Rh Incompatibility and Disease

Name - Vanshul Rana

Group - 173B

International Medical Faculty

Rh Disease

- Occurs during pregnancy when there is an incompatibility between the blood types of the mother and fetus

Blood Types

- A, B, O blood groups are specific types of proteins found on the surface of RBC's
- Also found in the cells and other body fluids (saliva, semen, etc)
- O represents neither protein being present on RBC
- Possible groups include: A, B, AB, or O
- A, B, O groups most important for transfusions

Rh Factor

- Proteins (antigens) occurring only on surface of RBC's
- Rh + if proteins present
- Rh – if proteins absent
- A+, A-, B+, B-, AB+, AB-, O+, O-
- Most important for pregnancy
- Inheritance is Autosomal Dominant
- 15% Caucasian population is Rh-

Nomenclature

- Correct to say Rh(D) + or –
- Rh blood system has other antigens: C, c, D, E, e
- D is by far the most common and the only preventable one
- Weak D (Du) also exists
- Also non Rhesus groups such as Kell, MNS, Duffy (Fy) and Kidd (Jk) exist

Why Does Rh Status Matter?

Fetal RBC cross to maternal circulation

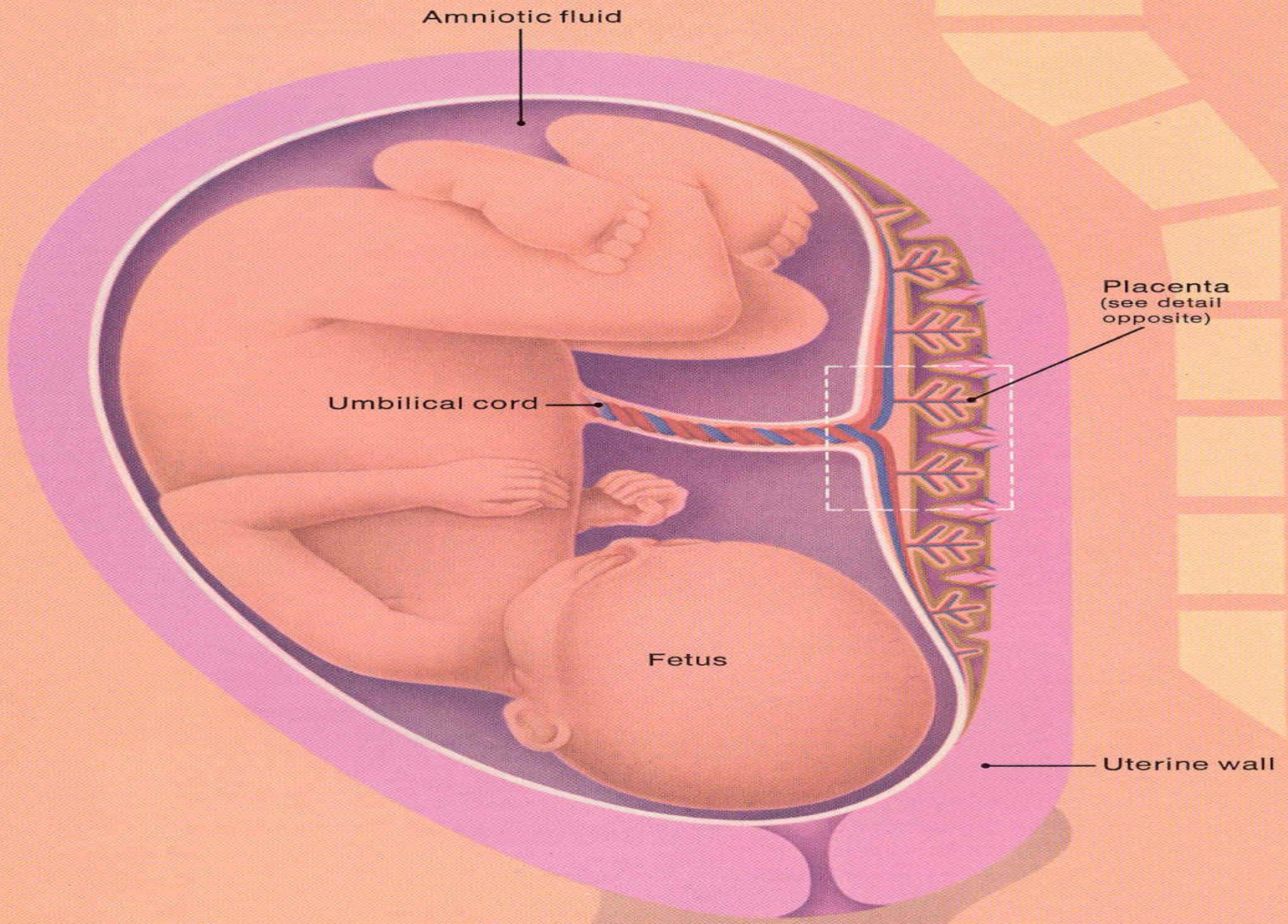
Maternal immune system recognizes foreign
antigens if fetus Rh + and mother Rh –

