

RH - ALLOIMMUNIZATION



Outline

- ⊕ Introduction***
- ⊕ Rh blood grouping system***
- ⊕ Incidence of Rh alloimmunization***
- ⊕ Pathophysiology of Rh alloimmunization***
- ⊕ Management principle of unsensitized pregnancy***
- ⊕ Management principle of sensitized pregnancy***

The Basics Of Blood

W.B.C. & Platelet

R.B.C.

Plasma

ANTIGEN

>400 Agglutinogens on the cell membrane

ANTIBODY

*Natural & Immune Agglutinins/
allo antibodies*

***Antigen-Antibody reaction on the
cell surface → HEMOLYSIS***

Cont'd.

- > 15 blood group systems are recognized
 - ◆ *ABO, Rh, Kell, Duffy, Lewis.....*
- Most of these blood group antigens have been found to be associated with hemolytic disease
- However— ABO & Rh account for **98%**

Cont'd.

- ***Natural antibodies*** are formed against most of the major group antigens & present in almost all individuals when the antigen is absent
 - ◆ Mostly of them are IgM type
 - ◆ Usually do not cross placenta
- ***Immune antibodies***:- In contrast it is IgG type
 - Best react at body temp. & readily cross placenta

Rhesus Blood Group System

- Rh antigen is found On the short arm of **chromosome 1**
- Each chromosome will be
 - ◆ D positive or D negative (no d antigen)
 - ◆ C or c positive
 - ◆ E or e positive
- The genes code for D,C(c),E(e) antigens
- Rh system means all the **five** antigens

Cont'd.

- ◆ Rh positive → Presence of D ,C,c,E ,e antigens
- ◆ Rh negative absence of D , C,c ,E,e
- ◆ Traditionally Rh positive implies presence of D antigen
- ◆ Rh neg absence of D antigen
- ◆ Because D is the most common Rh antigen and by far the most immunogenic
- ◆ The Rh pos men could be 40% heterozygous & 60% homozygous

Cont'd.

- ◆ The Rh D antigens appear at age of **30 days** in utero life
- ◆ The Rh antigens are transmembrane proteins located & thus integral components of the red cell membrane
- ◆ The precise function of Rh-antigen unknown; but probably in maintaining RBC membrane integrity

Cont'd.

- ◆ **Sensitization** ---production of antibodies against exposed antigens
- ◆ **“Allo”—different; “Iso”—same**
- ◆ Isoimmunization is the older term & now replaced by **alloimmunization** & can be interchangeably used with **Rh sensitization**

Cont'd.

- ◆ **Erythroblastosis fetalis**: before the advent of ultrasound the effect of this alloimmunization was only known by peripheral blood smear of high immature RBC called erythroblasts ;hence the name Erythroblastosis fetalis was used
- ◆ **Hemolytic diseases of the fetus & the newborn(HDFN)** –Currently used instead of Erythroblastosis fetalis

Incidence of RH alloimmunization

- ◆ **About 16%** of untreated Rh neg women become allo immunized in their Rh incompatible(ABO compatible)pregnancy

Pathophysiology RH alloimmunization

- Rh alloimmunization needs three conditions**
 - 1. Fetus Rh positive & mother Rh negative**
 - 2. Sufficient number of RBC must gain access to maternal circulation**
 - 3. Mother must have immunologic capacity to produce antibodies**

Cont'd.

Fetomaternal hemorrhage

- Fetal RBC may gain access to maternal circulation during **pregnancy & delivery**
- FMH increases as gestational age increases
- Chances of fetomaternal hemorrhage is only **5% in 1st trimester** but **50% in 3rd trimester**, many conditions can increase the risk
- Fetomaternal hemorrhage in a volume sufficient to cause alloimmunization is most common during delivery

Cont'd.

- ◆ **Factors that increase the amount of hemorrhage**
 - ◆ **Cesarean delivery**
 - ◆ **Multiple pregnancy**
 - ◆ **APH**
 - ◆ **Manual removal of placenta**
 - ◆ **Intrauterine manipulation**

Cont'd.

◆ Immunologic response

- ◆ The probability & severity of Rh alloimmunization depend on individual characteristics
- ◆ As many as **20%** of Rh negative
→ **nonresponders**
- ◆ **ABO incompatibility** will diminishes the risk of alloimmunization to **1.5%-2%**

Cont'd.

