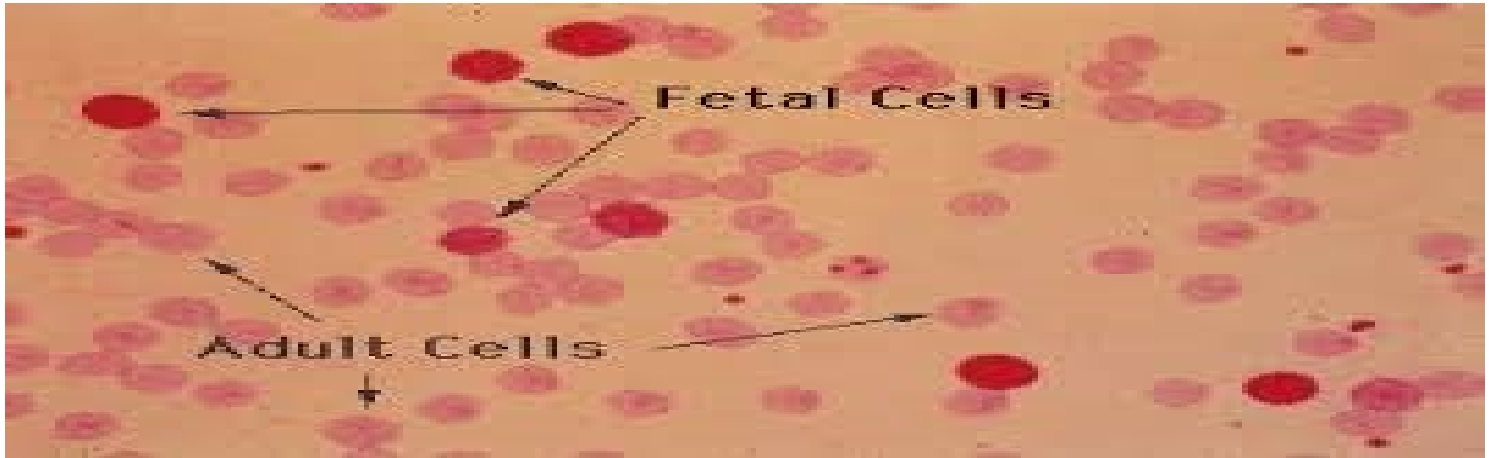
- Fetal erythrocyte contains Hb F which is more resistant to acidic solution (citric acid phosphate buffer) or alcohol denaturation than adult Hb A.





Kleihauer–Betke test:

- after exposure to acid only fetal cells remain
- The acid is able to elute adult hemoglobin, but not fetal hemoglobin
- from the red blood cells. As a result, on subsequent staining the fetal cells appear rose pink in color, while adult red blood cells appear as “ghosts.

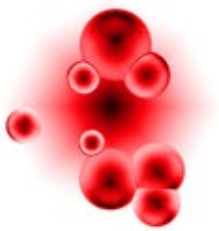


A young primigravida at 24 weeks attends the antenatal clinic. Her pregnancy till now has been smooth and uneventful. Routine investigations show her blood group to be

B Rh negative.

what is your management?

Management of patient found to be Rh-negative in ANC



Full history:

1. Husband blood group
2. in primigravida: previous history of blood transfusion
3. In a parous woman: a detailed obstetric history.

(i) History of fetal affection in the form of stillbirth or neonatal death

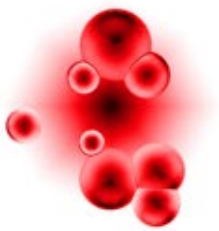
(ii) Previous history of hydrops fetalis

(iii) History of receiving anti-D immunoglobulin in previous pregnancies

(iv) Current pregnancy sensitizing events

Examination:

No specific finding is observed on general or systemic physical examination

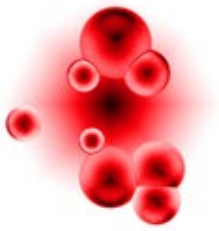


Investigations:

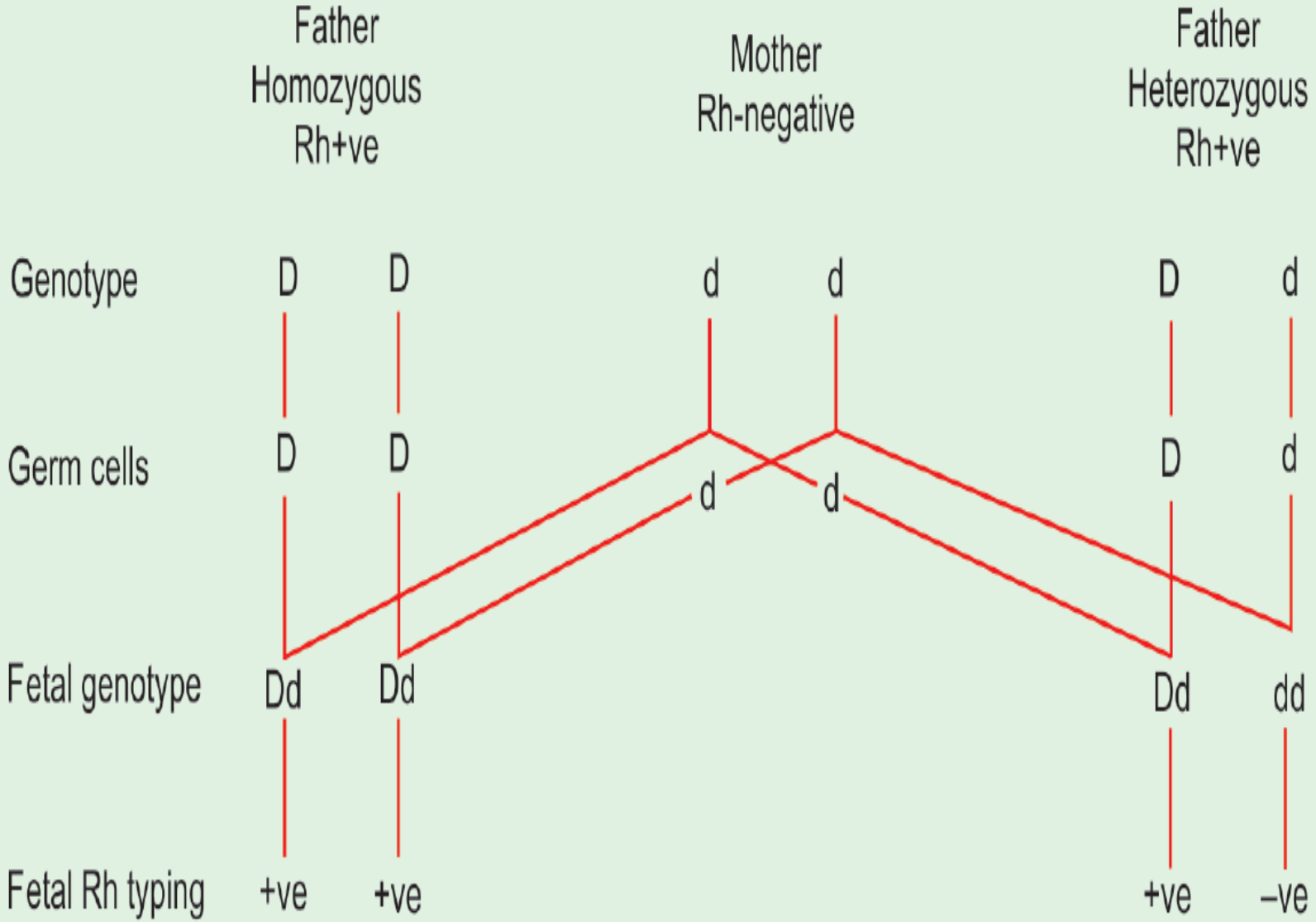
1-Blood group and Rh of the husband:

(If Negative: the baby will be Rh –ve so the pregnancy will be managed as normal. No need for any testing)

2-Indirect coomb's test



Mating of Rh-positive Male with Rh-negative Female and the Resultant Possible Rh-group of the Baby



Management

unsensitized pregnant woman	Sensitized pregnant woman
indirect coomb's test negative	indirect coomb's test positive

Group 1:

Management of :

Unsensitized Rh-negative pregnant woman

(indirect coomb's test negative)

1. ***Follow up***

- *by indirect coomb's test*

☒ *at booking visit*

- *if its negative repeat **it** at*

☒ *20 weeks.*

☒ *24 weeks.*

☒ *28 weeks.*


prevention

Prevention:

- ***Ensure*** *indirect coomb's test negative prior to prevention*

1-routine antenatal anti-D prophylaxis

- **Protocol**
- **either**
  - *1 dose at 28 weeks dose of (1500 IU)*
- **or**
  - *2 doses of Anti D, of 500 IU each,*
    - *are given at 28 weeks and 34 weeks*

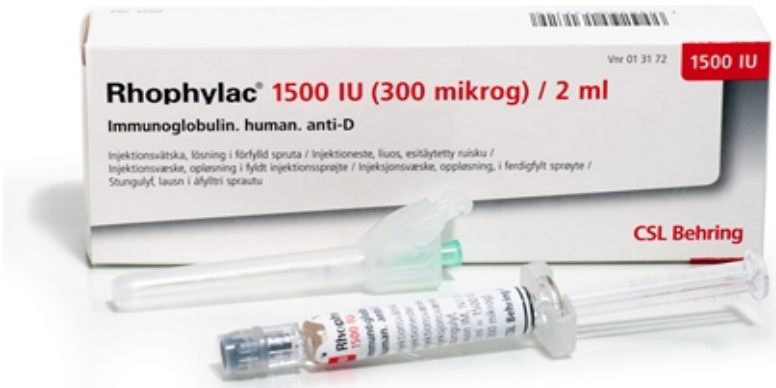
2-After the potentially sensitizing event

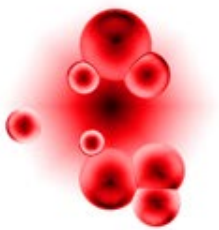
- **Time:** within 72 h of sensitizing event.