Antibodies are formed against fetal antigens

Subsequent pregnancy with Rh+ fetus,
immune system activated
and large amounts of Ab formed

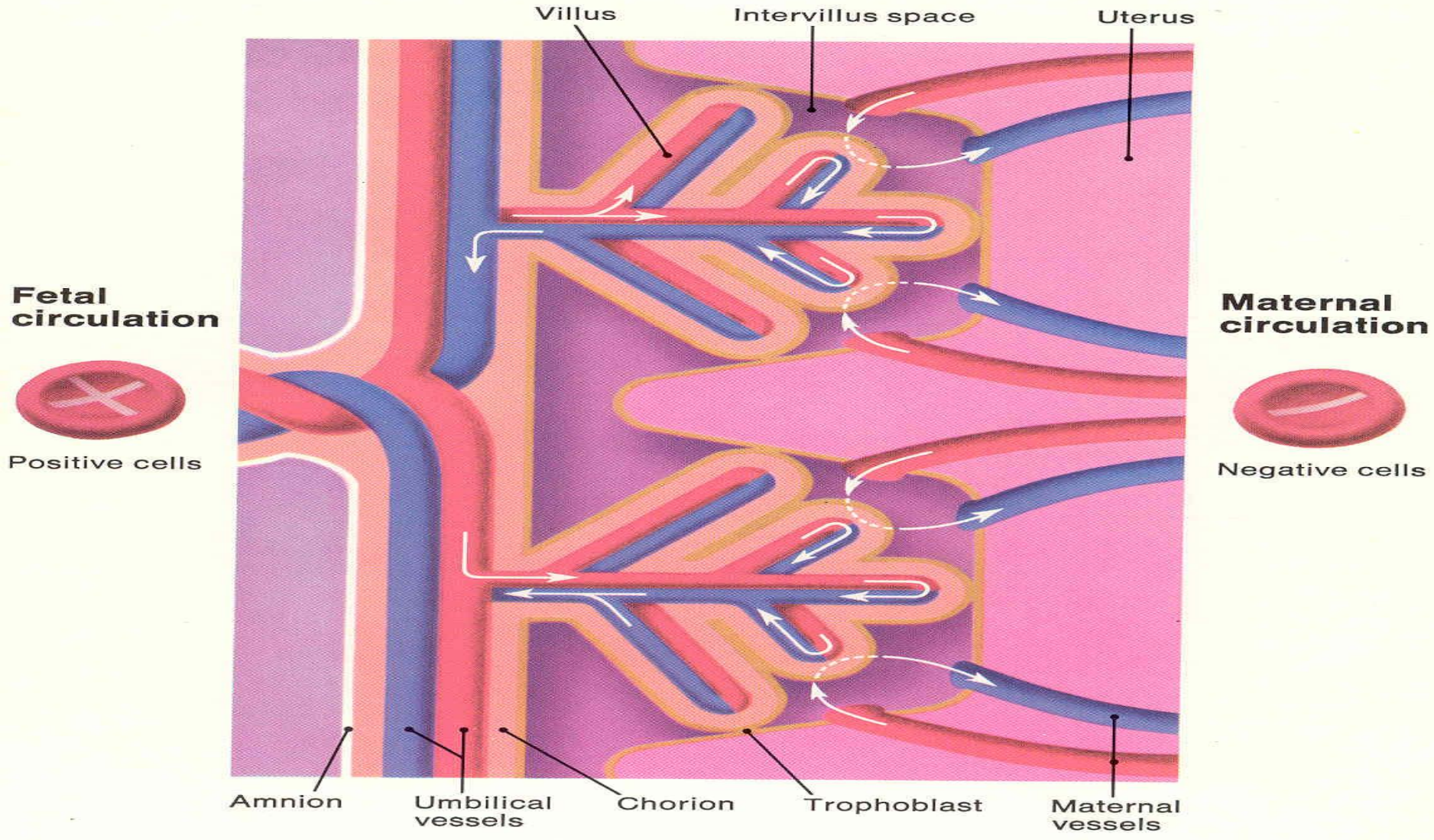
IgG Ab cross placenta & attack fetal RBC

Fetal anemia, hydrops, etc


Amniotic fluid
Placenta
(see detail
opposite)
Umbilical cord
Fetus
Uterine wall

Scheme of Placental Circulations

White arrows depict separate routes of fetal and maternal circulations within the placenta. Dotted lines represent oxygen, nutrient and waste exchange through the placental barrier.

