# RH-ISOIMMUNIZATION AND & ABO incompatibility


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***173-B***

# Rh- Iso imunization Definition

known as:

**Rhesus incompatibility**, **Rhesus disease RhD Hemolytic Disease of the Newborn.**

-When Rh– mother gets pregnant to Rh+ fetus —she may be sensitized to Rh antigen and develop antibodies. These will cross the placenta and cause hemolysis of fetal red blood cells.

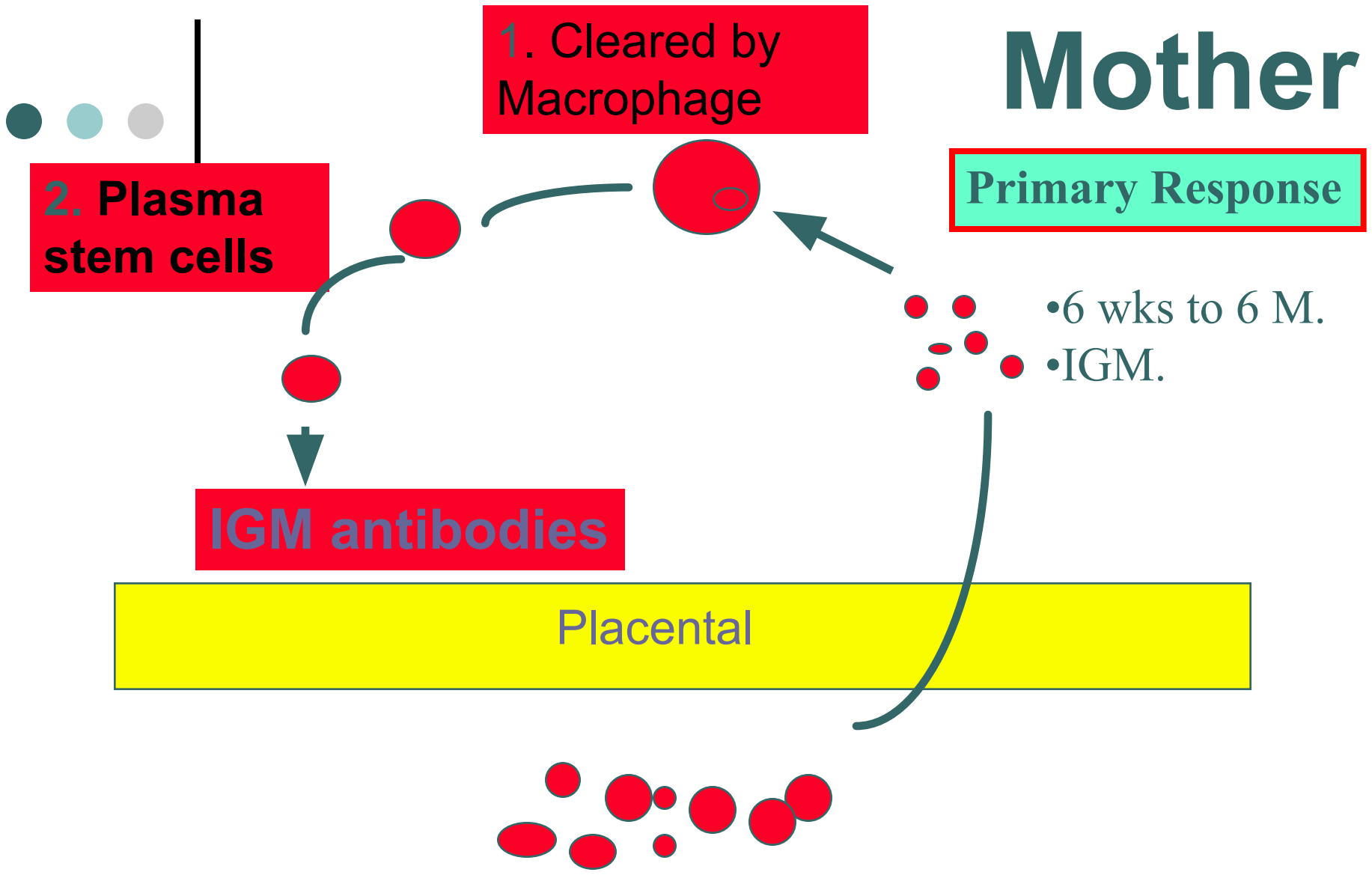
- The risk of sensitization after ABO incompatible pregnancy is only 2%

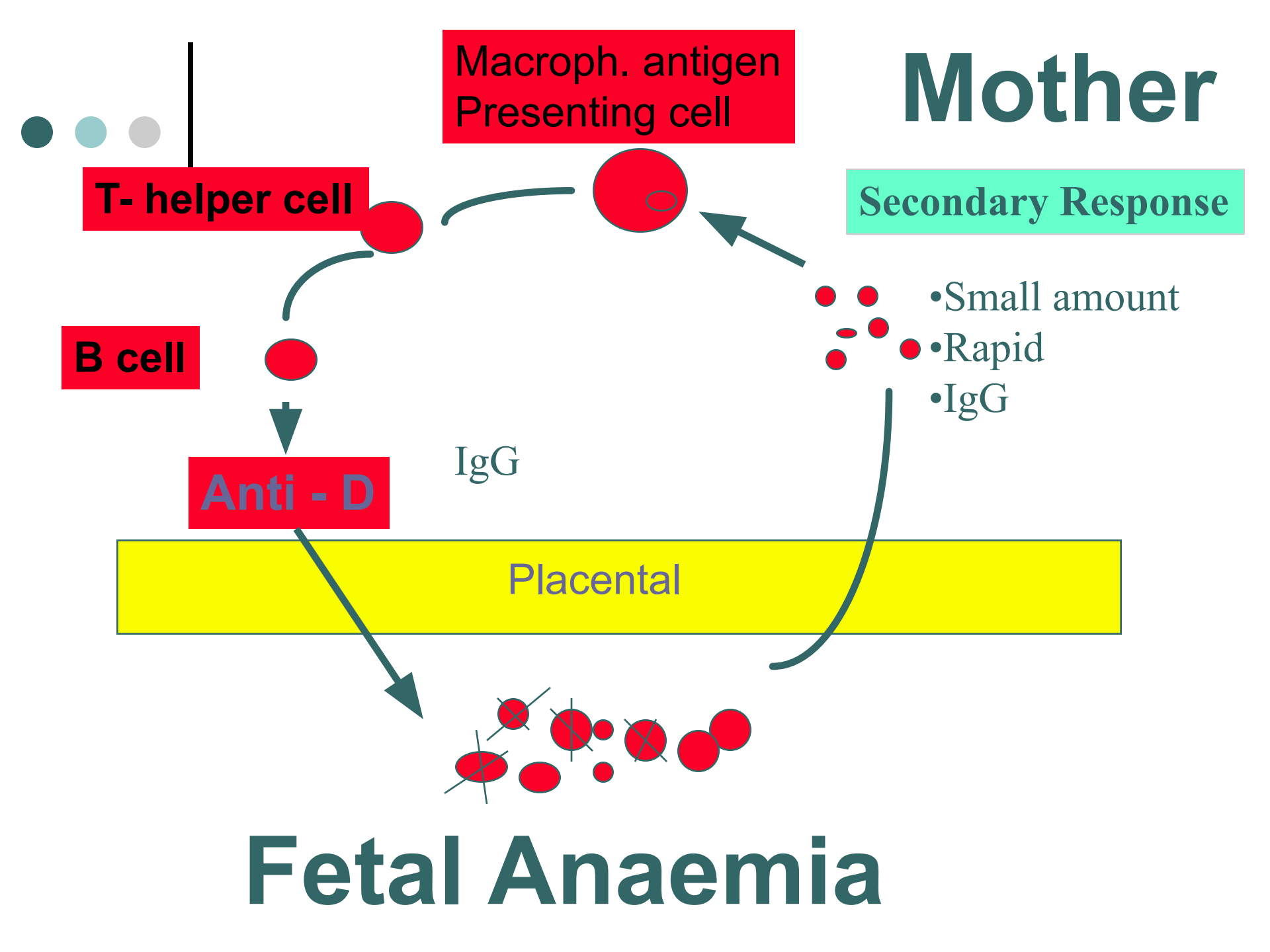
# Pathophysiology

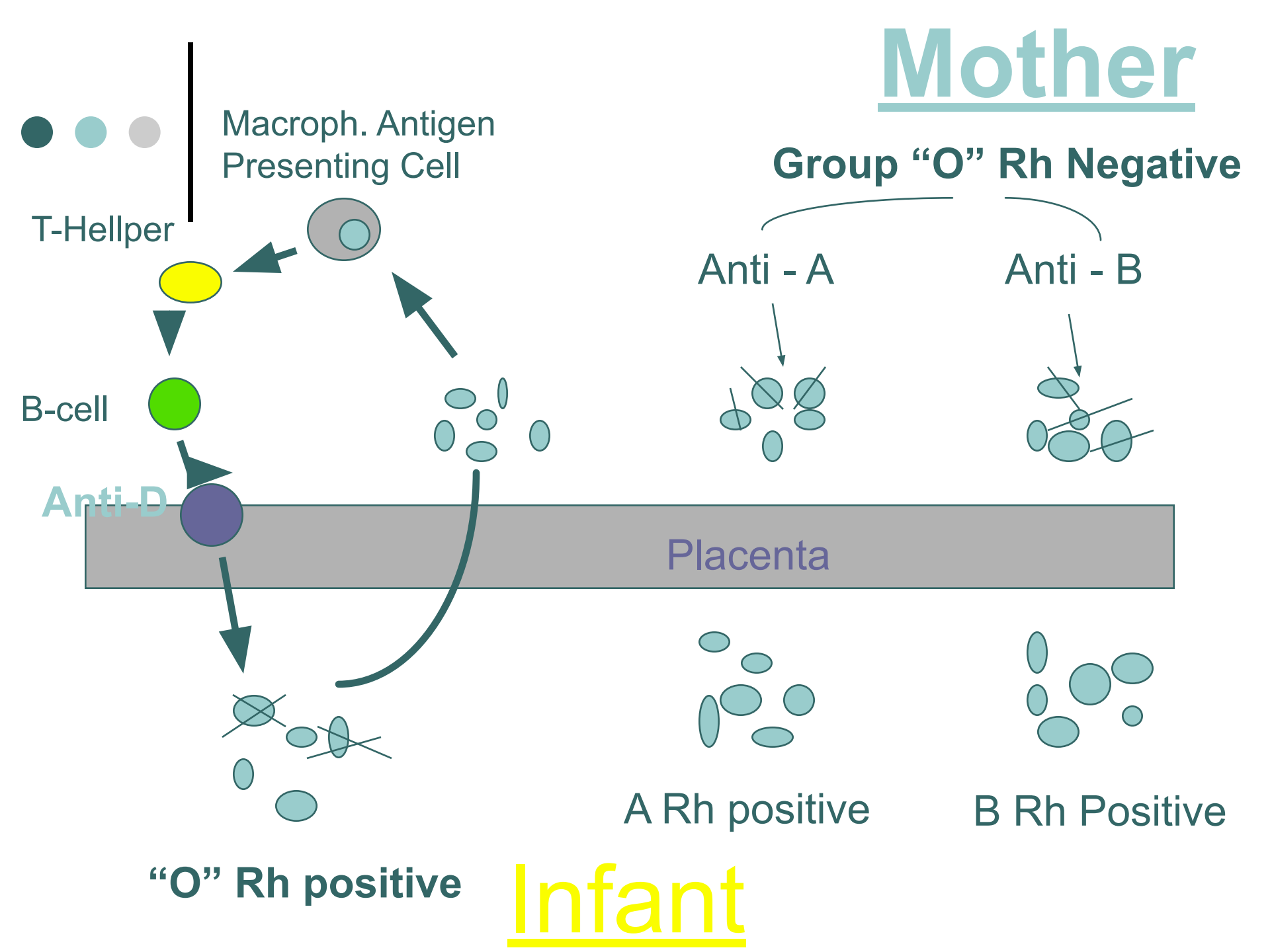
- The rhesus system which comprises number of antigens C, D, E, c, e.
- A person who lacks D antigen is called Rh negative.
- 15% of Caucasians, 5% African Americans and 2 % of Asians are Rh negative.
- Rh isoimmunisation is due to D antigen in more than 90% of cases.
- Occasionally hemolytic disease of the newborn is a result of maternal immunization to Irregular RBC antigens other than Rh group like anti- Kell and anti-Duffy