- **Dose**

- if <12 weeks, 250 IU of anti-D given IM- A Kleihauer test is **not required**
- if 12-20 weeks, 250 IU of anti-D given IM- A Kleihauer test is **required**
- if ≥20 weeks, 500 IU of anti-D given IM

APPENDIX 1 RH (D) IMMUNOGLOBULIN PATIENT CONSENT





NSW GOVERNMENT Health

Facility:

FAMILY NAME	MRN
GIVEN NAME	☐ MALE ☐ FEMALE
D.O.B. _____/_____/_____	M.O.
ADDRESS	
LOCATION / WARD	
COMPLETE ALL DETAILS OR AFFIX PATIENT LABEL HERE	

RH (D) IMMUNOGLOBULIN PATIENT CONSENT

SMR020060

Holes Punched as per AS2828.1: 2012

BINDING MARGIN - NO WRITING

CONSENT

I confirm that I have received information relating to Rh (D) immunoglobulin and that I understand that it is a blood product. I confirm that I understand the information provided and have had an opportunity to discuss the information, ask questions and have any concerns addressed.

I consent to receive the recommended administration of Rh (D) immunoglobulin as outlined in the information brochure provided to me in one or more of the following instances. This includes Rh(D) immunoglobulin for:

Tick as applicable

- ☐ **Potentially sensitising events both during and after the first trimester**
- ☐ **Routine antenatal prophylaxis during the third trimester**
- ☐ **Routine postnatal prophylaxis**

or at other times as recommended by the Health Service.

Printed Name .....

Signature ..... Date ...../...../.....

Interpreter ..... Date ...../...../.....

CLINICIAN PROVISION OF INFORMATION

I confirm that I have provided information relating to Rh (D) immunoglobulin which outlines the risks and benefits of receiving and/or declining Rh (D) immunoglobulin and the situations under which Rh(D) immunoglobulin is recommended. I have given the woman an opportunity to discuss the information, ask questions and have any concerns addressed.

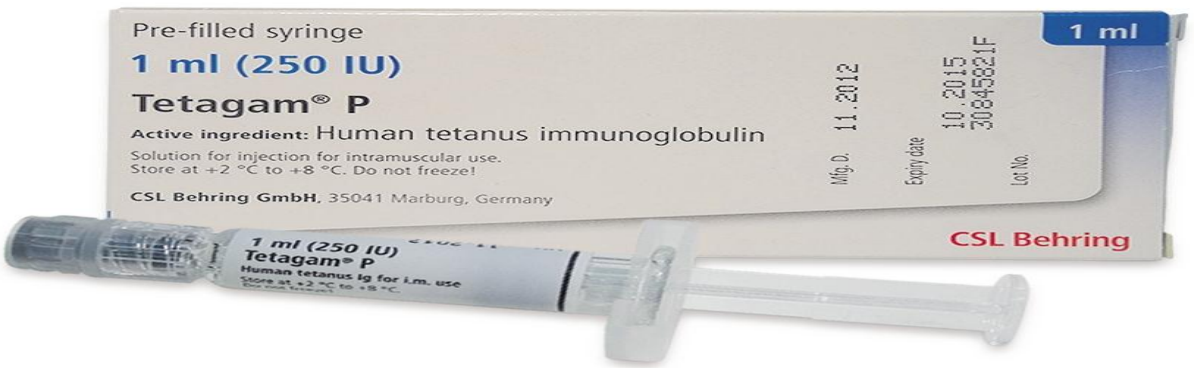
Printed Name ..... Designation .....

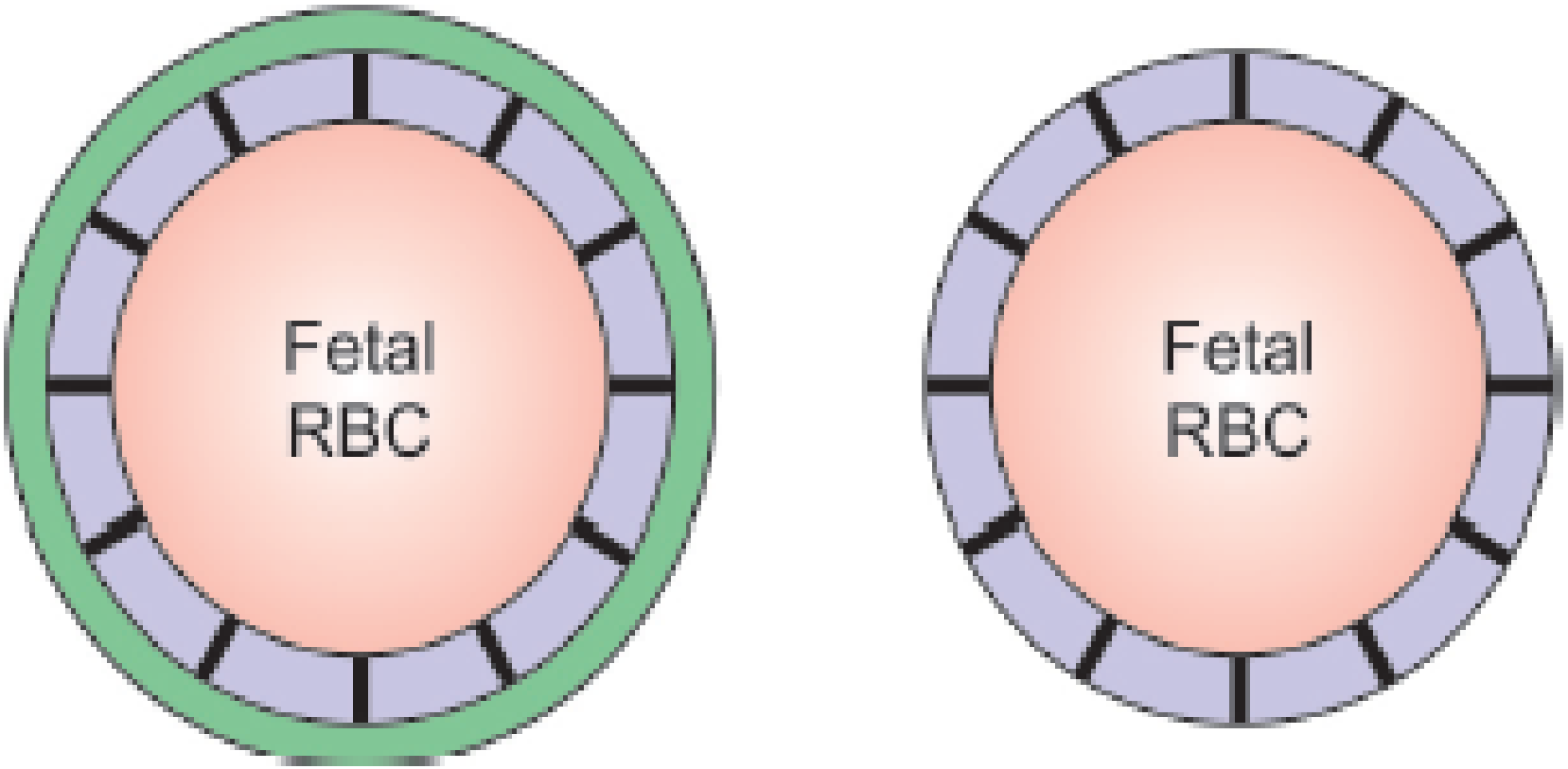
Signature ..... Date ...../...../.....

