RHESUS (Rh) ISOIMMUNIZATION

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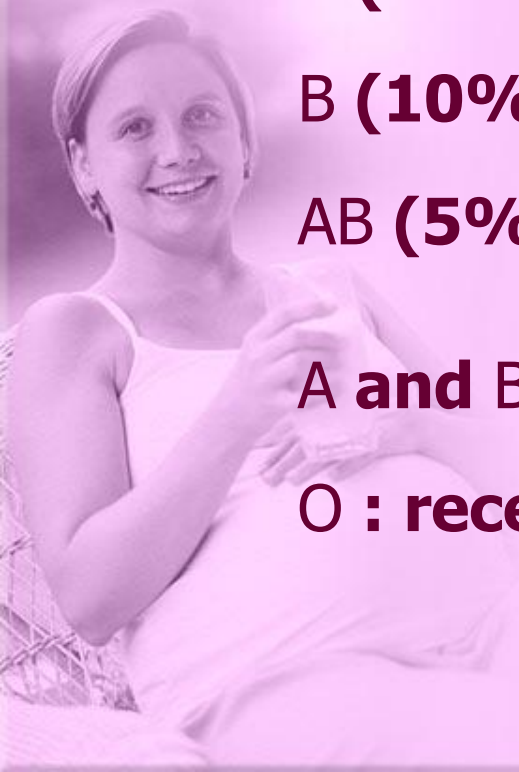
Rh ISOIMMUNIZATION

Blood groups (1900):

Antigens:	**Antibodies:**
O **(45%)**	**AntiA+Anti B**
A **(40%)**	**Anti B**
B **(10%)**	**Anti A**
AB **(5%)**	

A **and** B **: dominant**

O **: recessive**



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Rhesus factor (1940):

Agglutinogen (C,D,E) - mainly D

C,D,E - dominant antigen

d,e - recessive antigen

Rh ISOIMMUNIZATION

- Rh positive (85%) - homozygous (DD) (35%), or heterozygous (Dd) (50%)

- Rh negative (15%)

- Incidence of Rh-ve in far east is about 1%

Examples of Rh factor: (CDe=R1) , (Cde=r) (cDE=R2)

Other systems:

- kell-antikell,
- luther,
- Duffy, etc.

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- So in response to introduction of foreign protein (antigen) □ production of antibody to neutralize the antigen
- In ABO and other non Rh-incompatibility: It usually causes mild anaemia, mainly as there is no intrapartum boosting
- In Rhesus isoimmunization: mainly (D), but C, E can produce antibodies

Rh ISOIMMUNIZATION

Feto-maternal haemorrhage: during pregnancy leakage of fetal cells in the maternal circulation (Rh+ fetal cells in Rh- maternal circulation

<u>Examples:</u>

- **Spontaneous abortion**
- **Induced abortion**
- **APH**
- **E.C.V.**
- **Cordocentesis, CVS, amniocentesis**
- **Severe preeclampsia**
- **Ectopic pregnancy**
- **Caesarean section**
- **Manual removal of placenta**
- **Silent feto-maternal hage**

Rh ISOIMMUNIZATION

Development of Rhesus antibodies: depends on factors:

1- Inborn ability to respond

2- protection if ABO incompatible 1\10

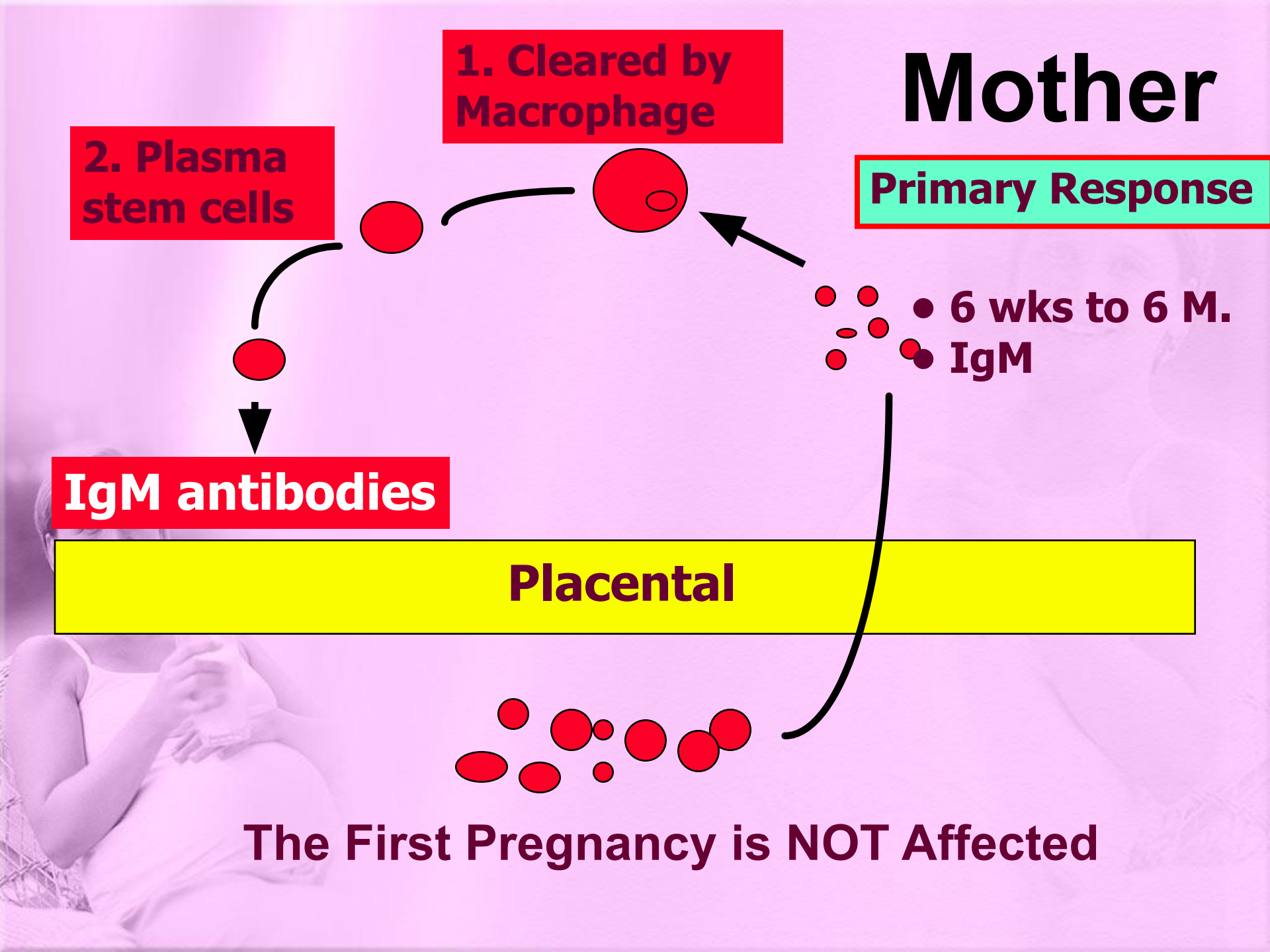
3- Strength of Rh antigen stimumlus (CDe=R1)