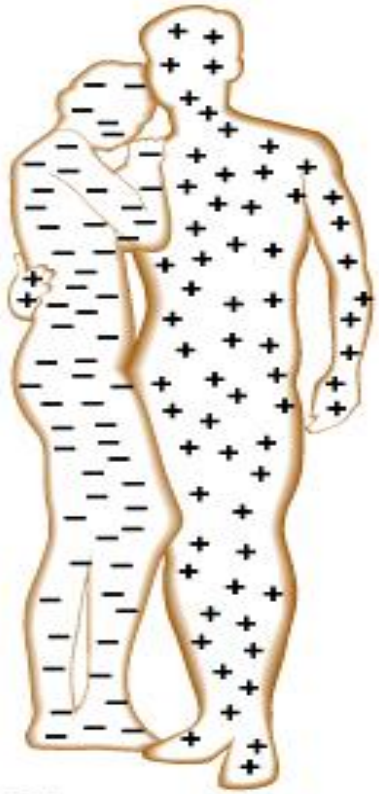
# Pathophysiology

- Initial response is forming IgM antibodies for short period followed by production of IgG which crosses placenta
- IgG antibodies adhere to the antigen site on the surface of erythrocytes causing hemolysis.
- The excessive removal of circulatory RBCs leads to severe anemia and hypoxia.
- Erythropoiesis results in hepatosplenomegaly.
- Tissue hypoxia and hypoproteinemia results in cardiac and circulatory failure, with generalized odema and hydrops

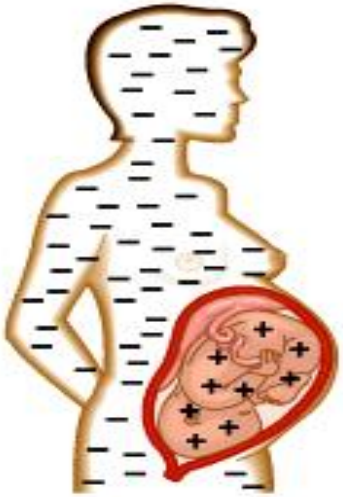

1. Cleared by Macrophage
Mother
2. Plasma stem cells
Primary Response
•6 wks to 6 M.
•IGM.
IGM antibodies
Placental
Fetal Anaemia


Macroph. antigen
Presenting cell
Mother
T- helper cell
Secondary Response
•Small amount
•Rapid
•IgG
B cell
IgG
Anti - D
Placental
Fetal Anaemia


Mother
Macroph. Antigen Presenting Cell
T-Hellper
Group “O” Rh Negative
Anti - A
Anti - B
B-cell
Anti-D
Placenta
A Rh positive
B Rh Positive
“O” Rh positive
Infant



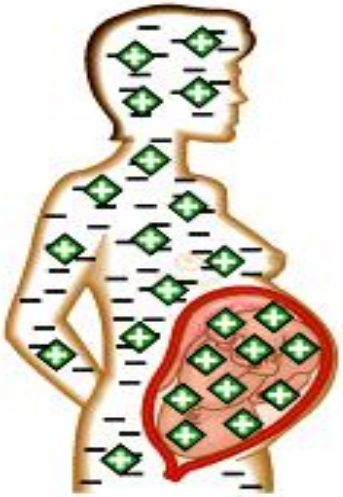
Rh-negative woman and Rh-positive man conceive a child



Rh-negative woman with Rh-positive fetus

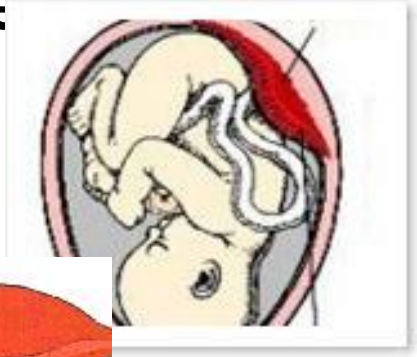
Cells from Rh-positive fetus enter woman's bloodstream

Woman becomes sensitized— antibodies (◇) form to fight Rh-positive blood cells

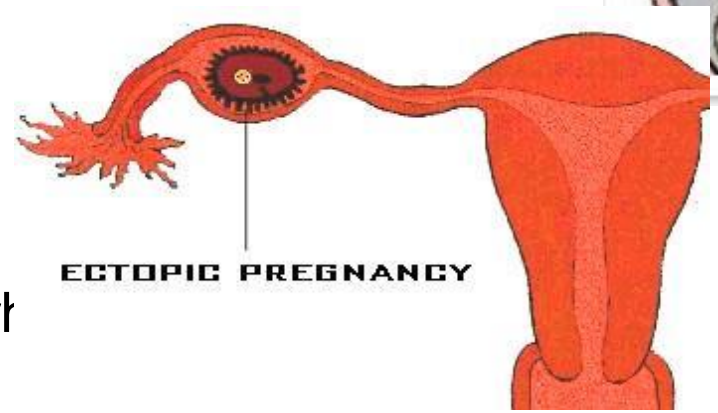


In the next Rh-positive pregnancy, maternal antibodies attack fetal red blood cells

# Fetomaternal hemorrhage as a reason of Rh –isoimmunization has bee documented in:

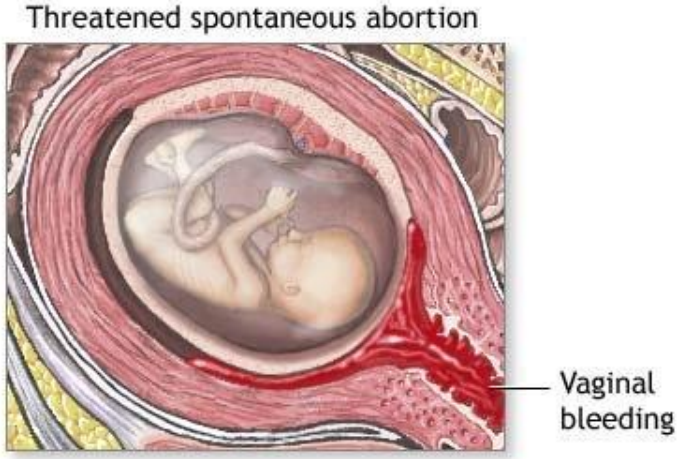


- 7% in the first trimester.
- 16% in the second trimester
- 29% in the third trimester




Risk of fetromaternal hemorrh is increased in **abruption placenta, threatened abortion, toxemia, after cesarean section, ectopic pregnancy, amniocentesis, intrauterine fetal transfusion.**

**And it occur during normal delivery**



Rh Antibodies

↓

Antibodies Coated Red Cells

↓

Destruction of Fetal Cells by Fetal RES

↓

**Fetal Anemia**

↓

Fetal Hypoxia and Stimulate of Erythropoitin

↓

Extra Medullary red Cells Synthesis

↓

Hepatomegally

↓

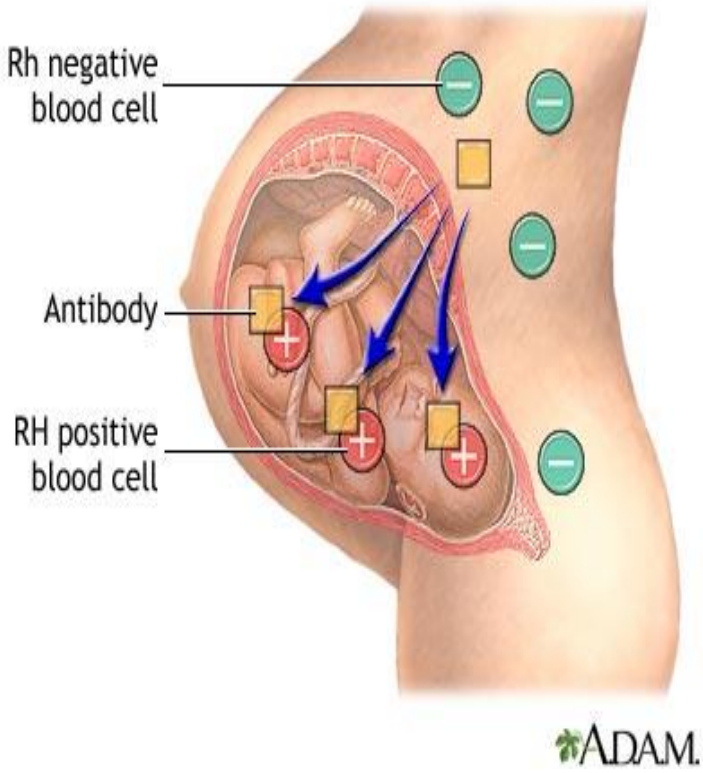
Hepatic Cell Failure

↓

Hypoproteinemia, Increased Intrahepatic Pressure, Portal hypertension

↓

Ascetic, Edema, hypoxia, Placental Thickness, Polyhydramnios, Pericardial effusion



# Complications of Fetal-Neonatal anemia:

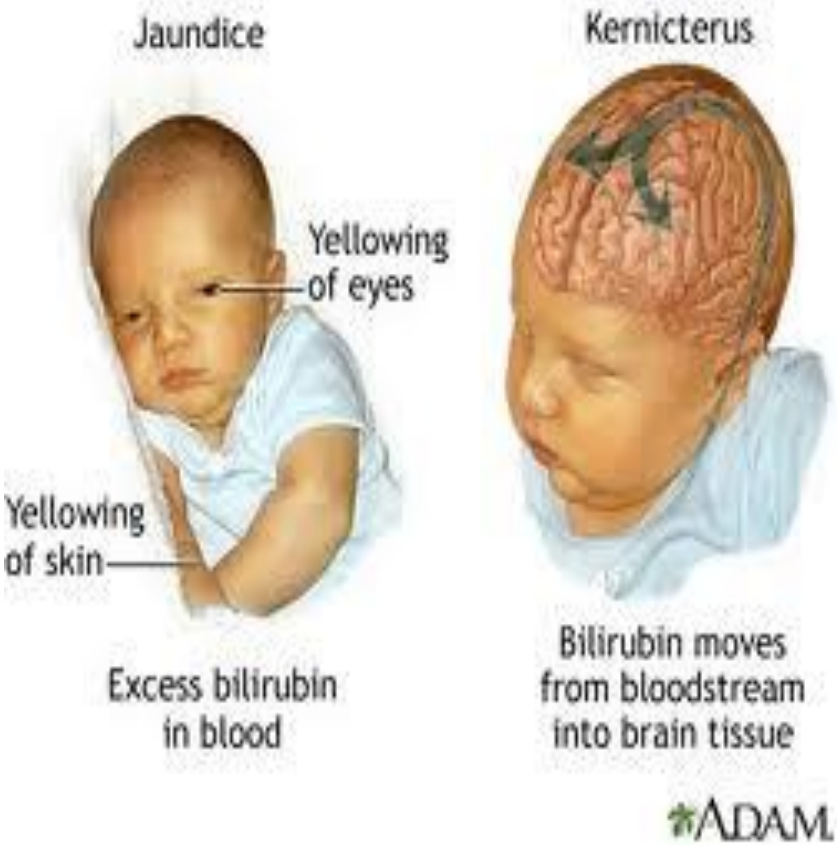
- Fetal Hydrops And Stillbirth
- Hepatosplenomegaly
- Neonatal Jaundice
- Compilations Of Neonatal Kernicterus (Lethargy, Hypertonicity, Hearing Loss, Cerebral Palsy And Learning Disability)
- Neonatal Anemia