NH00686 140314

NO WRITING

RH (D) IMMUNOGLOBULIN PATIENT CONSENT SMR020.060

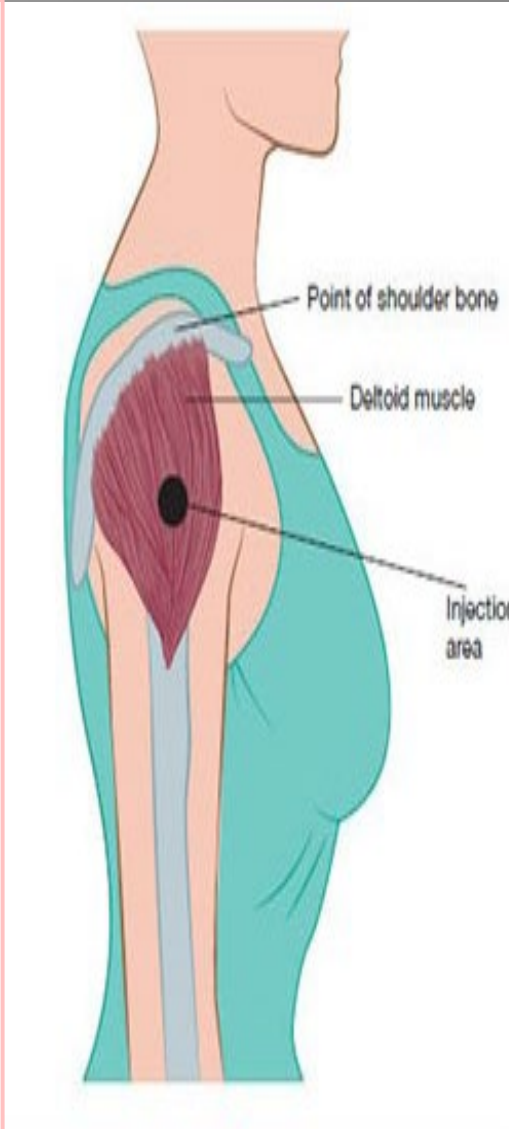

Pre-filled syringe
1 ml (250 IU)
Tetagam® P
Active ingredient: Human tetanus immunoglobulin
Solution for injection for intramuscular use.
Store at +2 °C to +8 °C. Do not freeze!
CSL Behring GmbH, 35041 Marburg, Germany
Mfg.D. 11.2012
Expiry date 10.2015
Lot No. 30845821F
1 ml
CSL Behring
1 ml (250 IU)
Tetagam® P
Human tetanus Ig for i.m. use



Flg. 22.2: Anti-D immunoglobulin injected into the mother surrounds the fetal RBC (thick green circle) preventing the antigen sites (spikes) to form antibody

Rout:

- ☒ *IM, into the deltoid muscle, (delayed absorption if given to gluteal region)*
- ☒ *If a bleeding disorder should receive anti-D Ig via the subcutaneous or intravenous route preparation.*



3-within 72 h of delivery. (postnatal prophylaxis): if

- *The infant is Rh +ve.*
- ***Dose:*** ***either***

☒ ***1500 IU****: Not need to send Kleihauer Betke screening test*

- ***Or***

☒ ***500 IU*** *of Anti D and sent Kleihauer Betke screening test within 2 hours after delivery to identify women who need additional Anti D*

4-preventive steps during labor

A. **not** allowed to become post date

B. **minimize the risk of fetomaternal hemorrhage**

- **During labor**

1. Not give ergometrine in second stage of labor.
2. Gentle handling of the uterus during the third stage.
3. gently manual removal of the placenta if needed

- **During cesarean delivery**

1. avoid blood spillage into the peritoneal cavity.
2. avoid routine manual removal of the placenta.
3. Early cord clamping.