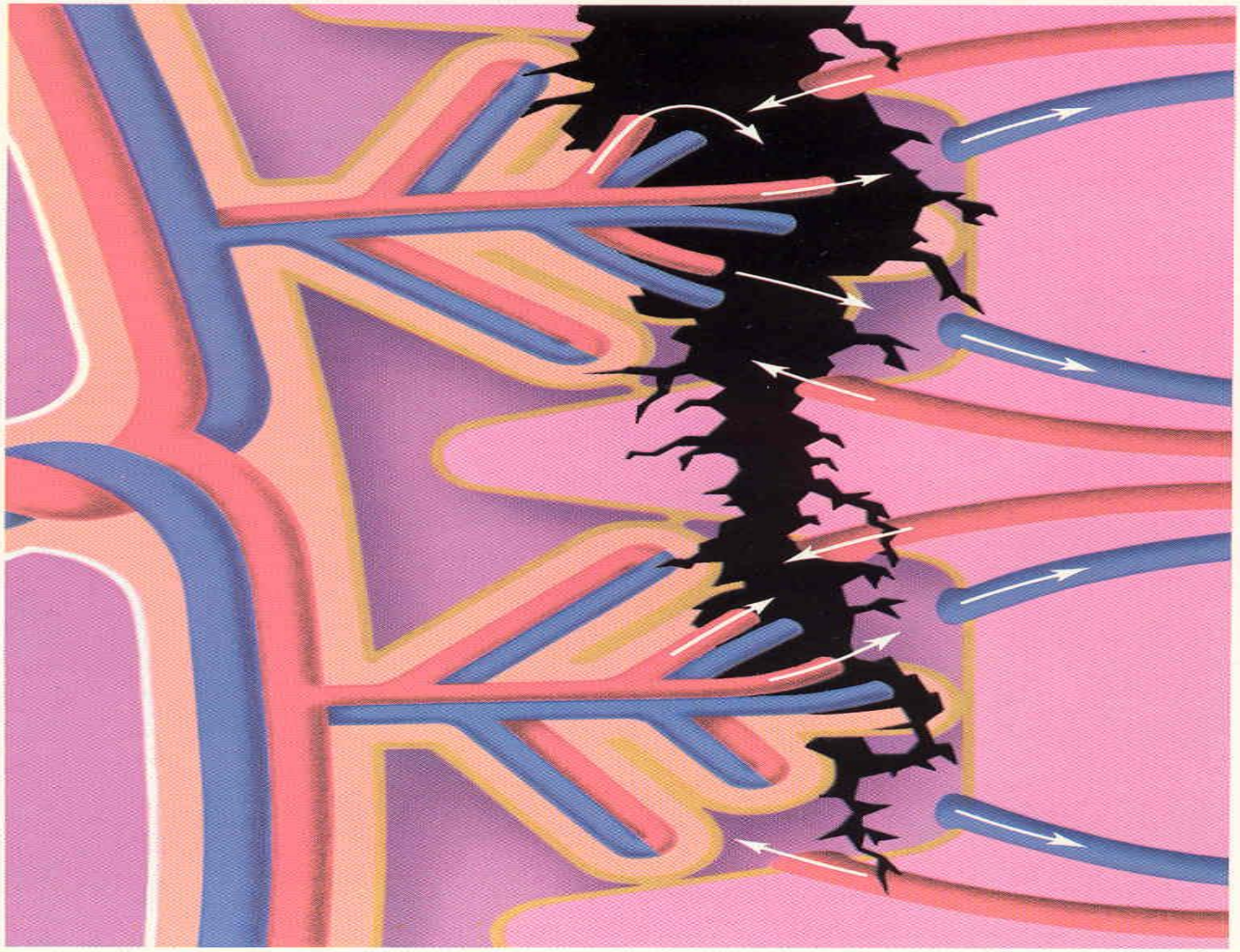


Separation of Placenta Following Delivery

Diagram portrays the rupture of placental vessels (villi) and connective tissue allowing escape of fetal blood cells. Prior to complete constriction of open-end maternal vessels, some fetal blood may enter maternal circulation.