# Kernicterus

Concentration of bilirubin in the newborn blood exceeds

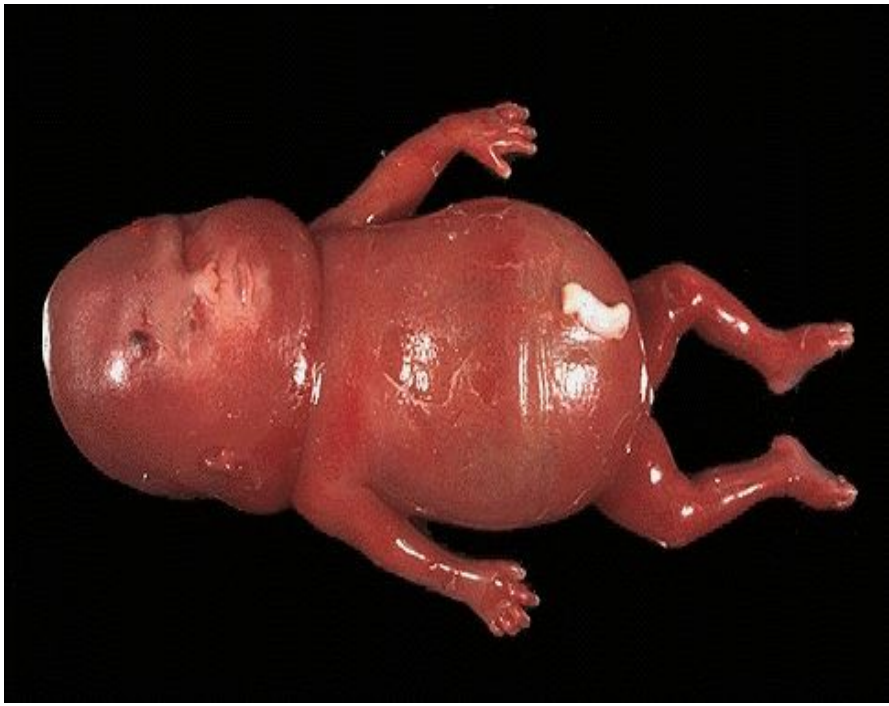
in-term fetus – 307,8 – 342 mkmoll/L

in pre-term fetus – 153-205 mkmoll/L,

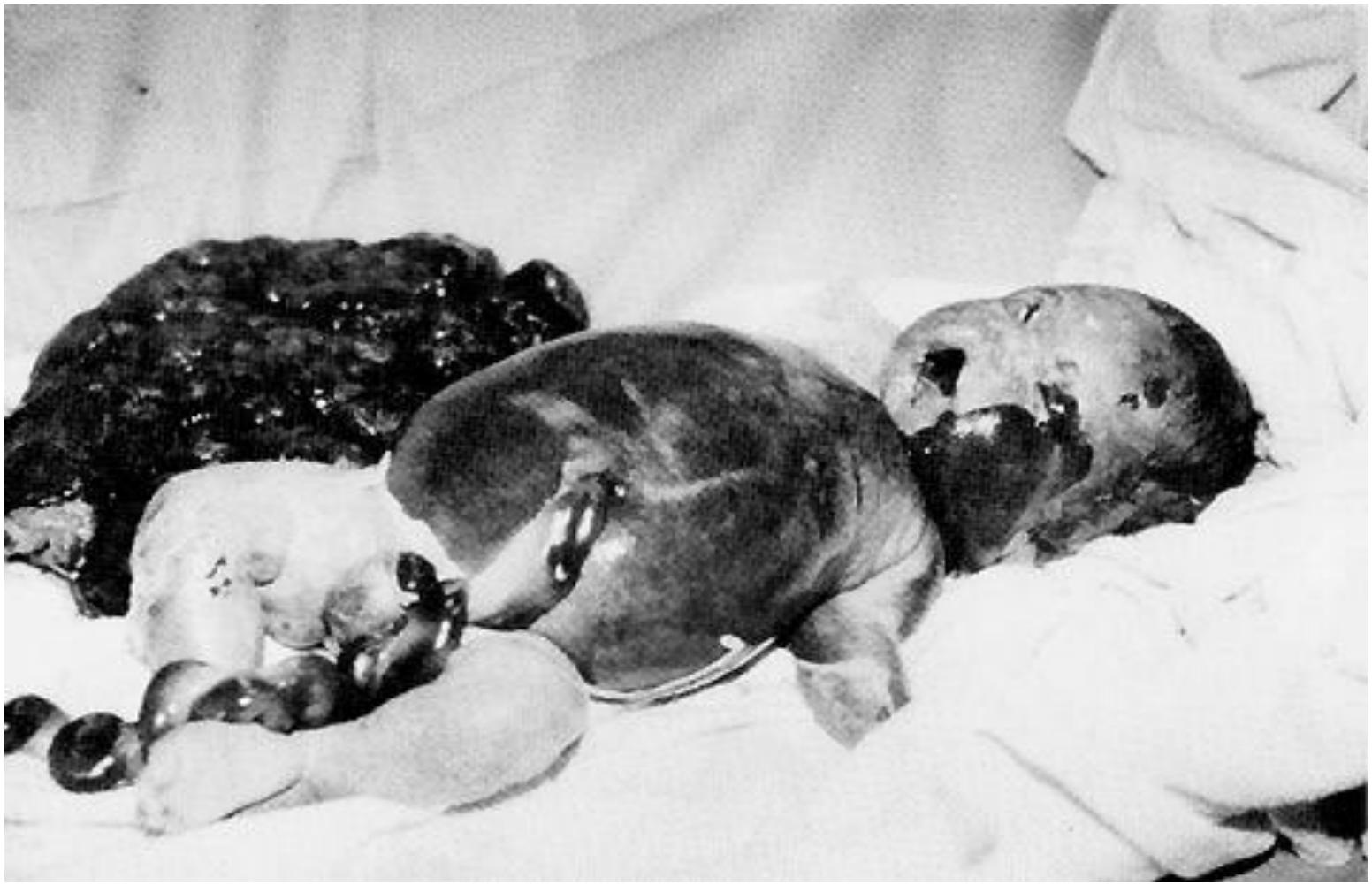


# Natural History

- 50% of affected infants have no or mild anemia, requiring either phototherapy or no treatment.
- 25% have some degree of hepatosplenomegaly and moderate anemia and progressive jundice culminating in kernicterus, neonatal death or severe handicap.
- 25% are hydropic and usually die in utero or in the neonatal period ( half of these the hydrops develops before 34 weeks gestation



# Hydrops fetalis

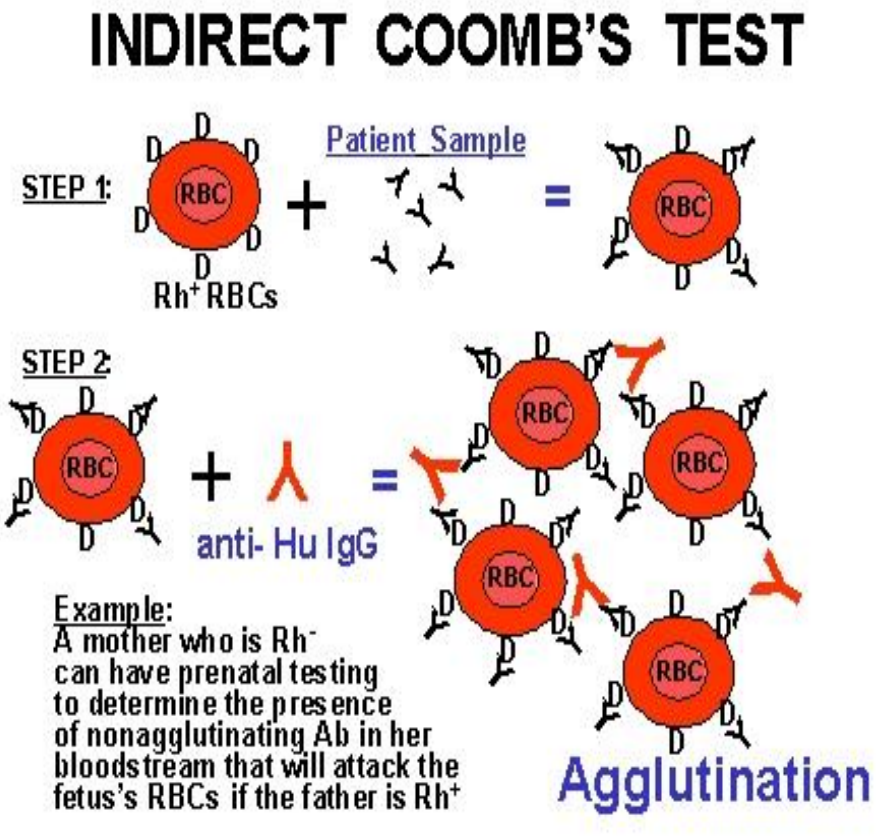


# The aim of antenatal management

- To predict which pregnancy is at risk
- To predict whether or not the fetus is severely affected.
- To correct anemia and reverse hydrops by intrauterine transfusion.
- To deliver the baby at the appropriate time, weighing the risks of prematurity against these of intrauterine transfusion.

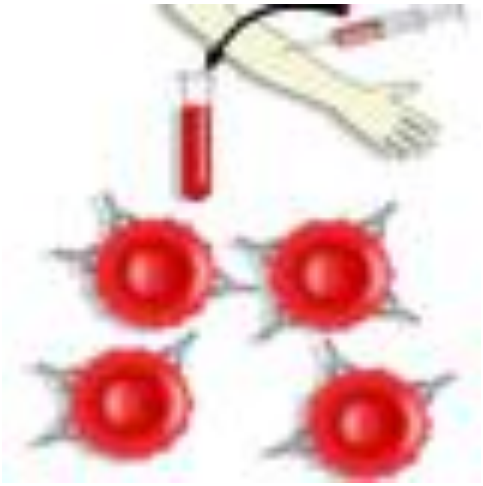
# Recognition of pregnancy at risk

- First ante-natal visit check blood group, antibody screening.
- If indirect coombs test is positive, the father's Rh sho be tested.
- Serial maternal Anti D titers should be done every 2- 4 weeks.
- If titer is less than 1/16 the fetus is not at risk.
- **If titer is more than 1/16 th severity of condition shou be evaluated.**