Group 2:

Management sensitized Rh-negative pregnant woman

G3P1A1 with 28 weeks pregnancy comes to you for antenatal care. Her previous pregnancy was uneventful. Her Blood group is B negative and Indirect coomb's test positive

What the management ?

Management

- the main objective of the management is to **diagnose** and **treat** fetal anemia as soon as possible.

1-Estimation of (Anti-D antibody) titer:

* repeat every **month** if stable
* every **2 weeks** (from 28 weeks until delivery or when there is rising titer)

☒ The **titer < 1:16, expectant management** until 38 weeks.

☒ if ≥**1:16**, the fetus at significant risk of hydrops ,investigate for fetal anemia every week by MCA Doppler

2-Rh antibody level:

- Levels of < 4 IU/ml= rarely associated with HDFN. follow up
- Between 4 and 15 IU/ml = moderate fetal hemolysis

1. monitoring levels every 3 weeks
2. Referral for a fetal medicine opinion examine the baby for signs of anemia

- Levels >15 IU/ml =severe hemolysis (high risk of hydrops fetalis) requiring intervention

3-The ultrasound :

also may reveals frank evidence of hydrops when the fetal Hb is less than 6 g/dl.

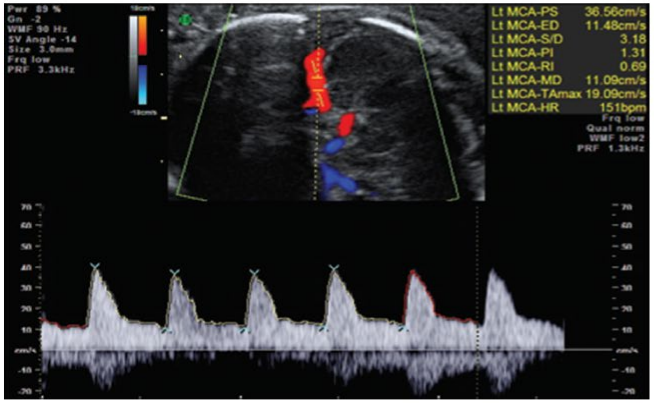
e.g.:

- ☒ ***Ascites***
- ☒ ***pleural or pericardia effusion***
- ☒ ***enlarged fetal heart***
- ☒ ***subcutaneous edema***

4-Doppler US:

for Middle cerebral artery (MCA)-peak systolic velocity (PSV)

- *at **18 weeks** of gestation*
- *Repeat at 2-week interval*



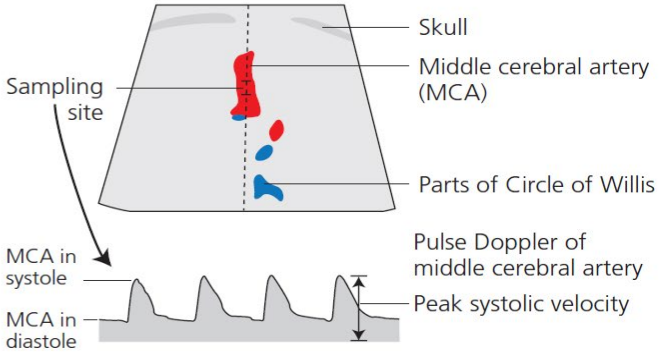


Fig. 22.3 Middle cerebral artery (MCA) Doppler.

Doppler US:

1-If MCA-PSV: ≤1.5 MoM for gestational age:

1)Continuo follow up every 2 weeks

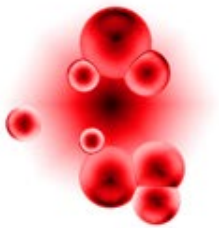
2)from 32 weeks every 2 weeks evaluated :(nonstress tests, biophysical profile, Doppler assessment)

2-If MCA-PSV >1.5 multiples of the median (MOMs) for gestational age: This severely affected fetus so referral to a fetal medicine specialist

Feto Maternal & GenetYX Center

Referral to a fetal medicine specialist *when:*

- *there are rising antibody levels/titres*
- *ultrasound and doppler features suggestive of fetal anemia.*



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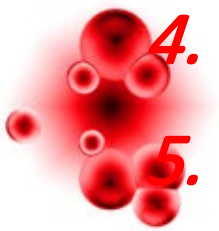
If the fetus is preterm

cordocentesis (percutaneous umbilical cord blood sampling) is recommended at this stage to directly assess :

1. *the fetal hematocrit*
2. *fetal blood grouping and Rh type*
3. *direct Coombs' test*
4. *reticulocyte count*
5. *total bilirubin level*