- ◆ The Rh D is highly immunogenic in subjects who are not immunosuppressed
- ◆ As low as **0.1ml** can produce antibodies
- ◆ Only **20%** produced anti D in malignancy & AIDS patients

Cont'd.

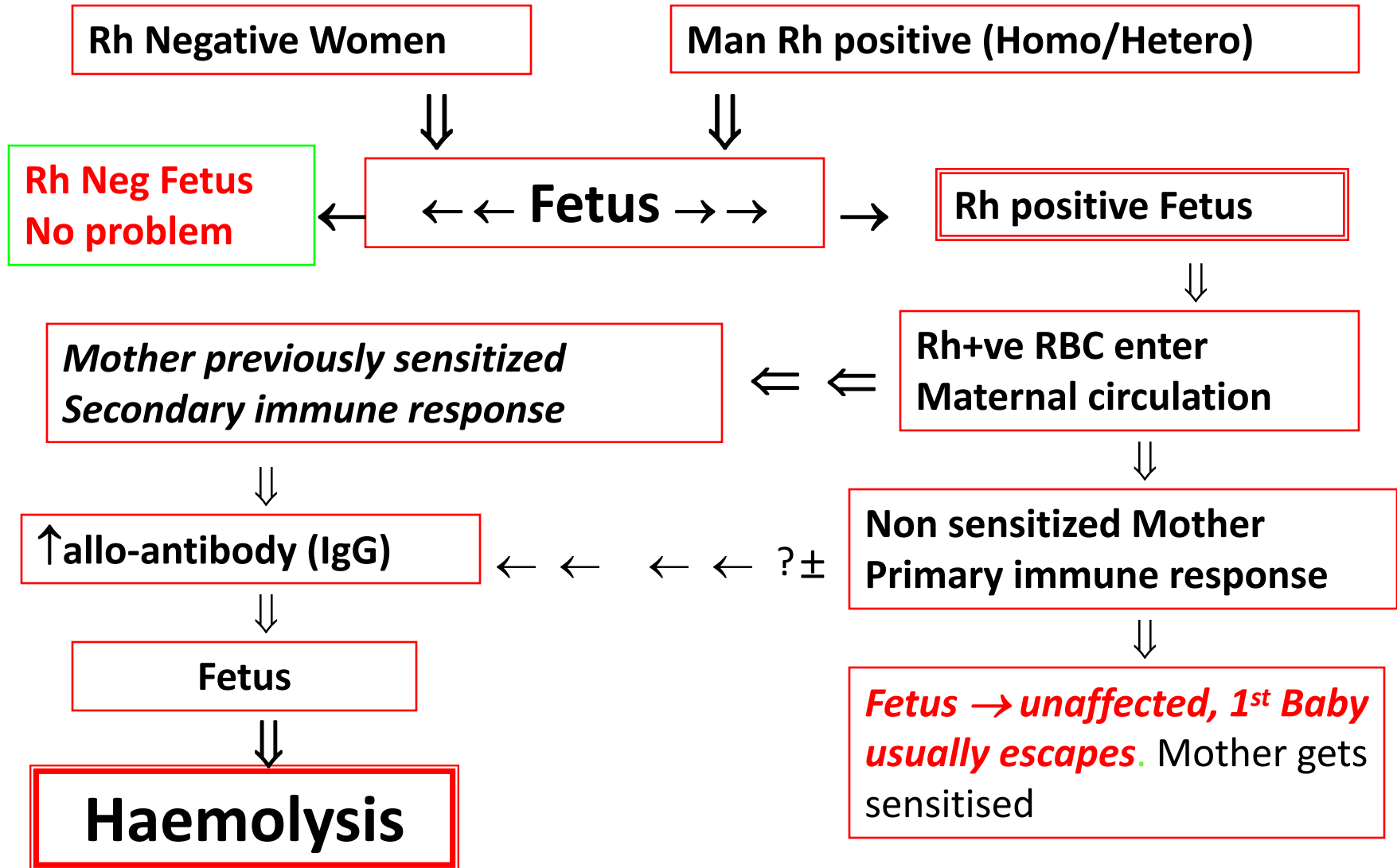
◆ Primary immune response

- ▶ Slow in response
- ▶ Initially IgM (900,000) can not cross the placenta → no hemolysis
- ▶ Later IgG (160000) cross the placenta & cause hemolysis