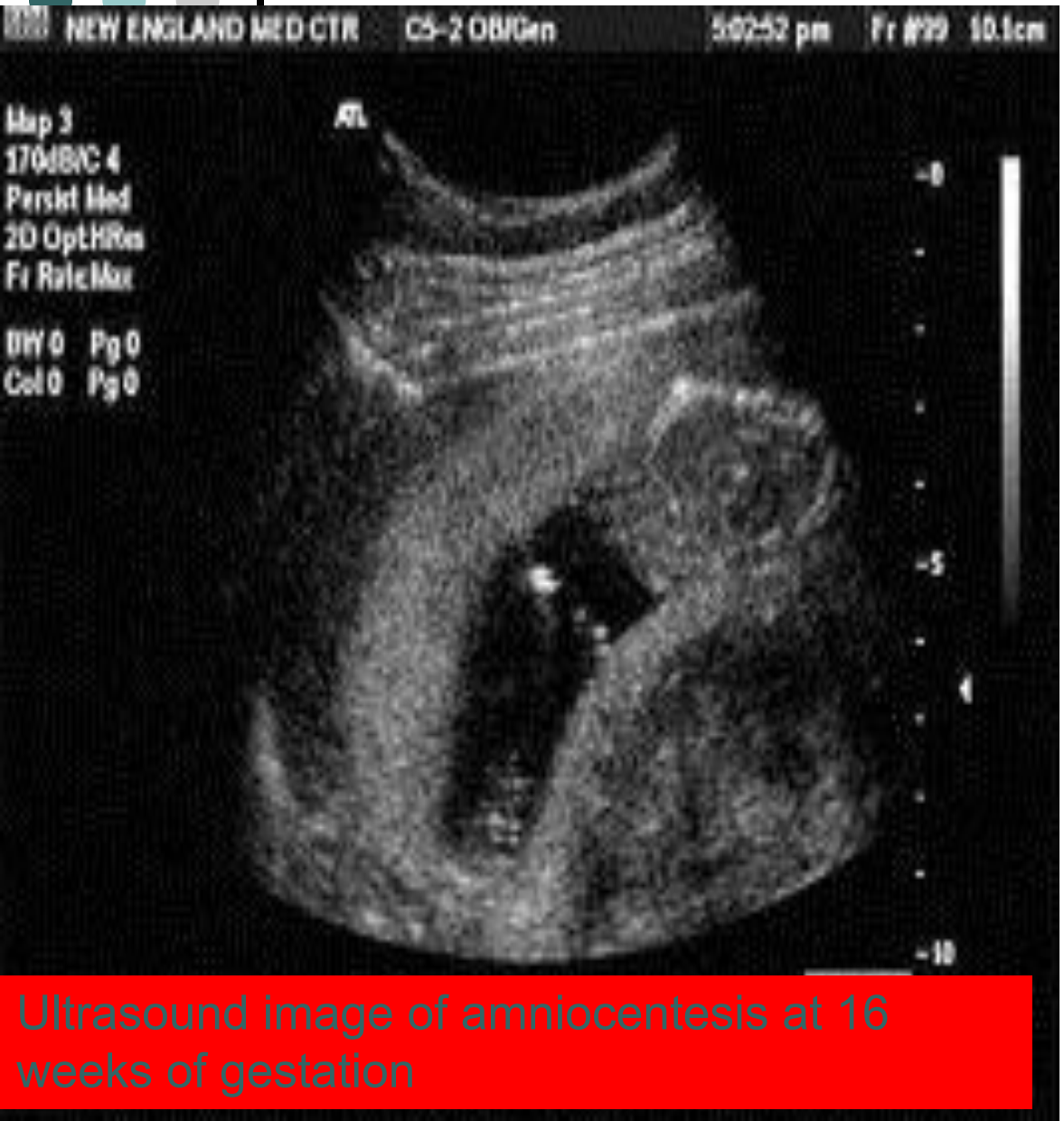


# Prediction of the severity of fetal hemolysis

- History of previous affected pregnancies
- The levels of maternal hemolytic antibodies
- Amniocentesis
- Biophysical surveillance
- Fetal blood sampling



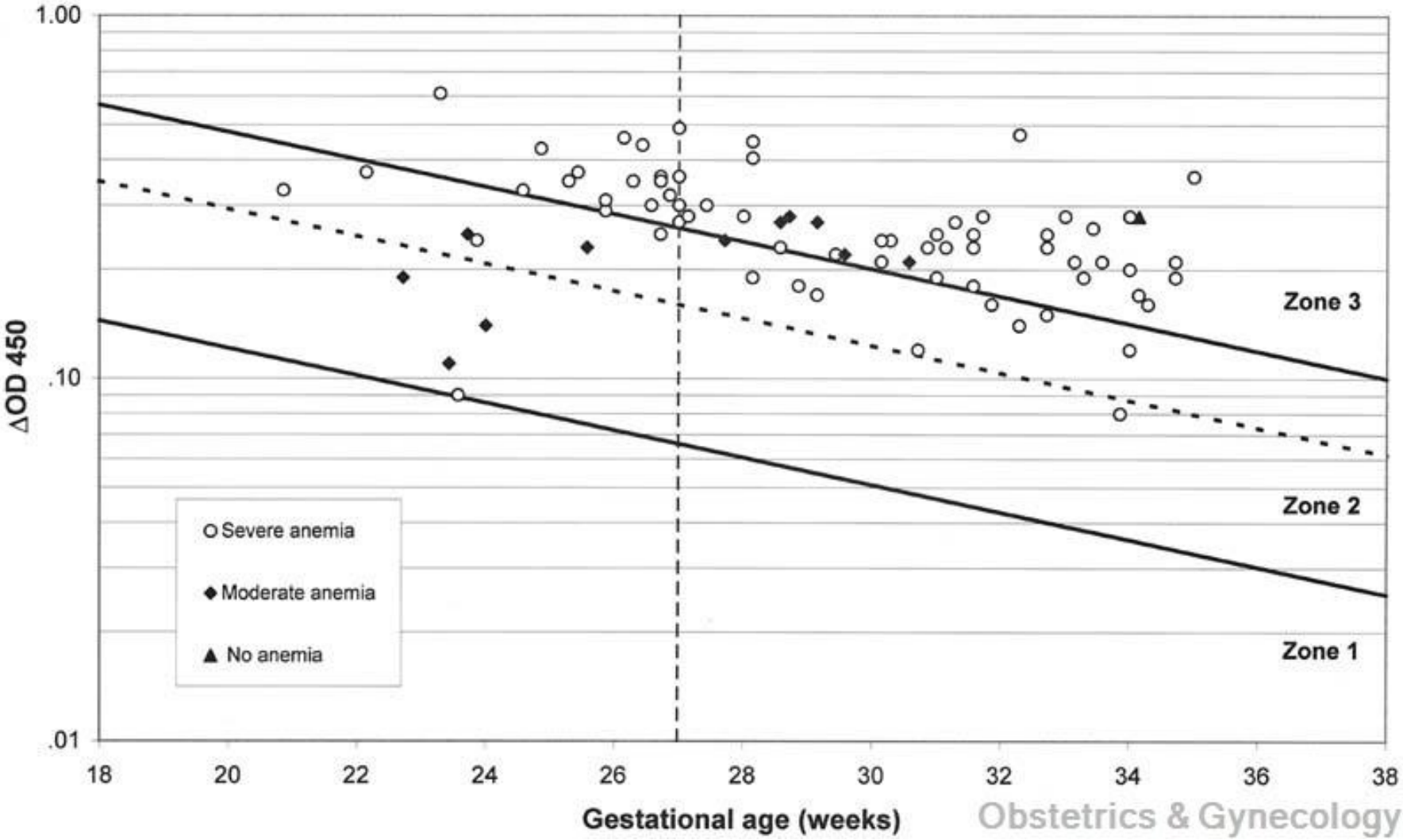
# Amniocentesis – at 16 weeks




Ultrasound image of amniocentesis at 16 weeks of gestation

- There is an excellent correlation between the amount of bilirubin in amniotic fluid and fetal hematocrit.
- the optical density deviation at 450 nm measures the amniotic fluid unconjugated bilirubin.

# Amniocentesis



# Amniocentesis

- Normally Bilirubin In Amniotic Fluid Decreases With Advanced Gestation.
- It Derives From Fetal Pulmonary And Tracheal Effluents.
- Its Level Rises in Correlation With Fetal Hemolysis.

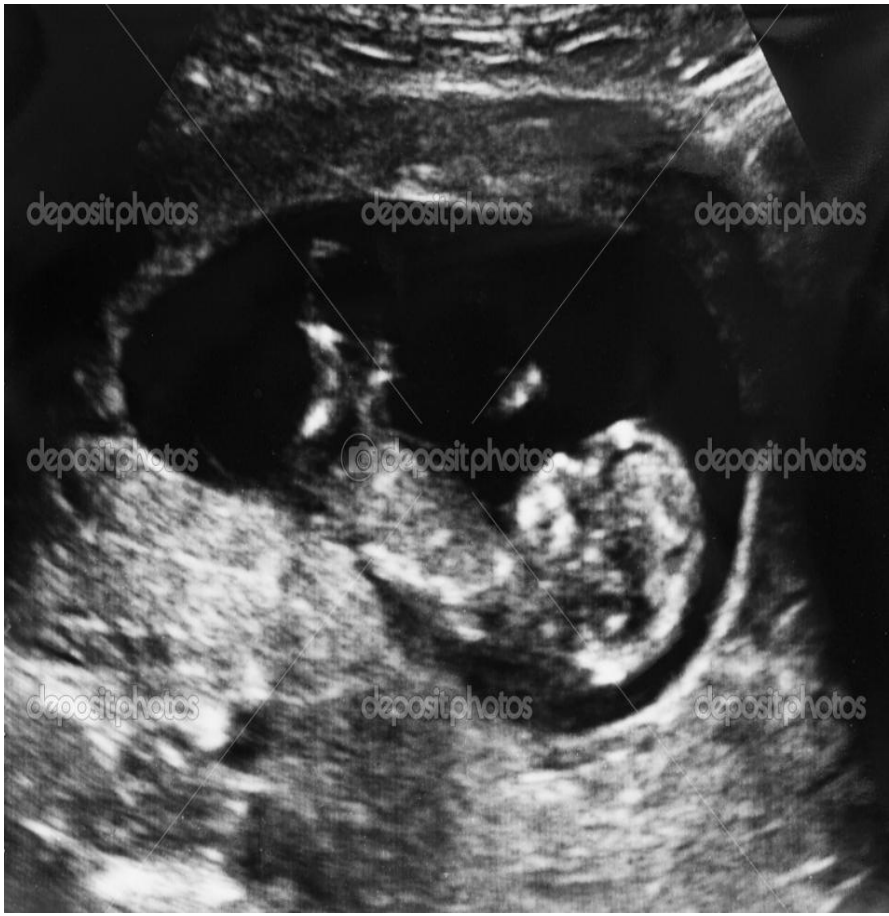
**Determination Of Amniotic Fluid Bilirubin:**

By The Analysis Of The Change In Optical Density Of Amniotic Fluid At 450 nm On The Spectral Absorption Curve (delta OD450)

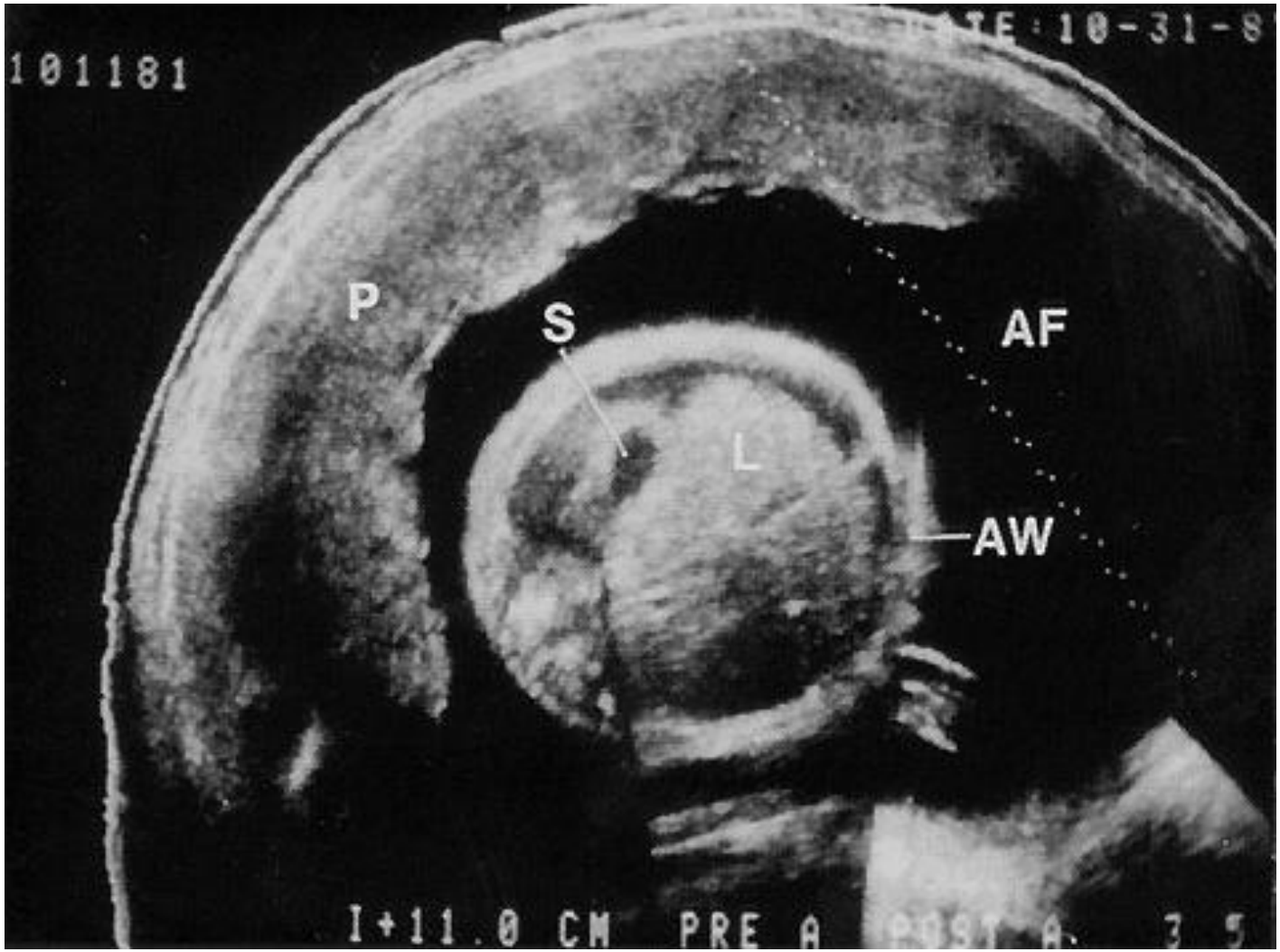
Procedures Are Undertaken At 10-15 Days Intervals Until Delivery Data Are Plotted On A Normative Curve Based Upon Gestational Age.