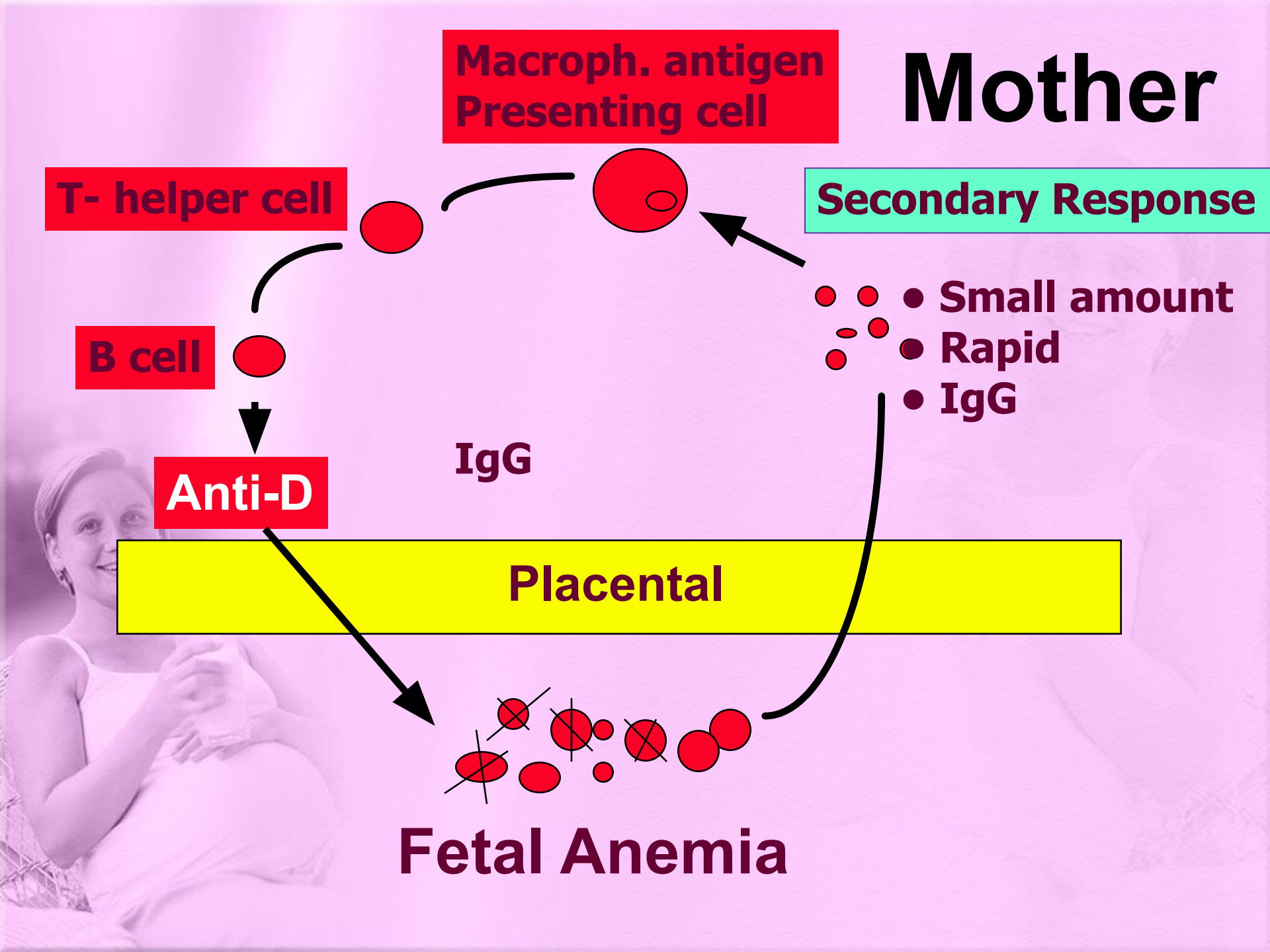
4- Volume of leaking feta blood (0.25ml)

IgM (7 days) doesn't cross placenta, then IgG 21 days - crosses placenta

1- If ABO is incompatible:

Red blood cells is easily destroyed, so not reaching enough immunological component to cause antibody response and reaction


1. Cleared by Macrophage
Mother
2. Plasma stem cells
Primary Response
• 6 wks to 6 M.
• IgM
IgM antibodies
Placental
The First Pregnancy is NOT Affected