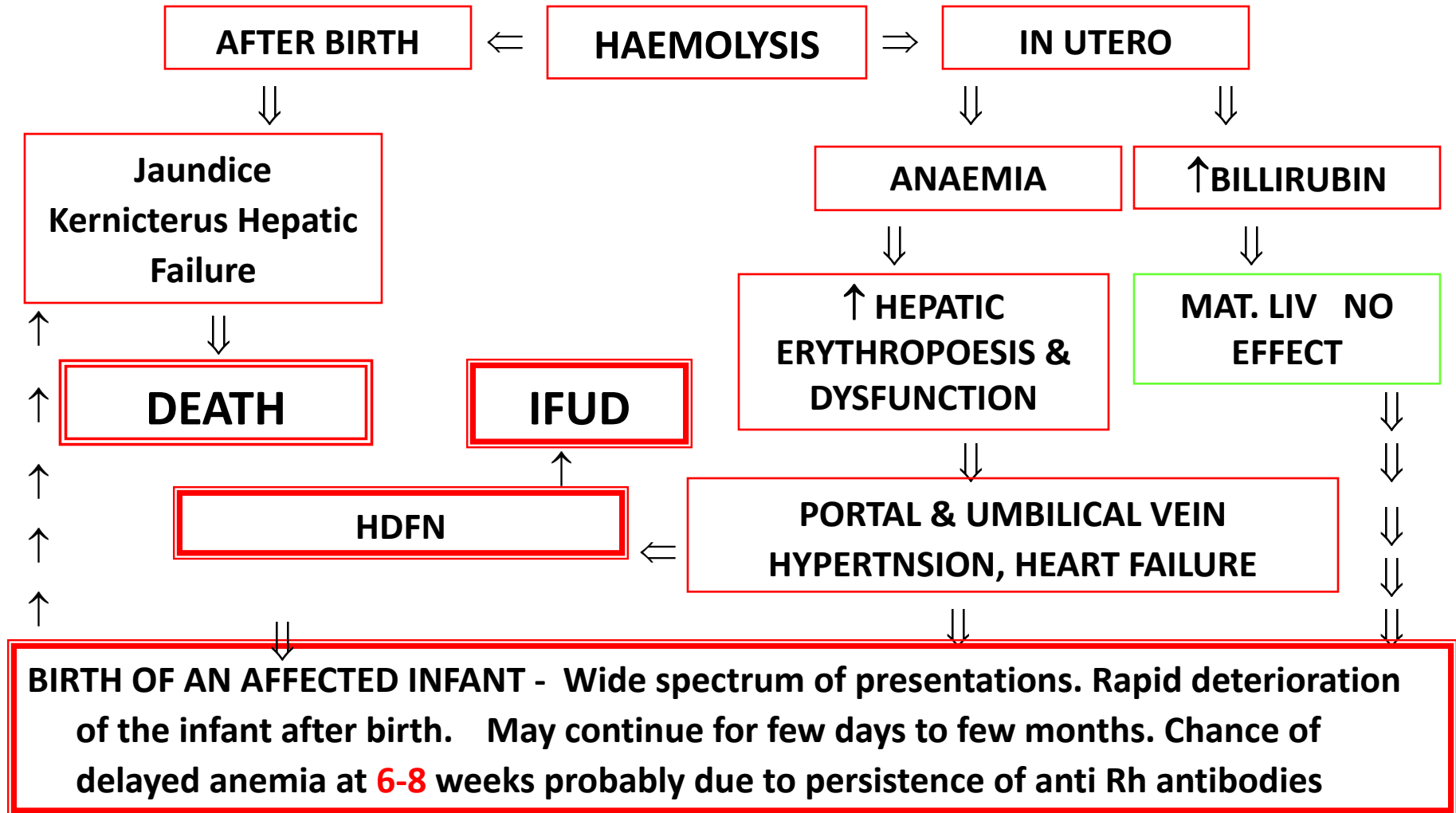
◆ Secondary immune response

- ▶ Fast & totally IgG → hemolysis

Pathogenesis Of Rh Allo-immunisation



Pathology Of allo-immunisation



Management of Unsensitised Pregnancy

- ◆ **Blood typing at 1st visit**
 - ◆ If negative → husband's typing
 - ◆ If husband is also negative → no treatment
 - ◆ If husband is positive
 - ◆ Do Indirect Coomb's test of mother – and if negative repeat at 28 weeks
 - ◆ If negative, 300 g of Rh immunoglobulin (RhIgG) is given
 - ◆ If Positive → ***Sensitized***

Cont'd.