# Ultrasound detection of Rh Sensitization

- Placental size and thickness and hepatic size.
- Fetal hydrops is easy to diagnose when finding one or more of the following: Ascites, pleural effusion, pericardial effusion, or skin edema.
- Doppler assessment of peak velocity of fetal middle cerebral artery proved to valuable in predicting fetal anemia

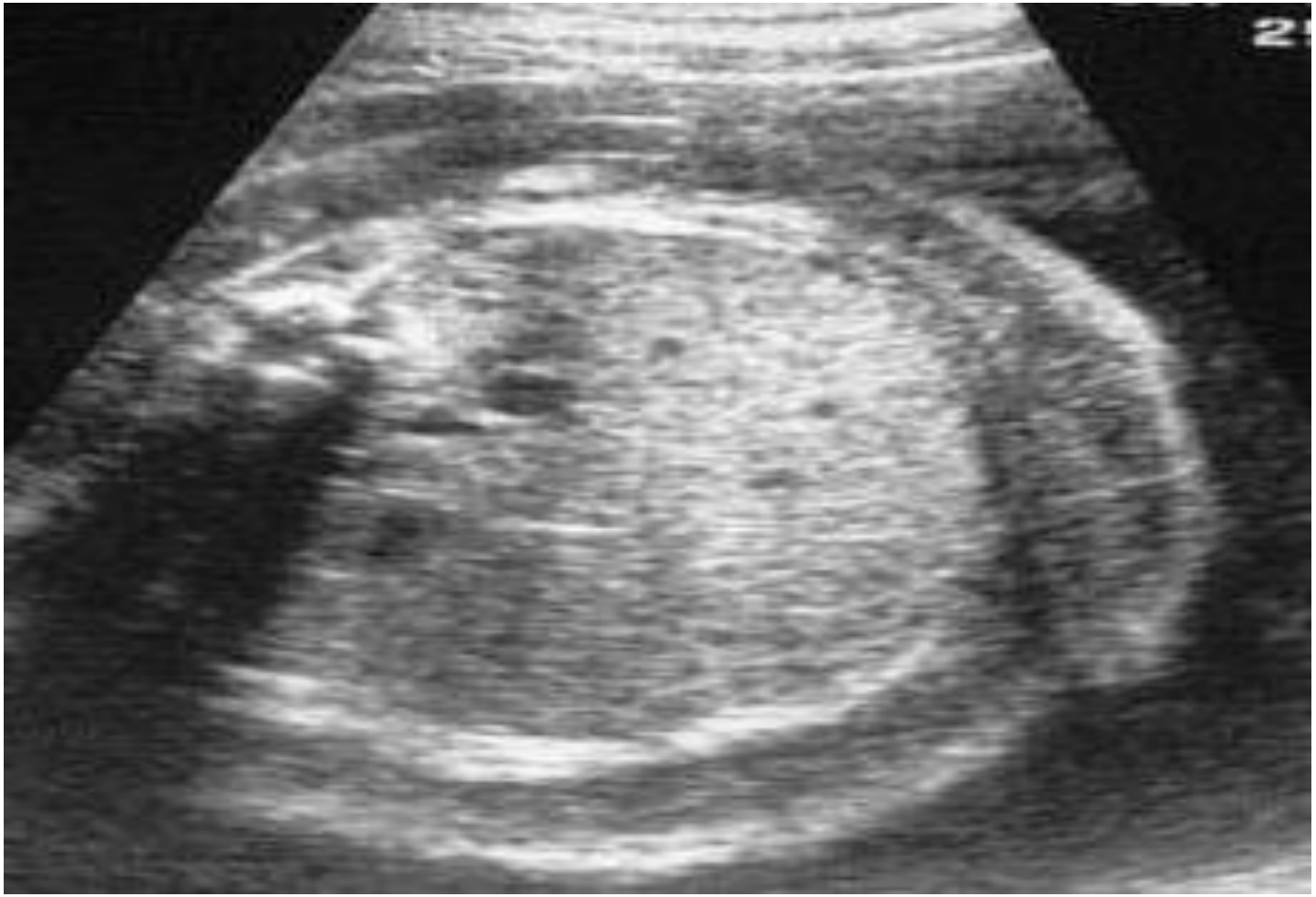