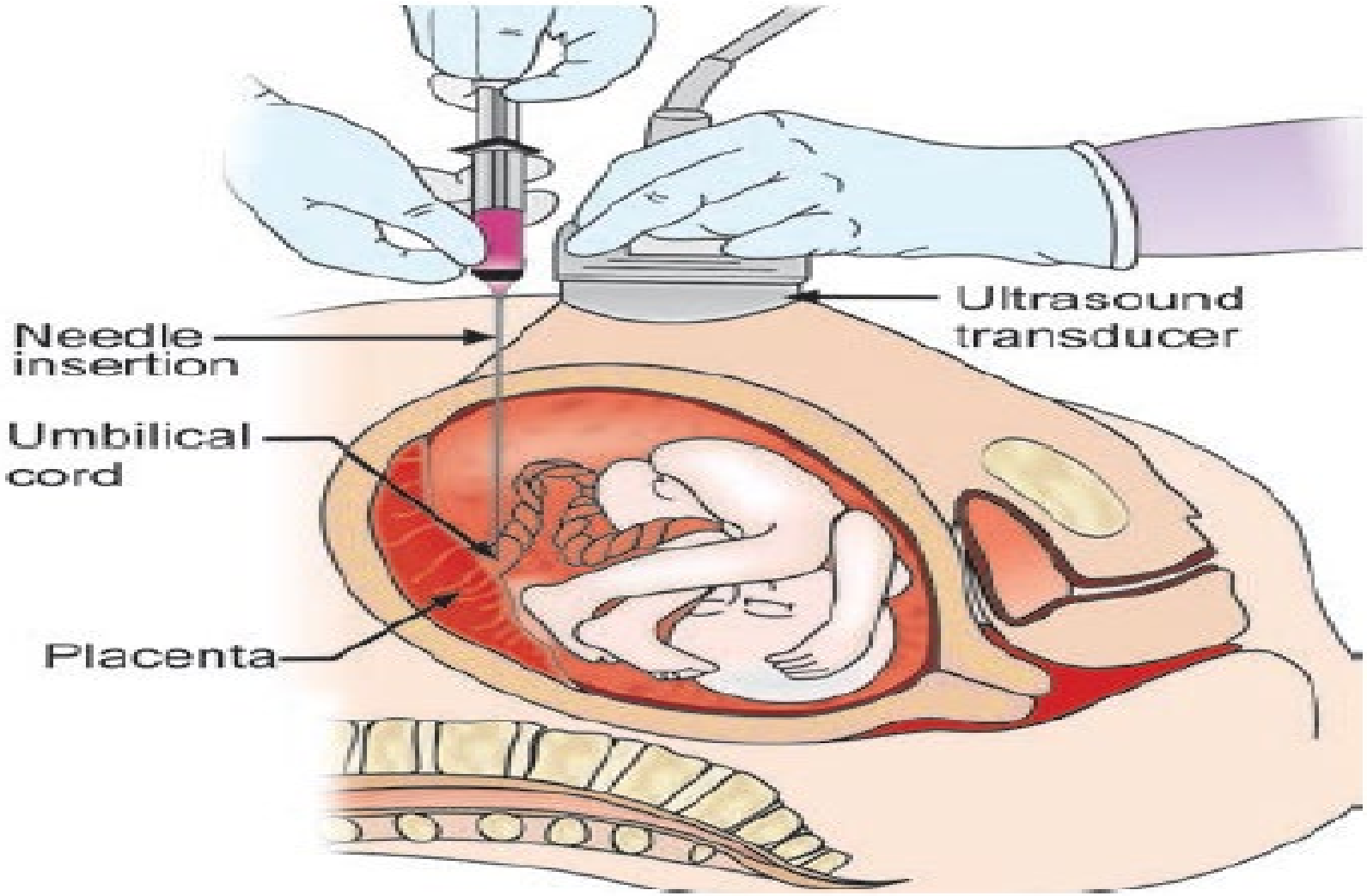


Fig. 6.6: Procedure of cordocentesis

Fetal blood transfusion

If severe anemia is confirmed:

intrauterine transfusion can be performed directly into the umbilical vein.