Fetal circulation

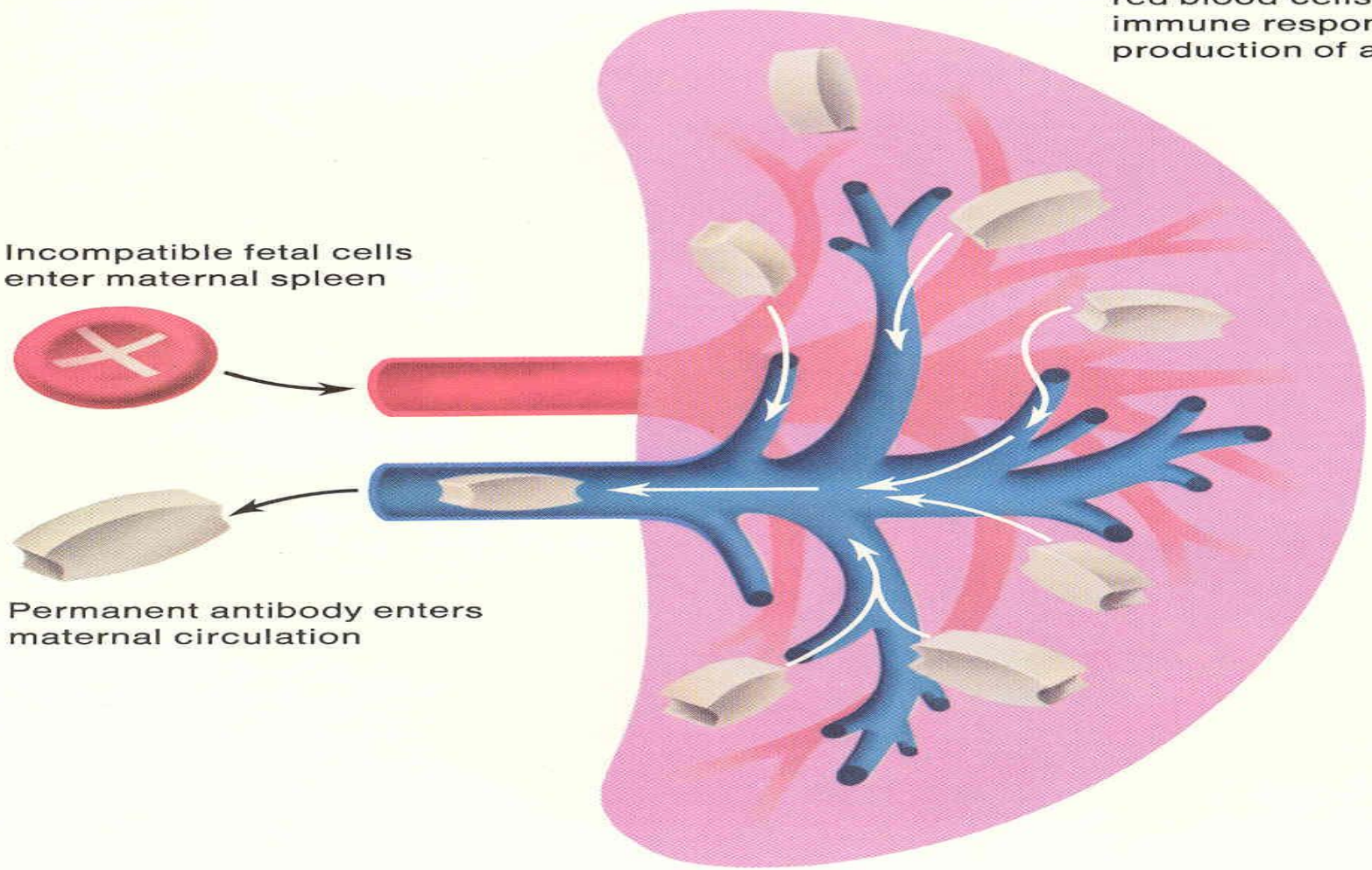
Positive cells



Maternal circulation

Invading fetal (positive) cells

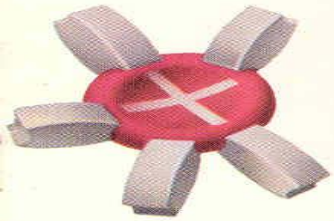
Mother's Spleen After Delivery of Incompatible Infant