- ◆ At birth- cord blood for ABO/Rh typing, direct coombs test
 - ◆ Baby Rh negative – Be happy
 - ◆ Baby Rh positive - 300mcg anti-D immunoglobulin be given within **72** hours after delivery (shown to be effective in preventing allo immunization if given up to **28** days after delivery)

Cont'd.

- ◆ In Abortion, Ectopic
 - ◆ Pregnancy < 12 weeks- *50mcg Anti D*
 - ◆ Pregnancy >12 weeks- *300mcg Anti D*
 - ◆ *GTD-300mcg*
- ◆ APH, Amniocentesis, Abdominal trauma ,Any procedure associated with Fetal-maternal hemorrhage
➔ *300mcg Anti D*

Rh D immune globulin & the prevention of alloimmunization

- ◆ Prior to anti-D immunoglobulin **16%** of Rh(D) negative women will be sensitized
- ◆ The rate will fall to **2%** after single dose & further reduced to **0.1%** after additional dose in the third trimester
- ◆ Anti-D is a sterile solution containing **IgG anti-D** manufactured from human plasma
- ◆ A single 300microgram (1microgram=5IU) contains sufficient anti-D to suppress immune response to 15ml of RBC(30ml of whole fetal blood)

Mechanism of action of Anti D

◆ **Unproven**

◆ **Possibilities**

1. Rapid macrophage mediated clearance of anti D coated RBC

2. Down regulation of antigen specific B cells before an immune response

Management of Sensitized Pregnancy

- ◆ Sensitized = antibody titer of $\geq 1:4$
- ◆ Antibody titer should be followed Q 4weeks until 24weeks and then Q 2weeks in first affected pregnancy until **critical titer**
- ◆ Critical titer is the anti D antibody titer after which hydrops fetalis is high likely to occur
- ◆ Its value is **1:32**

Cont'd.

- Below critical titer mild to moderate anemia can occur, but **severe anemia is unlikely**
- Further diagnostic methods are not recommended at values below critical titer
- There are two approaches for those above the critical titer level and for those having a **previously affected fetus or new born**

Cont'd.

- 1. Middle cerebral artery(MCA) Doppler studies** should be commenced 2 weeks after critical titer.(the base is peak systolic velocity increases as anemia increases)
 - If MCA Doppler **>1.5MoMs**, Cordocentesis is recommended for hematocrit level