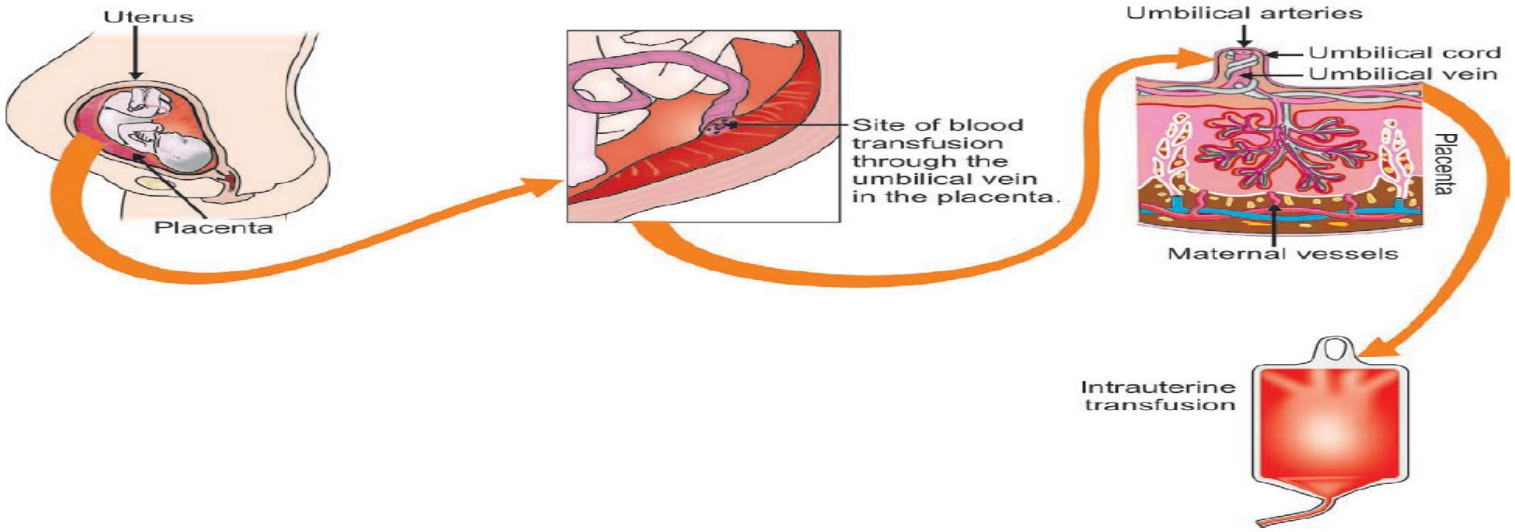


Fig. 6.7: Process of exchange transfusion

- started at 18 weeks
- repeated at intervals of 1–3 weeks up to 32–34 weeks

using

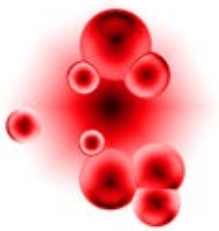
- 0-negative
- cytomegalovirus-negative
- washed
- leukocyte depleted
- irradiated packed red cells

Delivery:

- terminate the pregnancy around 34 weeks after steroid administration;
- neonatologist must be present at delivery, as exchange transfusion may be required If the baby has anemic

Fetal hydrops

- 90% are due to a non-immune cause
- 10% have an immune etiology.



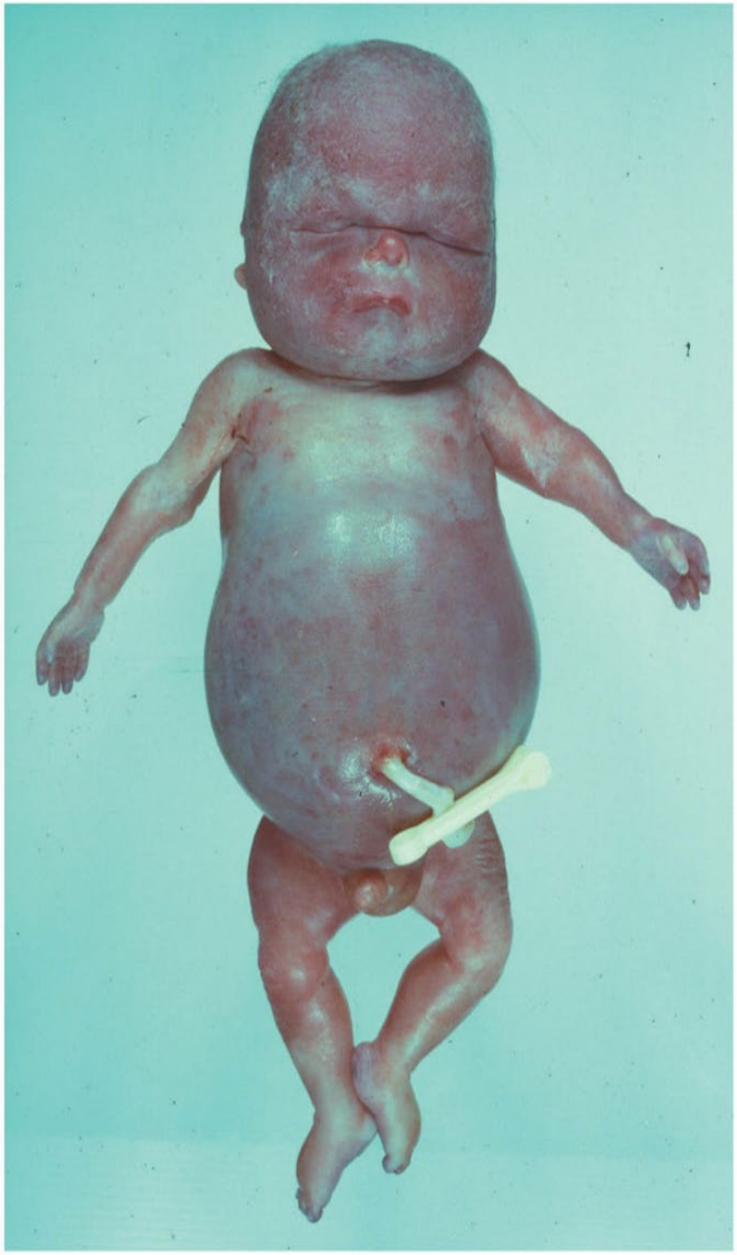
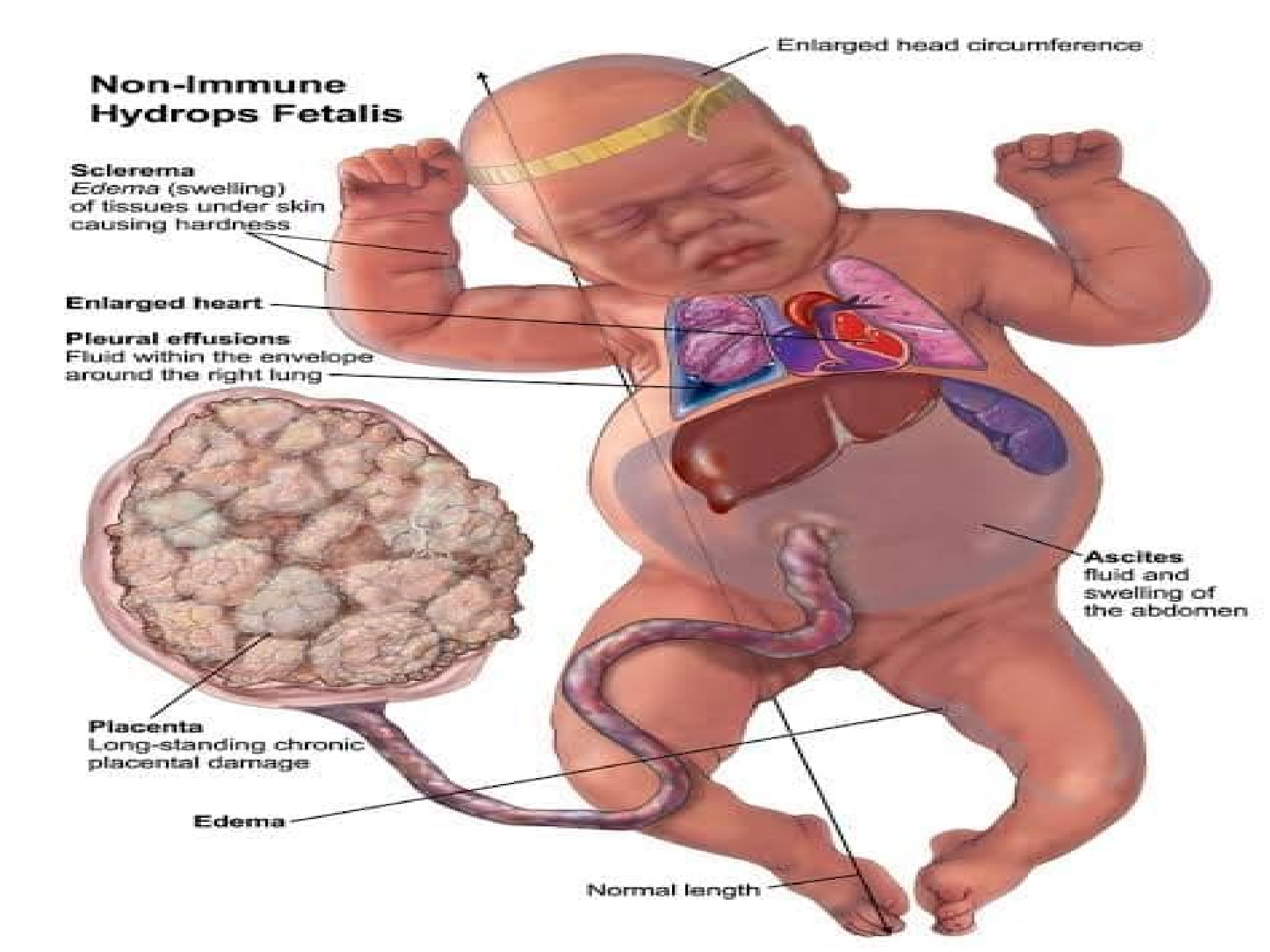