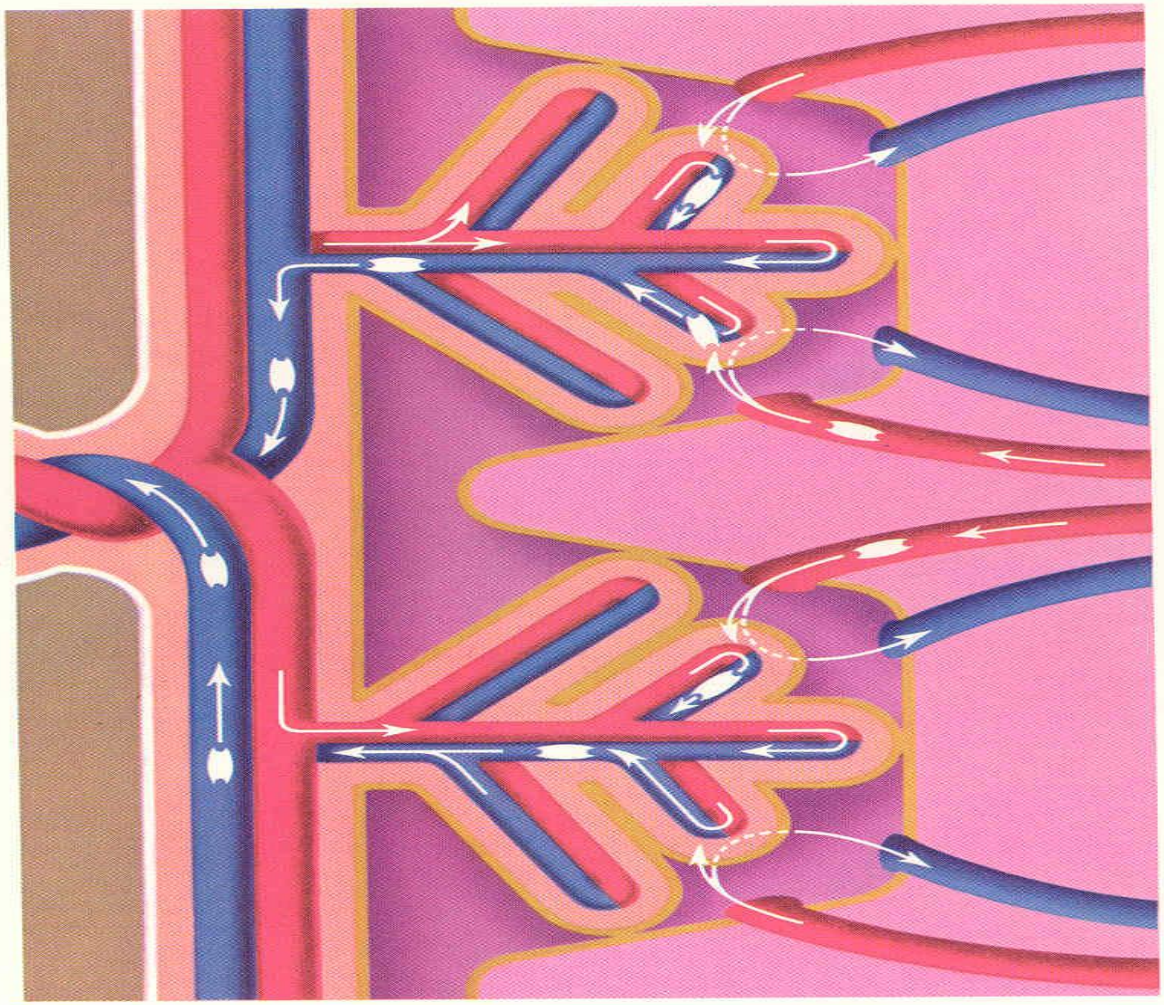
Subsequent Incompatible Pregnancy

Residual antibodies produced as a response to red cells of a previous incompatible fetus or donor are transported through the placental barrier. They attach to the specific red cell antigen sites of the incompatible fetus of the current pregnancy. Sensitized cells do not have a normal life span; the baby suffers from anemia and its consequences.