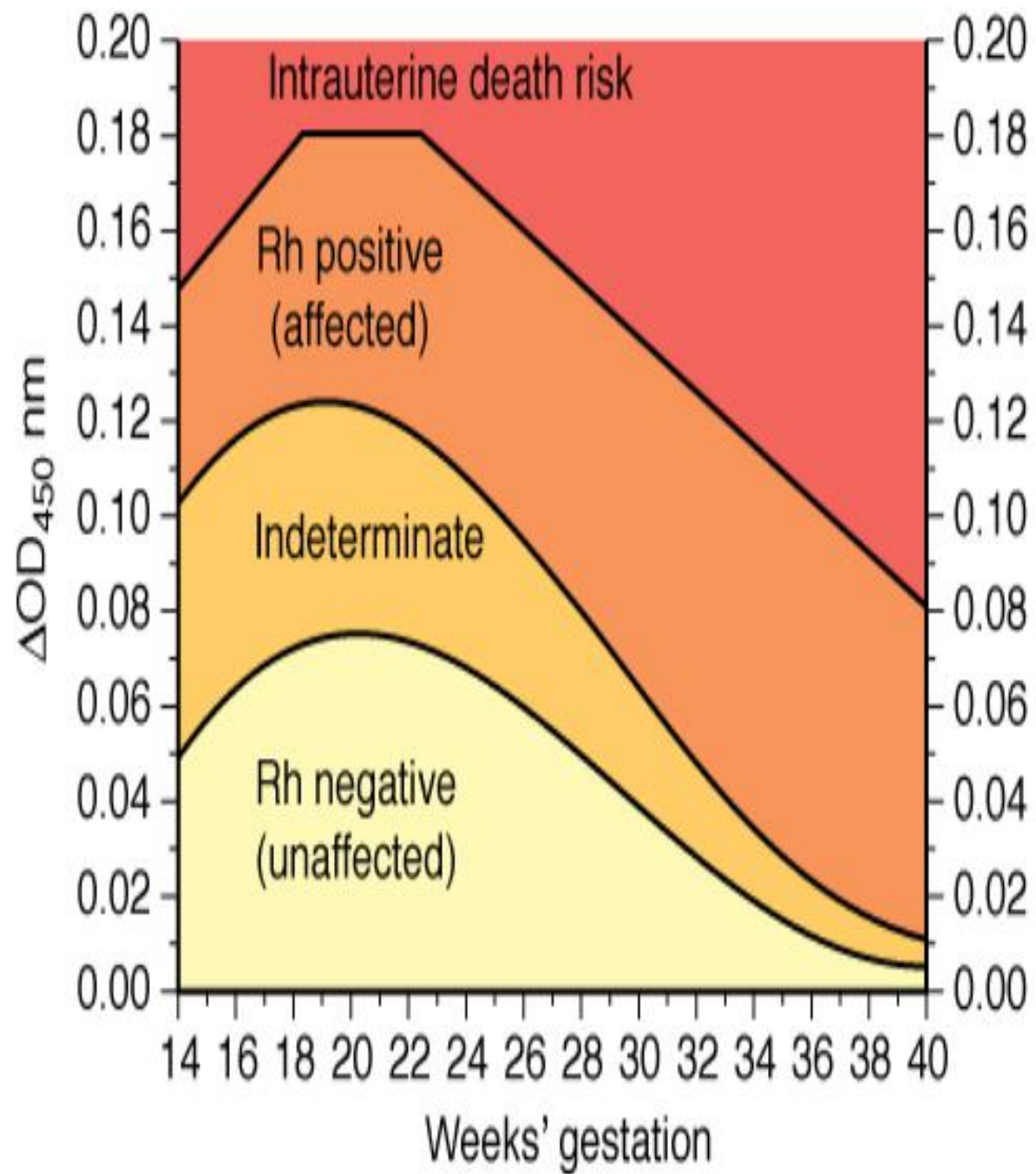
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2. Amniocentesis

- Serial procedures are undertaken at 2 weeks intervals
- Hemolysis bilirubin excreted to amniotic fluid
- High bilirubin → Increased hemolysis
- Analysis of the change in optical density(OD) of amniotic fluid at wave length of 450nm
 - OD is defined as the measure of the transmission of an optical medium for a given wave length

Cont'd.

- ◆ AF analysis for Liley's chart follow-up
 - ***Mildly Affected Fetus*** (falls into **zone 1**)
 - Is considered to unaffected or mildly affected
 - Testing repeated every 2–3 weeks, and
 - Delivery at term
 - ***Moderately Affected Fetus*** (falls into **zone 2**)
 - Should be tested more frequently, every 1–2 weeks
 - Delivery may be prior to term (as pulm. maturity is reached)
 - ***Severely Affected Fetus*** (falls into **zone 3**)
 - Has frank evidence of hydrops (ascites, pleural or pericardial effusion, subcutaneous edema)
 - Consider termination of pregnancy or intrauterine transfusion based on GA



Summary

- ➡ Most of HDFN are associated with **ABO & RH** incompatibility
- ➡ There are many factors which affect the **incidence & severity** of RH sensitization
- ➡ Administration anti-D both ante partum & postpartum doesn't **totally prevent** the risk of sensitization
- ➡ **Antibody titer** level is not used for follow up in a woman having **previously affected** pregnancy
- ➡ Once the **critical titer** level is reached **MCA doppler velocimetry** or **Amniocentesis** can be used to indirectly assess the level of anemia
- ➡ If the indirect methods show that the risk of anemia is **high** taking blood directly from the fetus for **HCT** determination is recommended
- ➡ Based on the **HCT** result & **GA** either **termination** of the pregnancy or **intrauterine transfusion** may be considered

THANK YOU!