# Ultrasonographic investigation



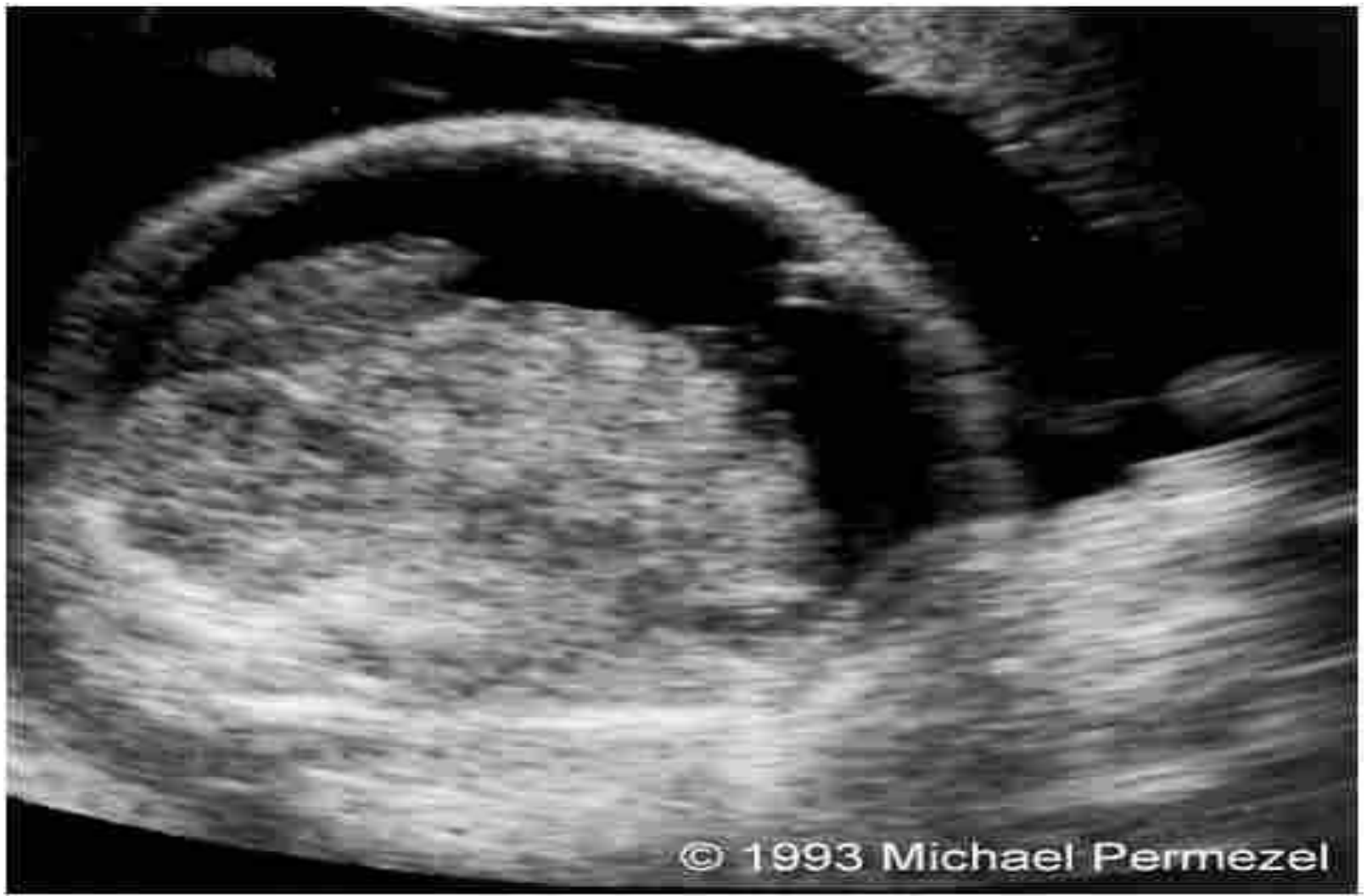
# Rh- Iso imunization

**Body wall edema**
**hydropic fetus**



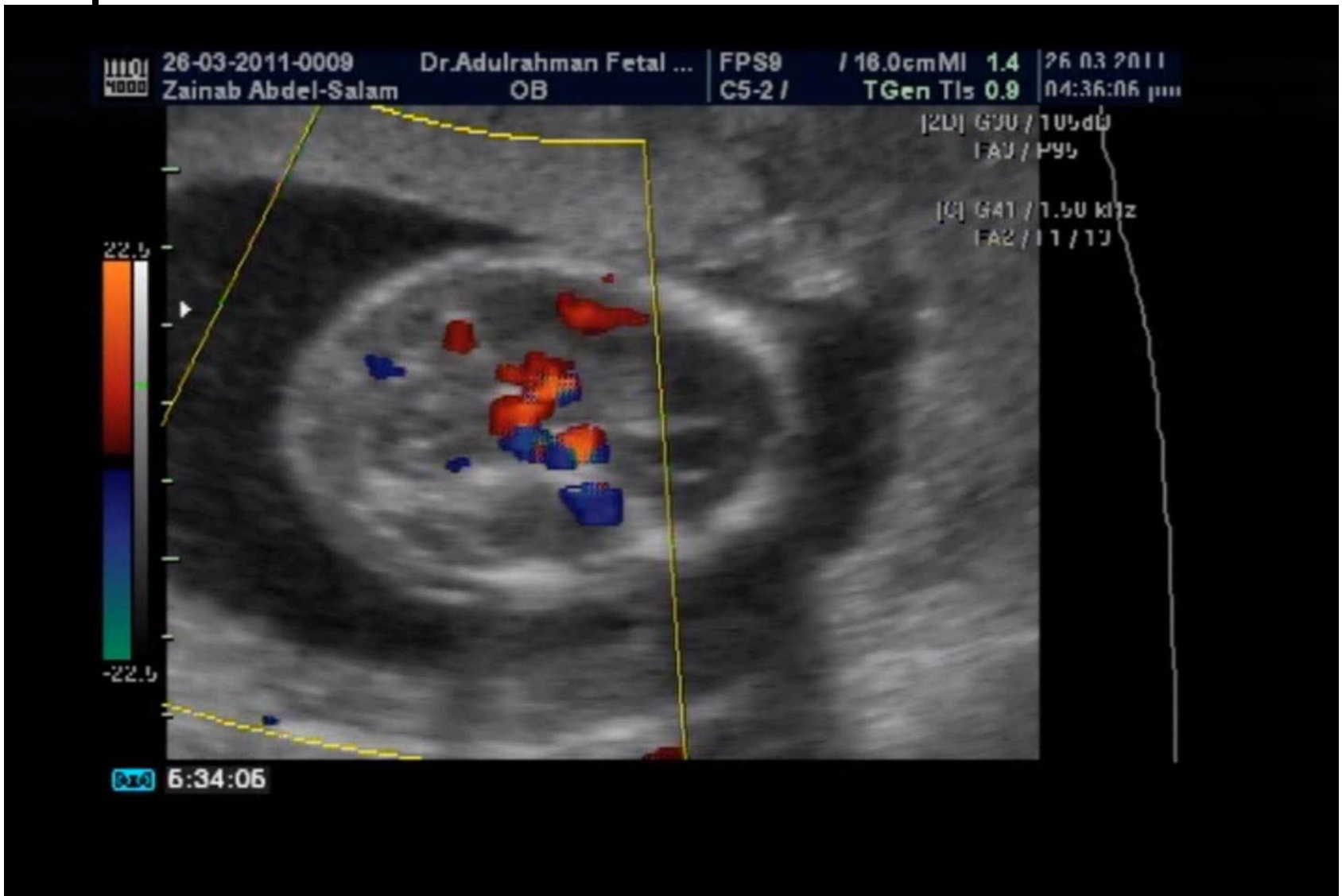
# Rh- Iso imunization

**Fetal Ascites**



# Biophysical surveillance

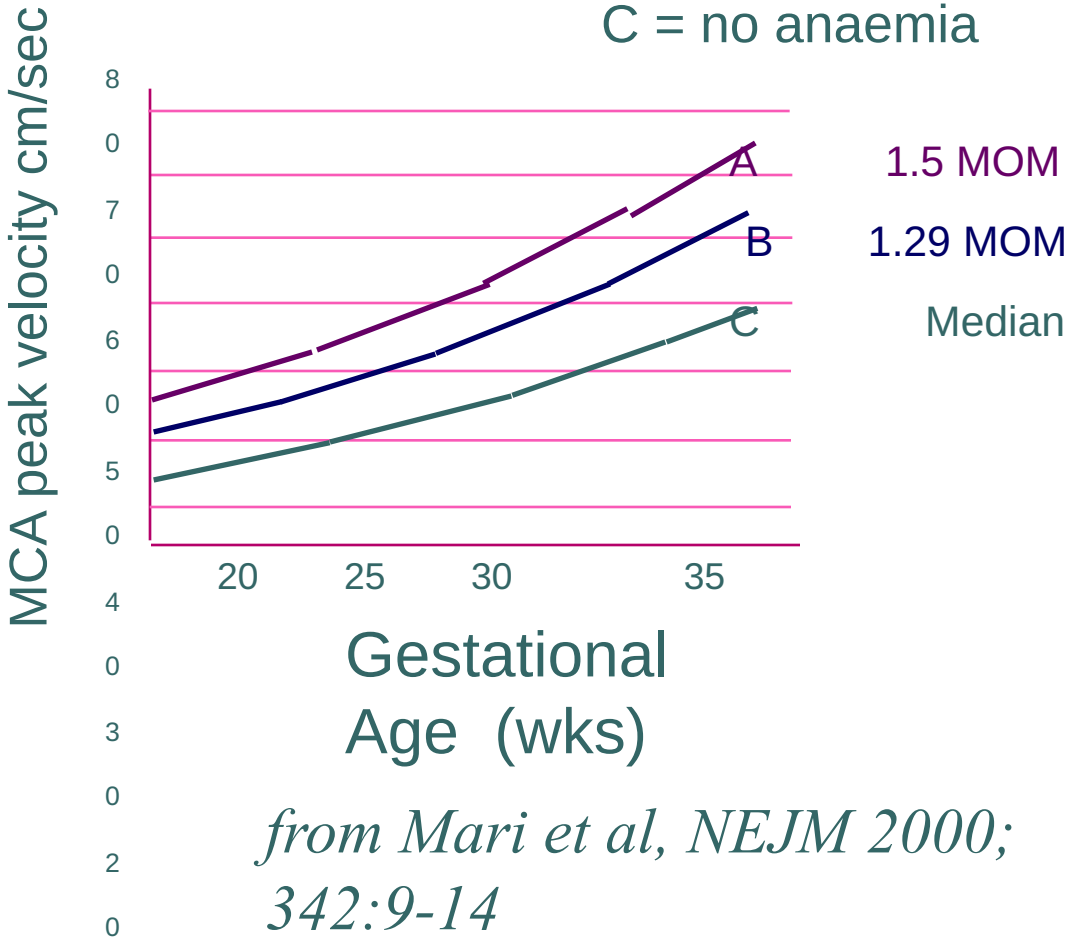
## Middle cerebral artery peak velocity



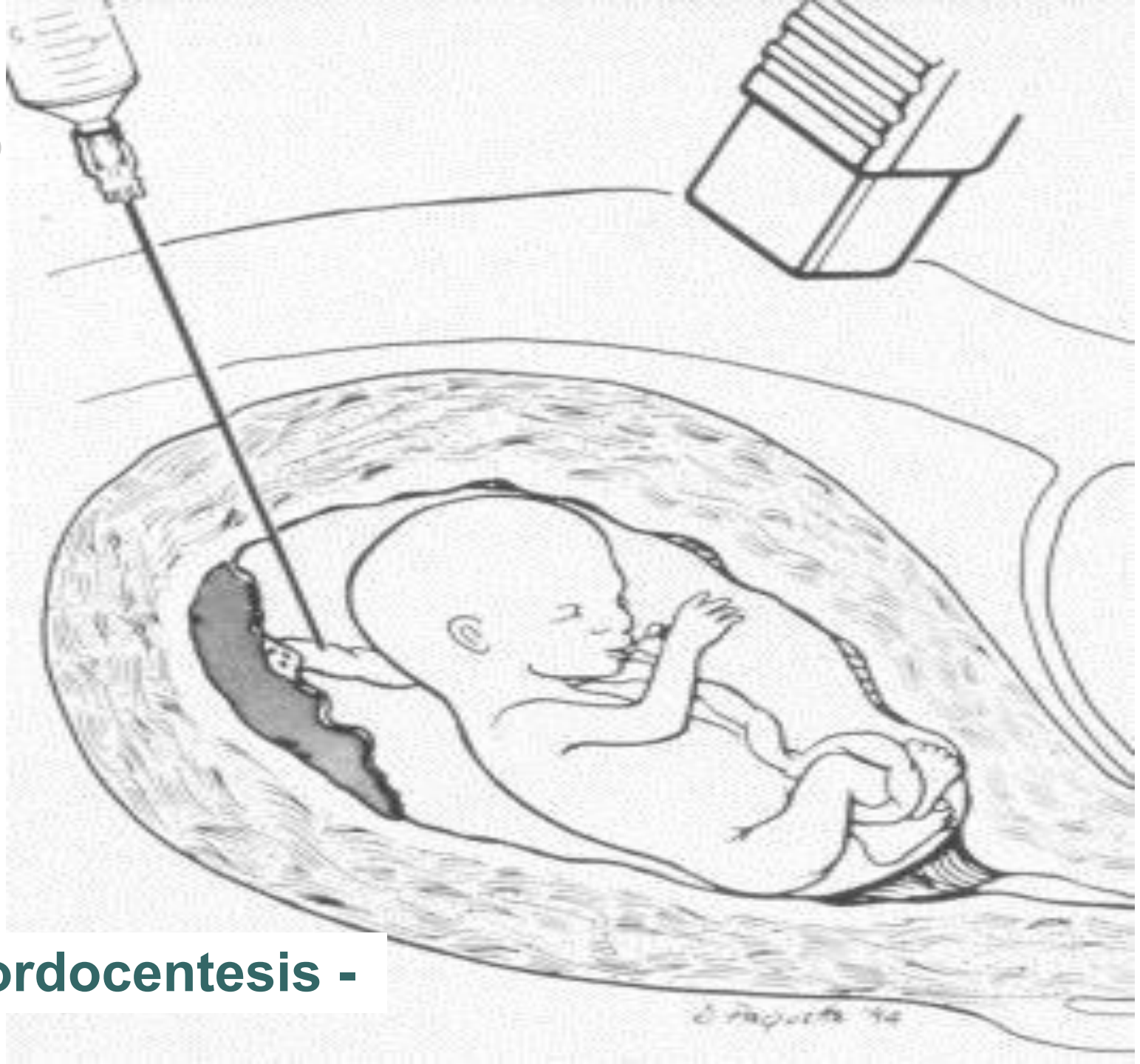
# Biophysical surveillance

## Middle Cerebral Artery peak systolic velocity

A = moderate-severe anaemia