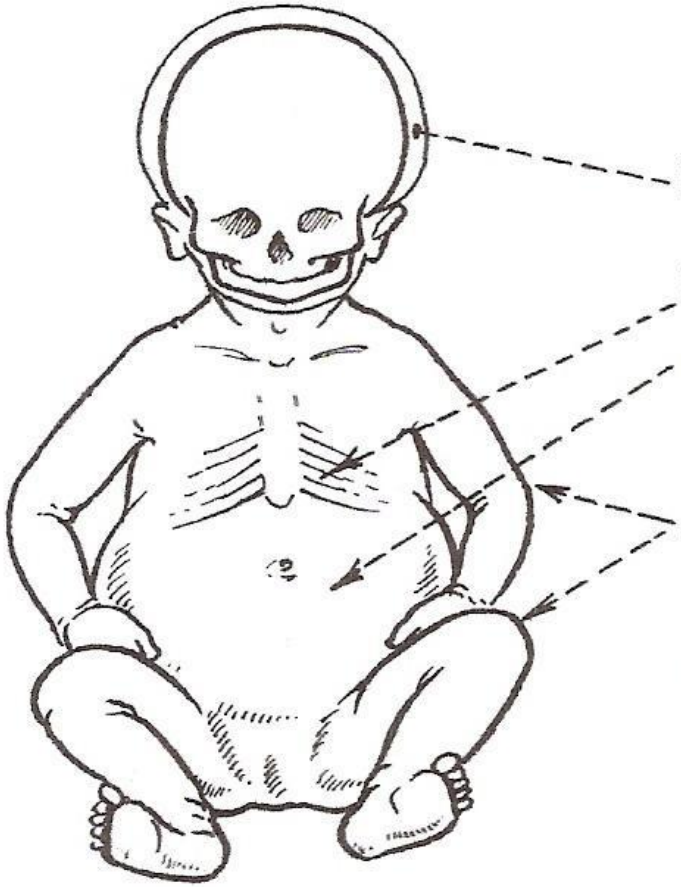

Macroph. antigen Presenting cell
Mother
T- helper cell
Secondary Response
Small amount
Rapid
IgG
B cell
IgG
Anti-D
Placental
Fetal Anemia

2 - If ABO is compatible:

Rh+ fetal cells □ remain in circulation (life span) until removed by (R.E.S) □ destroyed □ liberating antigen (D) □ isoimmunization

It takes time:

- **1st pregnancy is almost always not affected:**
  - **1% - during labour or 3rd stage)**
  - **10% - 6 months after delivery**
  - **15% by the 2nd pregnancy**



X-RAY APPEARANCES

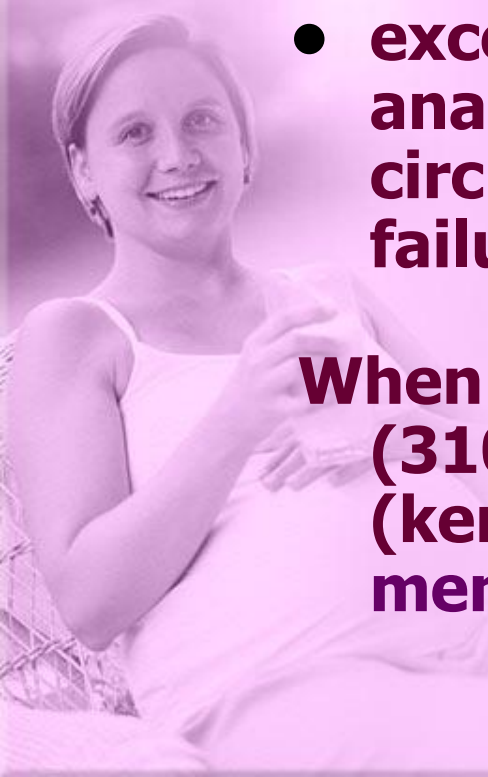
Halo round head due to oedema of scalp

Splaying of ribs
Enlargement of abdomen
} Due to enlarged liver and spleen

Abduction of limbs (Buddha attitude) due to enlarged abdomen

There is loss of flexion due to enlarged abdomen

Rh ISOIMMUNIZATION



Mild Cases:

- **fetal (RBC) destruction □ from anti-D (IgG): □ anaemia □ compensating haemopoiesis □ excess of unconjugated bilirubin**