Fetal circulation

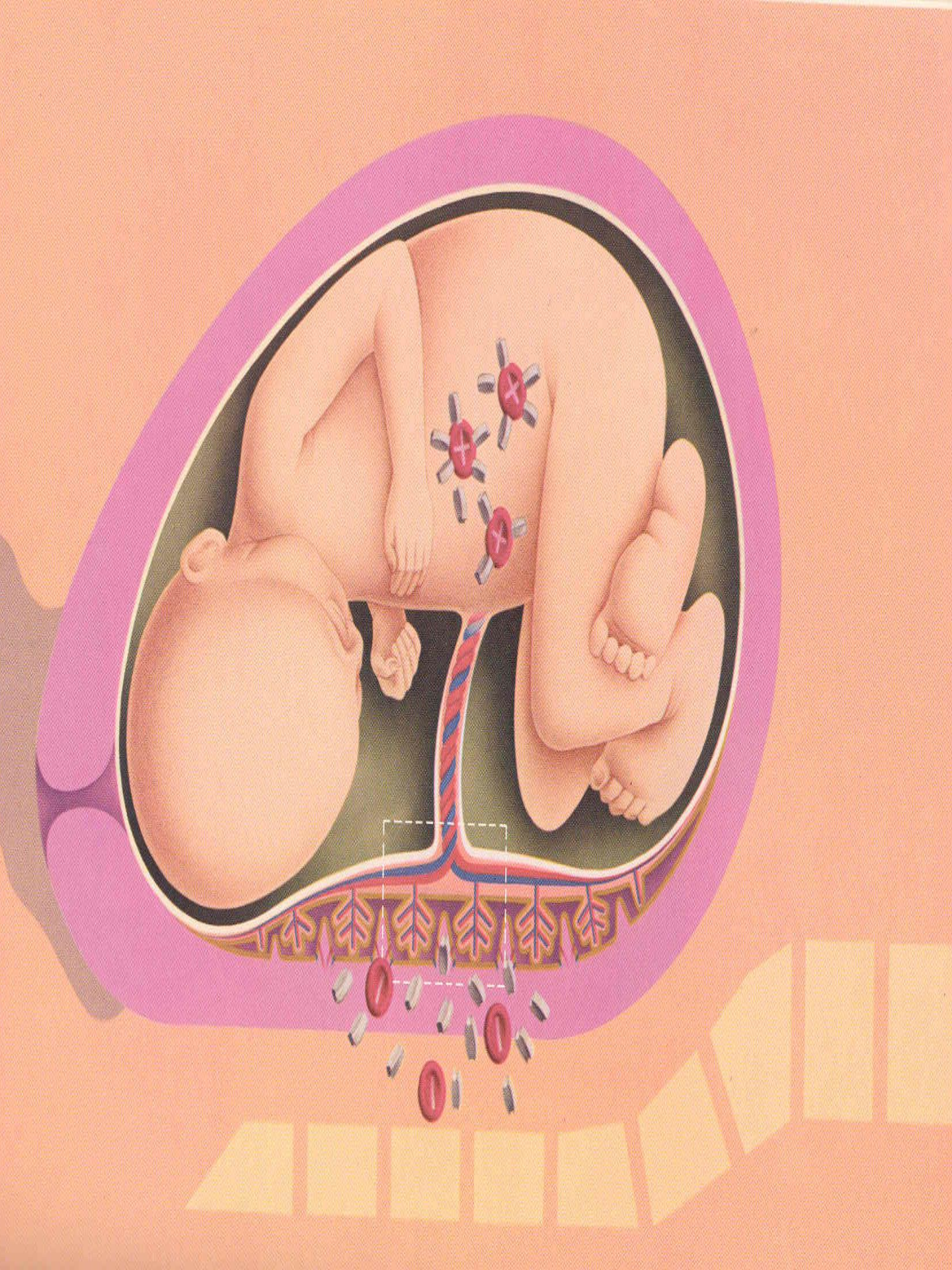


Maternal antibodies attach to incompatible fetal cells



Maternal circulation

Circulating maternal antibodies produced by previous isoimmunization enter placenta



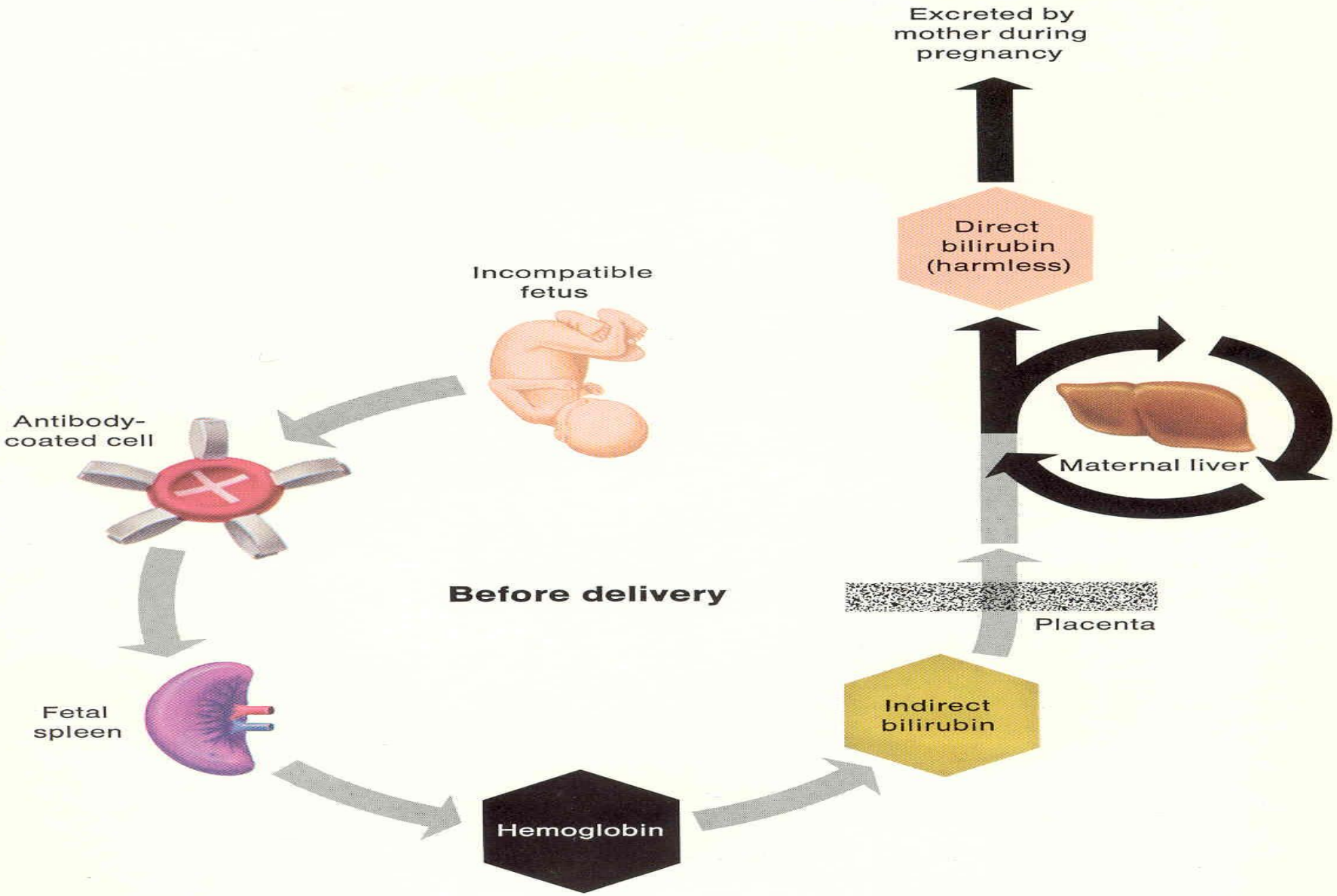
Pathophysiology

- Rh(D) antigen expressed by 30 d GA
- Many cells pass between maternal & fetal circulation including at least 0.1 ml blood in most deliveries but generally not sufficient to activate immune response
- Rh antigen causes > response than most
- B lymphocyte clones recognizing foreign RBC antigen are formed