B = mild anaemia
C = no anaemia

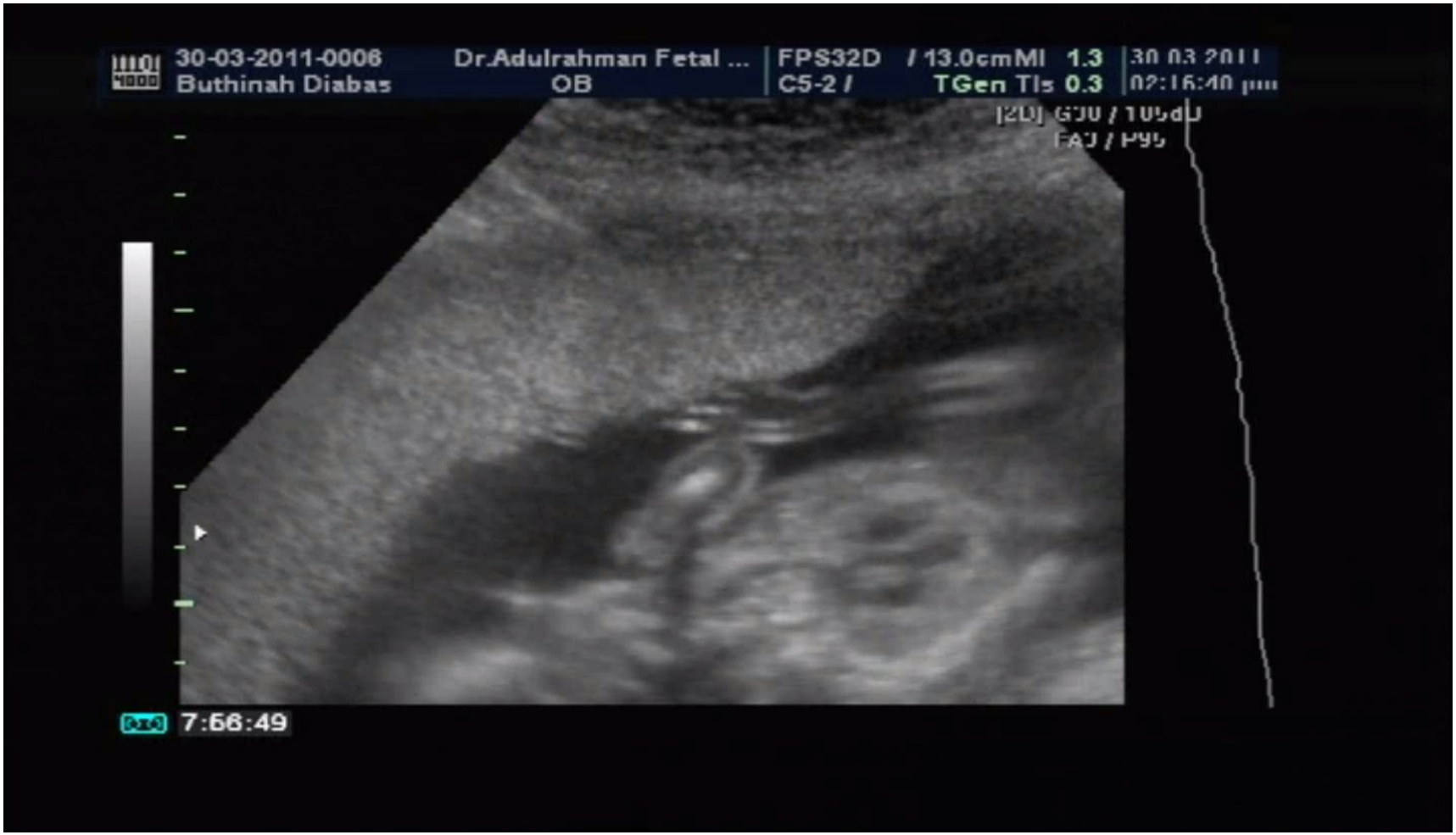


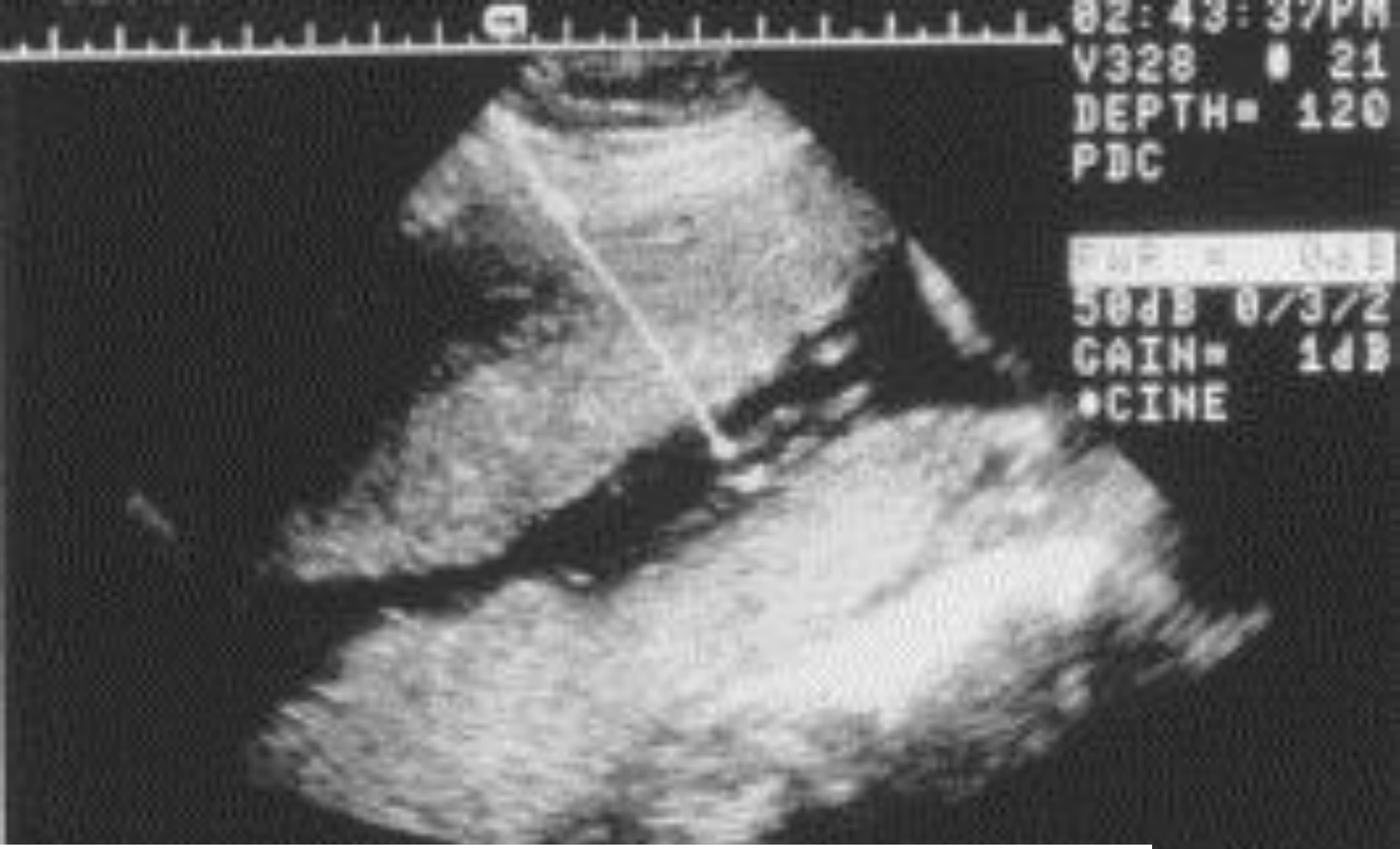

*from Mari et al, NEJM 2000; 342:9-14*



## Cordocentesis -

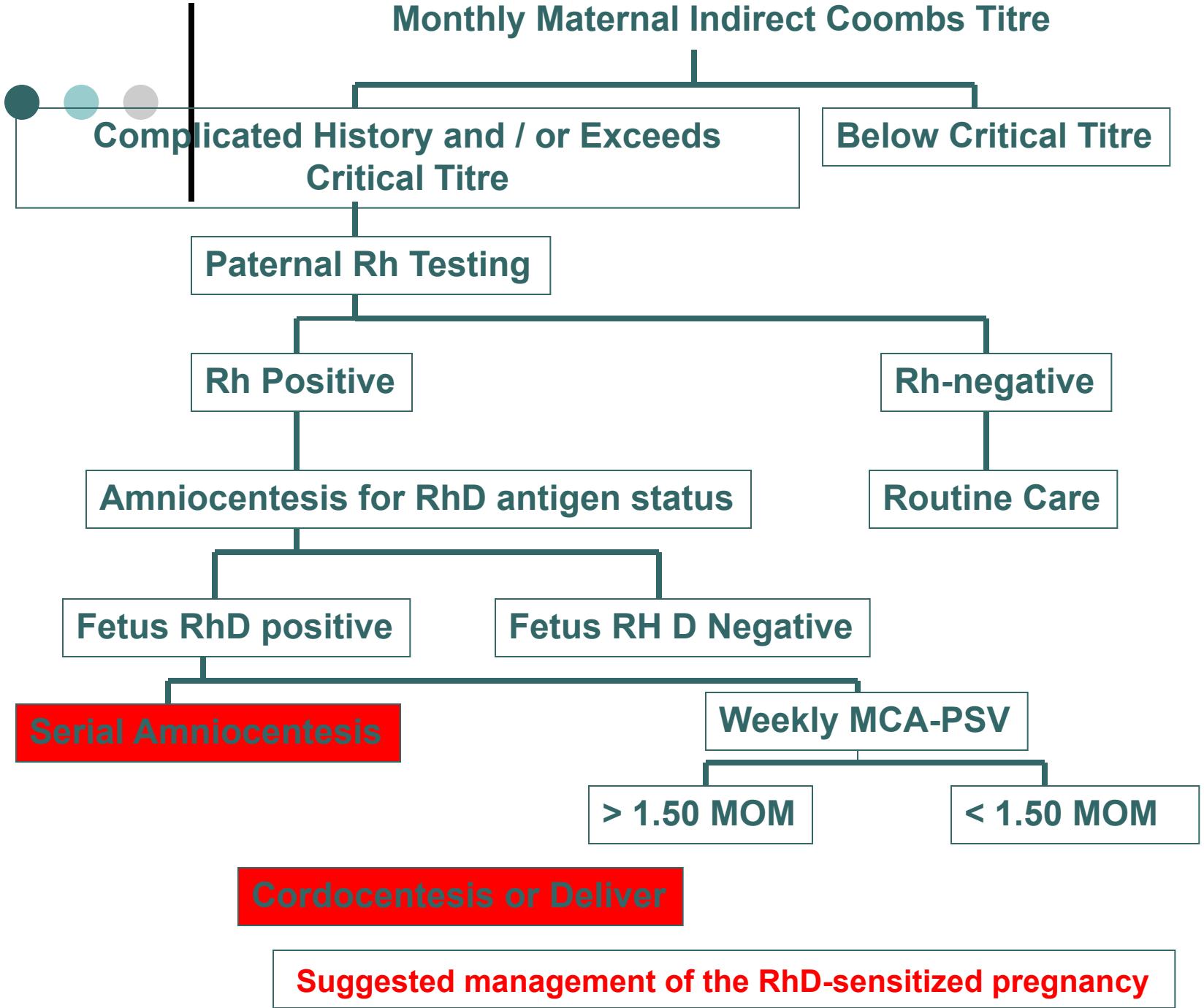
**Percutaneous Fetal Blood Sampling -** allows measurement of fetal Hb, Hct, pH, reticulocytes



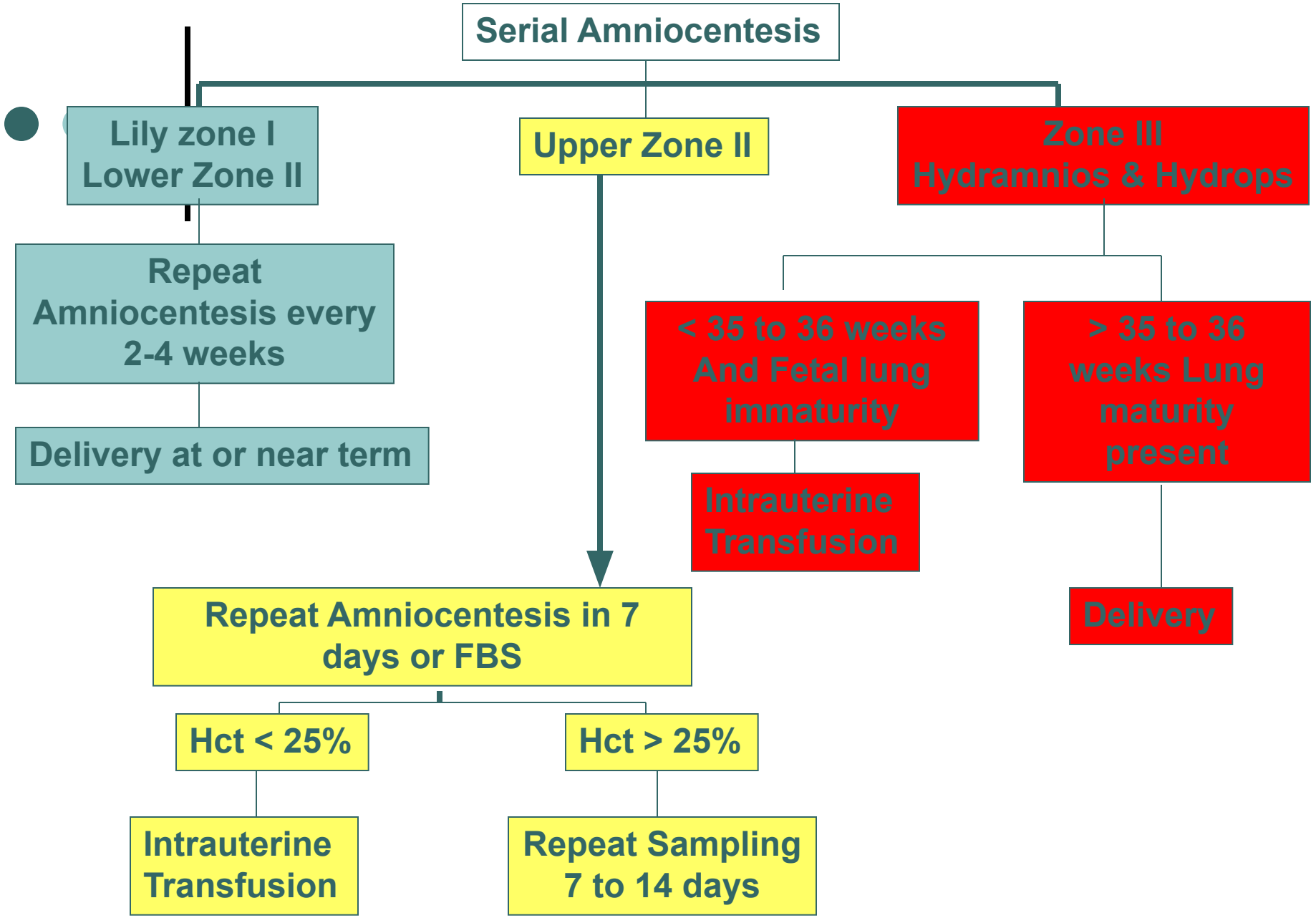



Is the gold standard for detection of fetal anemia.