FIGURE 7-3. Fetal hydrops caused by the accumulation of fluid in fetal tissues. (From Sadler TW. *Langman's Medical Embryology,* 10th ed. Philadelphia, PA: Lippincott


Non-Immune
Hydrops Fetalis
Enlarged head circumference
Sclerema
Edema (swelling)
of tissues under skin
causing hardness
Enlarged heart
Pleural effusions
Fluid within the envelope
around the right lung
Ascites
fluid and
swelling of
the abdomen
Placenta
Long-standing chronic
placental damage
Edema
Normal length

Category	Condition	Category	Condition
Cardiovascular	Tachyarrhythmia Congenital heart block Anatomical defects (ASD/VSD, TOF, hypoplastic left heart, pulmonary valve insufficiency, Ebstein subaortic stenosis, and single ventricle)	Urinary	Urethral stenosis or atresia Posterior neck obstruction Prune belly
Chromosomal	Trisomies, Turner syndrome, and triploidy	Gastrointestinal	Jejunal atresia Midgut volvulus Malrotation of intestines Duplication of intestinal tract Meconium peritonitis
Malformation syndromes	Thanatophoric dwarfism Arthrogryposis multiplex congenital Osteogenesis imperfecta Achondroplasia	Medications	Antepartum indomethacin (taken to stop preterm labor, causing fetal ductus closure and secondary nonimmune hydrops fetalis)
Hematological	**α-Thalassemia = MC cause of NIHF** Arteriovenous shunts (vascular tumors) Kasabach-Merritt syndrome	Infections	TORCH Syphilis Parvovirus Leptospirosis
Twin pregnancy	Twin-twin transfusion syndrome Acardiac twin syndrome		
Respiratory	Diaphragmatic hernia Cystic adenomatous malformation Pulmonary hypoplasia	Miscellaneous	Amniotic band syndrome Cystic hygroma Congenital lymphedema Congenital neuroblastoma Tuberous sclerosis Sacrococcygeal teratoma

Thank you

Good luck