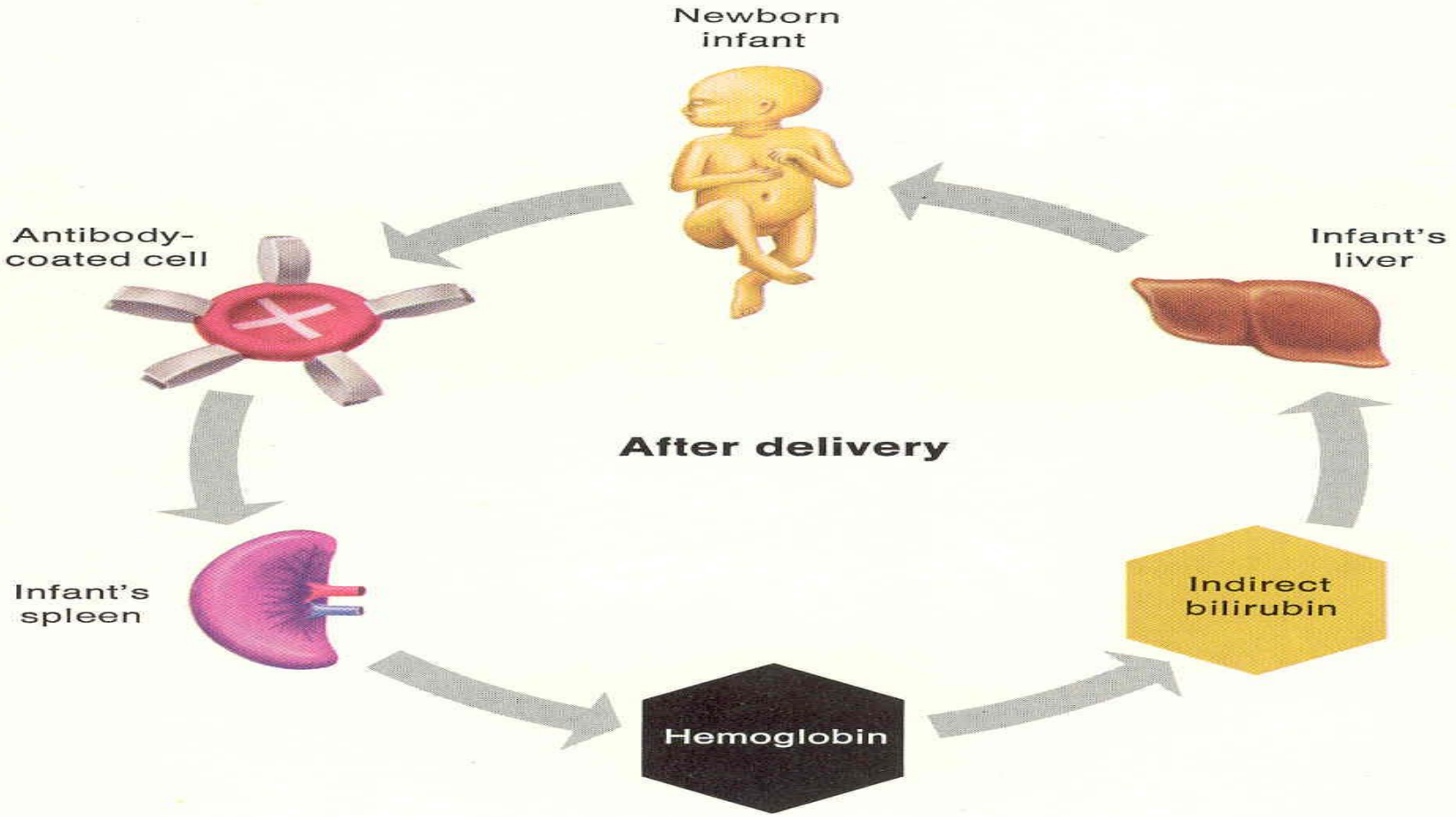
Pathophysiology cont…

- Initial IgM followed by IgG in 2 wks- 6 mths
- Memory B lymphocytes activate immune response in subsequent pregnancy
- IgG Ab cross placenta and attach to fetal RBC's
- Cells then sequestered by macrophages in fetal spleen where they get hemolyzed
- Fetal anemia

Metabolism of Bilirubin



Jaundice does not occur before delivery because bilirubin produced by the breakdown of cells in the fetal spleen passes via the placenta to the maternal circulation. Serum albumin transports the fetal bilirubin to the maternal liver where an enzyme (glucuronyl transferase) converts it to excretable direct bilirubin. The liver of the neonate does not produce glucuronyl transferase and cannot convert bilirubin to an excretable form. Consequently, bilirubin accumulates and if not removed will collect in tissues causing jaundice and brain tissue damage.