Reserved for cases with: - With an increased MCA-PSV

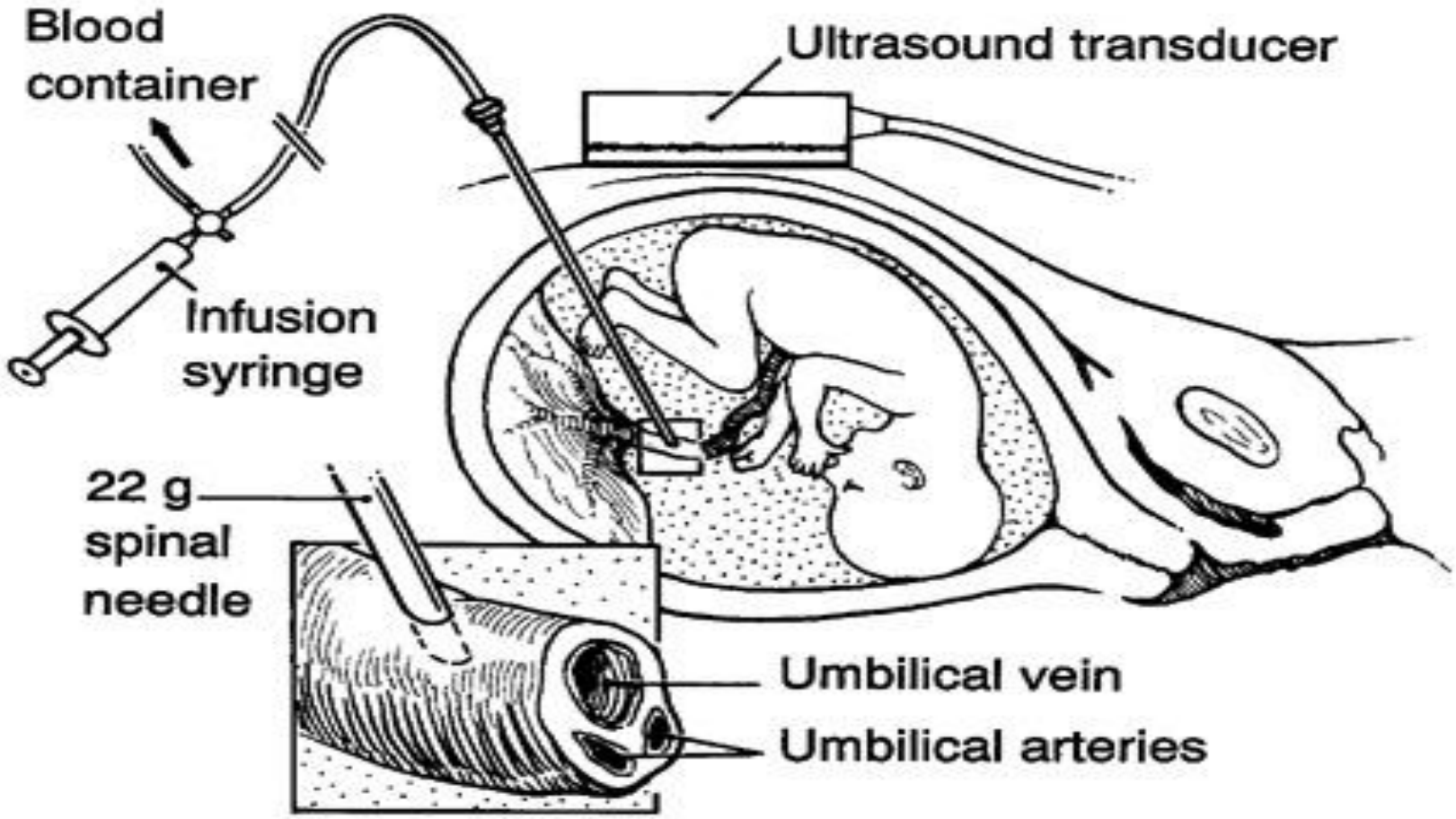



Suggested management of the RhD-sensitized pregnancy




Suggested management after amniocentesis for ΔOD 450

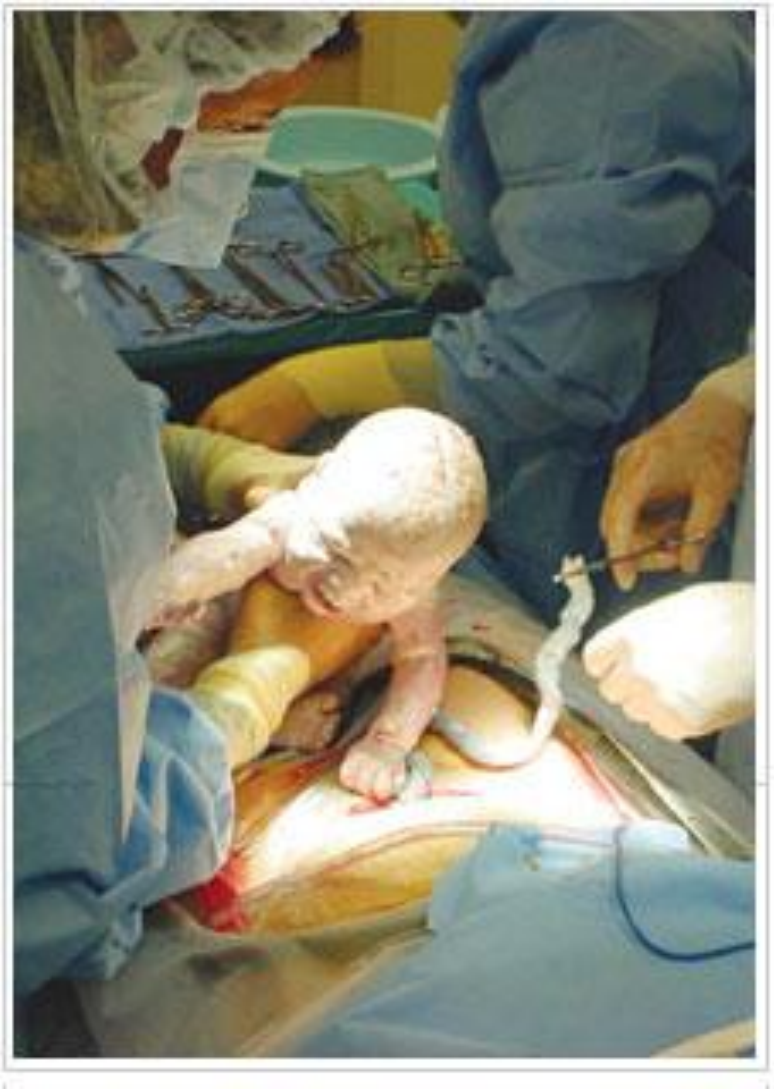
# Direct fetal intravascular transfusion



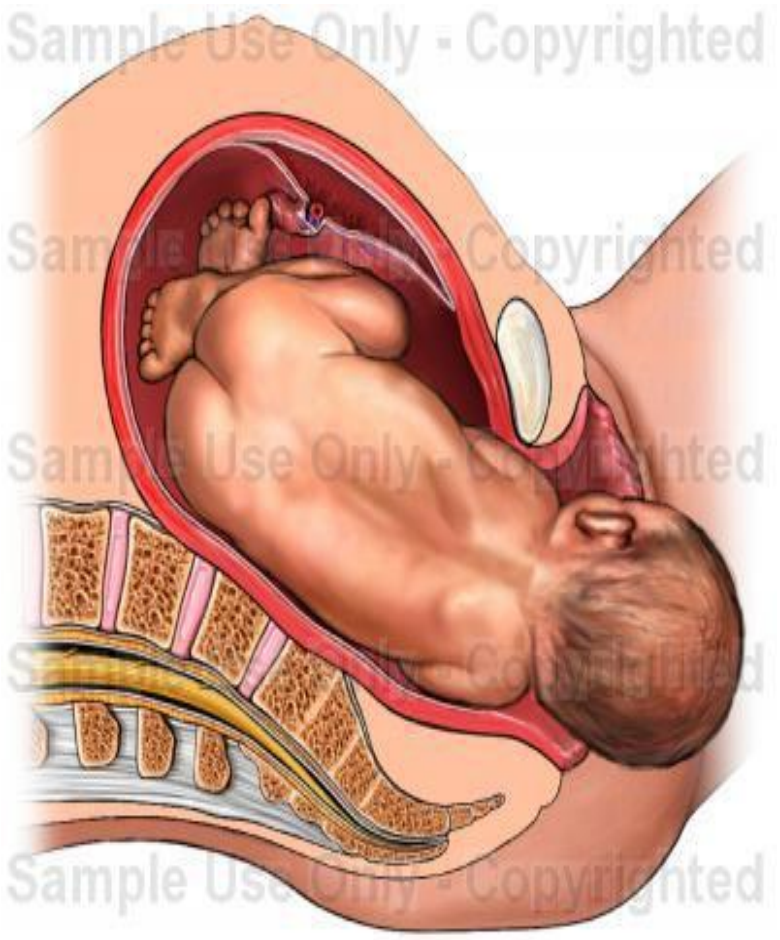
# *Pregnant women undergo cesarean section in isoimunization:*

- Severe form of hemolytic infant disease in the term 34-35 weeks after previous antenatal prevention of fetal hyaline membranes syndrome;

- Hydrops fetalis in any gestation term because of interm pregnancy would provoke antenatal fetal death.



# Vaginal delivery in Rh-isoimmunization



- In the second stage of labor pudendal block and episiotomy are indicated (they decreasing fetal trauma).
- In the all others cases pregnant women with the diagnosis of Rh- disease undergo delivery **in the term of 37-38 weeks of gestation**.
- Induction of labor is performen by prostaglandin (in the case of “unripe” uterine cervix) or by intravenous oxytocin infusion administration (in the case of “ripe” uterine cervix).

# Rh- Iso imunization Prevention

- Screening of all pregnant mothers to Rh D antigen and antibody screening for Rh D negative mothers.

-**Prophylactic anti D immunoglobulin** to all Rh – mothers after delivery if the fetus is Rh+ or( at 28, 36 weeks of pregnancy) and after abortion, amniocentesis, abruption.

# Rh- Iso imunization Prevention


**The standard dose of anti D is 0.3 mg** —will eradicate 15 ml of fetal red blood cells (routine for all Rh –ve pregnancies) within 3 days of delivery.

-If more feto-maternal bleeding is suspected as in abruption or ante partum hemorrhage-Do **Kleihauer –Betke** test to **estimate the amount of fetal red cells in maternal circulation** and re-calculate the dose of the anti-D.

# Management of sensitized newborn

Mild anemia (Hb <14gm/dl, cord bilirubin>4 mg/dl)---Phototherapy

-Moderate to severe----Exchange transfusion.

-Mild Hydrops improves in 88% of cases

-Severe hydrops—Mortality is 39%

# Indications to exchange blood transfusion in infants

| Laboratory symptom | In -term fetus : | | | Pre-term fetus | | |
|---|---|---|---|---|---|---|
| | 1 day | Repeated | 5 day | 1 day | Repeated | 5 day |
| Indirect bilirubin, mkmoll/L | > 68,42 | | 300,7 | 59,9 | | 273,6 |
| Indirect bilirubin per hour, mkmoll/L | 6,8 | 6,8 | | 5,1 | 5,1 | |
| Hemoglobin, g/L | < 150 | | | < 150 | | |
| Hematocrit | <0,4 | | | < 0,4 | | |


Thanks for attention