Severe Cases:

- **excessive destruction of fetal (RBC) □ severe anaemia □ hypoxia the tissues □ cardiac or circulatory failure □ generalized edema □ (H. failure) □ ascitis □ IUFD**

When excess of unconjugated bilirubin > (310-350 mol/L) □ It passes brain barrier □ (kernicterus) □ permanent neurological and mental disorders

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Kleihauer-Betke technique:

- **(acid elution test) - measure amount of feto-maternal haemorrhage**
- **If 0,1-0,25 ml of fetal blood leakes (critical volume) □ isoimmunization represented by 5 fetal cells in 50 low power microscopic field of peripheral maternal blood**
- **So 1 ml is represented by 20 fetal cells**

Rh ISOIMMUNIZATION

Fetal and Neonatal Effects:

- **Haemolytic anaemia of newborn Hb=14-18g/dl**
- **Icterus gravis neonatorum Hb=10-14g/dl**
- **Hydrops fetalis (Erythroblastosis fetalis)**

MANAGEMENT OF Rh ISOIMMUNIZATION

I) PROPHYLAXIS

1 - Prevention of Rhesus isoimmunization: Anti D (RhoD IgG)

- **Standard dose for > 20 wks, and ½ standard dose for < 20 wks - given within 72hours of the incident**
- **SD: i.m. injection: 500 iu = 100 ugm (UK), 1500iu = 300 ugm (USA)**
  - **1500iu = 300 ugm □ neutralize 15ml**
  - **500 iu = 100 ugm □ neutralize 5ml (4ml+1ml)**
  - **4ml = 4x20 f.cells = 80 fetal cells**

MANAGEMENT OF Rh ISOIMMUNIZATION

K-B test if large amount of leaking □ another SD if mother is Rh-, baby Rh+ with no isoimmunization (checked by indirect or direct Coombs test)

2 - A.P. administration of anti-D

- SD at 28 wks or at 28 and 36 wks will reduce Rh isoimmunization

MANAGEMENT OF Rh ISOIMMUNIZATION

II) 1- Antibody Screening:

- **for all pregnant women in ANC for irregular antibodies (mainly for Rh- women), then start at 20 wks , and every 4 weeks**

MANAGEMENT OF Rh ISOIMMUNIZATION

2 - Management following detection of Rh antibodies

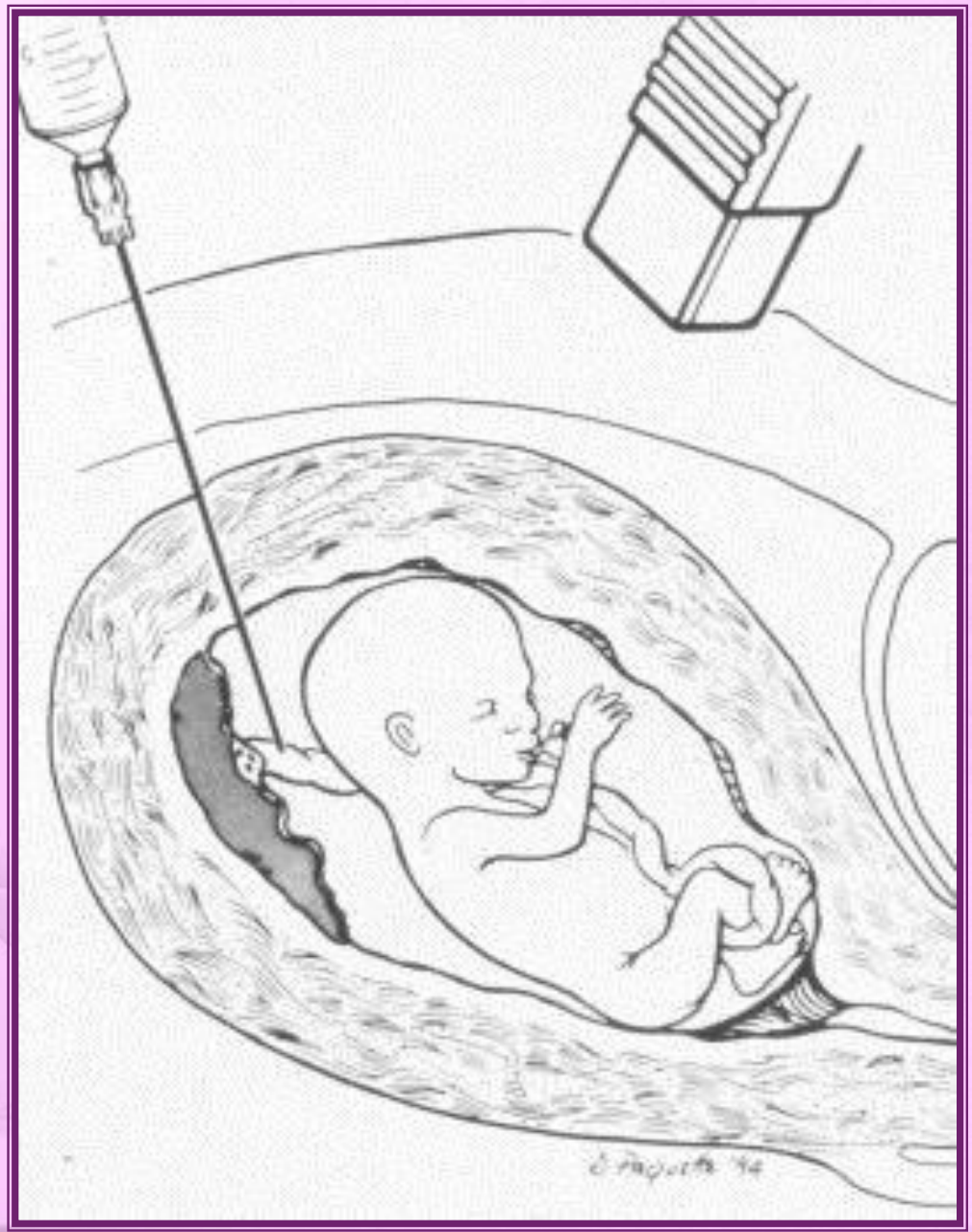
- **Should be treated in specialized centres**
- **Quantitative measures of antibodies + husband genotype**
- **Repeat titration (indirect Coombs, detecting of antibodies) titre or specific enzymes for antibodies IU**
- **Amniocentesis once necessary**
- **Obstetrical management based on timing of I.U. transfusion (now cordocentesis + fetoscopy) versus delivery**

MANAGEMENT OF Rh ISOIMMUNIZATION

3 - Amniocentesis:

- **Should be performed under ultrasound guidance if titre > 1\16 = 0.5-1 ugm □ 2.5-5 I.U**
- **Timing: 1st amniocentesis - 10 weeks before previous IUFD**
- **Start from 20-22 weeks, 2-4 weekly or more frequent if needed**
- **Amniotic fluid analysis - spectrophotometry: optical density at the height of optical density deviation at wave length 450 nM**

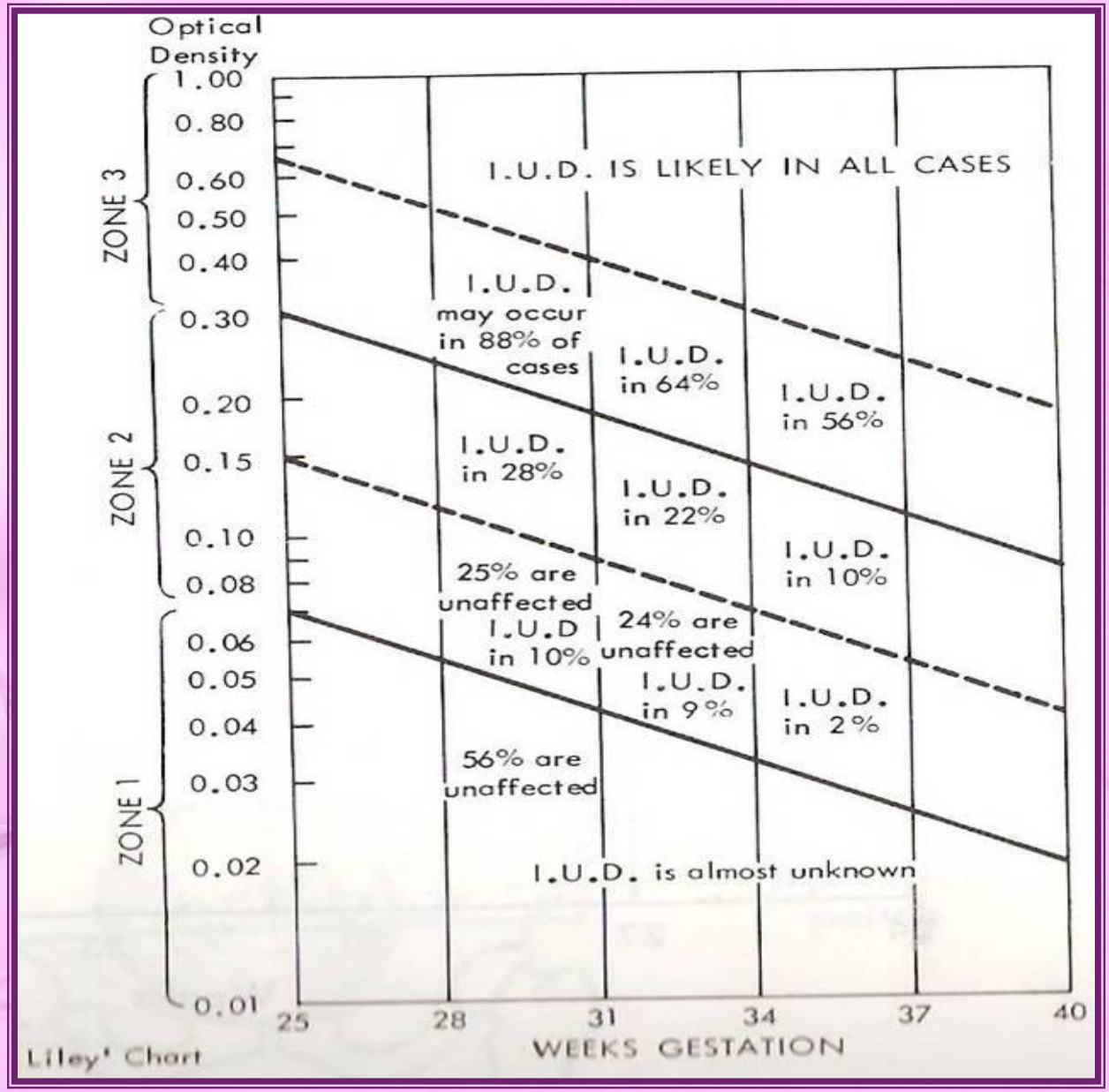
CORDOCENTESIS



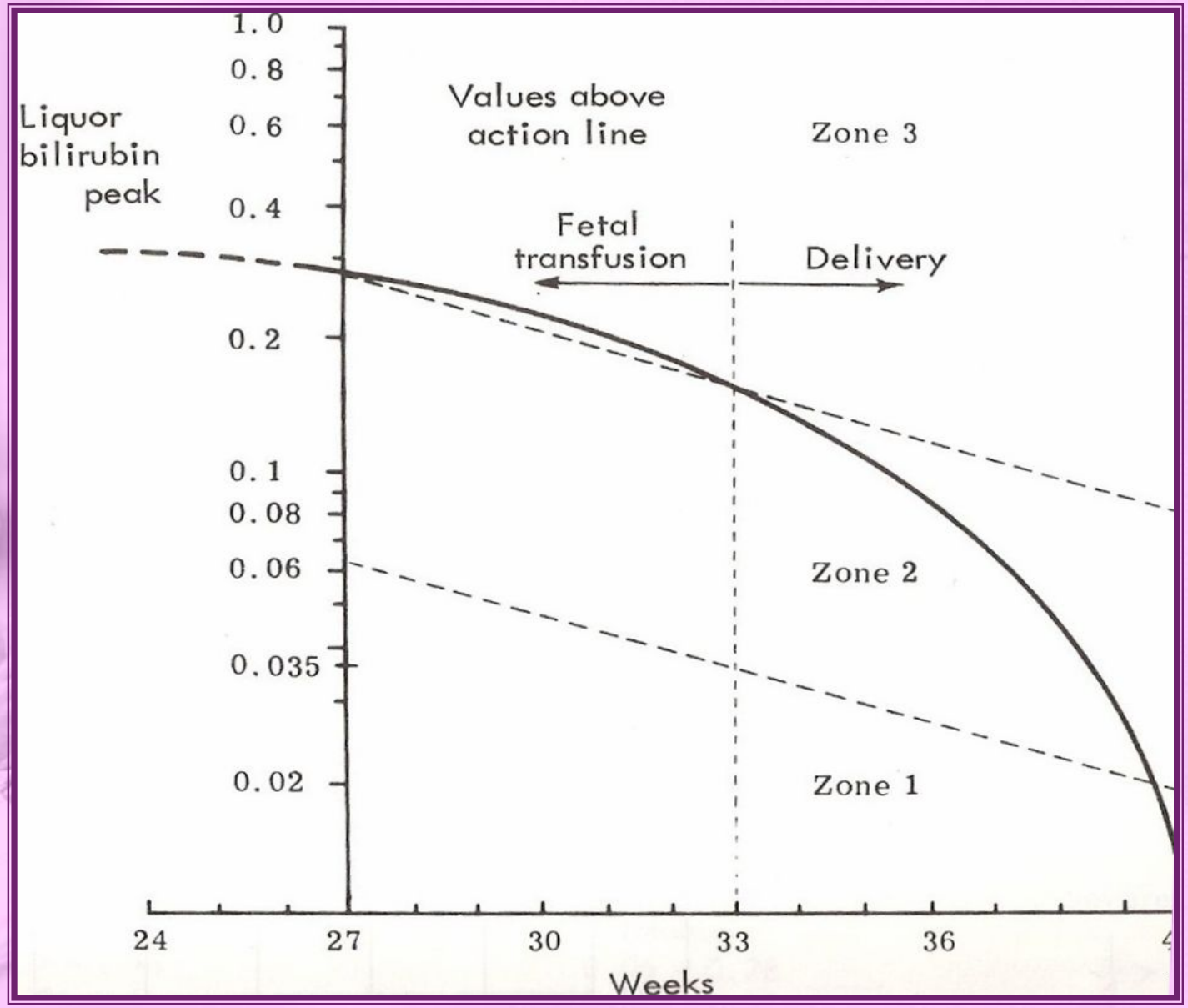
MANAGEMENT OF Rh ISOIMMUNIZATION

- IU transfusion (cordocentesis, in the past intraperitoneal transfusion) versus delivery of the baby:
  - Using Liley's chart
  - Prediction chart (Queenan curve)
  - Whitefield's action line

LILEY'S CHART



WHITEFIELD' ACTION LINE



MANAGEMENT OF Rh ISOIMMUNIZATION

- Alternatively follow up with Doppler study for the fetal middle cerebral artery
- <u>Prognosis</u> depends on:
  - obstetrical history
  - paternal genotype
  - maternal history (blood transfusion, antibody titre)
  - amniocentesis results
- <u>Delivery</u>: Vaginal versus C-Section

MANAGEMENT OF Rh ISOIMMUNIZATION

- **Intensive plasmaphoresis: when severe cases anticipated, using continous flow cell separator, as early as 12 wks**

- **Postnatal management: for the neonate:**
  - **Direct Coombs test, blood group, Rh type, Hb, bilirubin**
  - **Mild cases: phototherapy - correction of acidosis**
  - **Severe cases: exchange transfusion**