Causes of RBC Transfer

- abortion/ectopic
- partial molar pregnancy
- blighted ovum
- antepartum bleeding
- special procedures (amniocentesis, cordocentesis, CVS)
- external version
- platelet transfusion
- abdominal trauma
- inadvertent transfusion Rh+ blood
- postpartum (Rh+baby)

General Screening

- ABO & Rh Ab @ 1st prenatal visit
- @ 28 weeks
- Postpartum
- Antepartum bleeding and before giving any immune globulin

- Neonatal bloods ABO, Rh, DAT

Gold Standard Test

- Indirect Coombs:

-mix Rh(D)+ cells with maternal serum

-anti-Rh(D) Ab will adhere

-RBC's then washed & suspended in Coombs serum (antihuman globulin)

-RBC's coated with Ab will be agglutinated

- Direct Coombs:

-mix infant's RBC's with Coombs serum

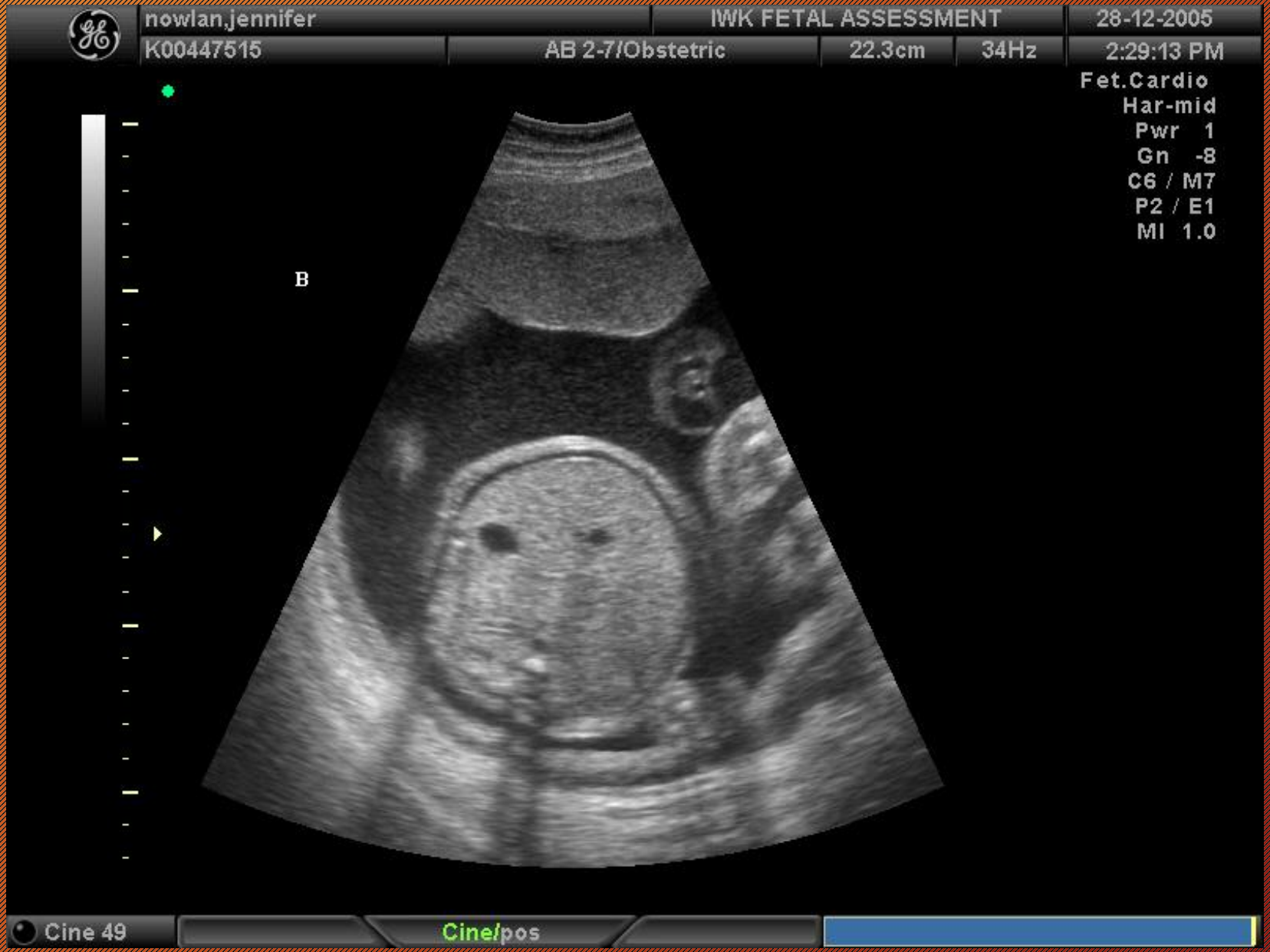
-maternal Ab present if cells agglutinate

+ Rh(D) Antibody Screen

- Serial antibody titres q2-4 weeks
- If titre ≥1:16 - amniocentesis or MCA dopplers and more frequent titres (q1-2 wk)
- Critical titre – sig risk hydrops
- ** amnio can be devastating in this setting
- U/S for dating and monitoring
- Correct dates needed for determining appropriate bili levels (delta OD450)

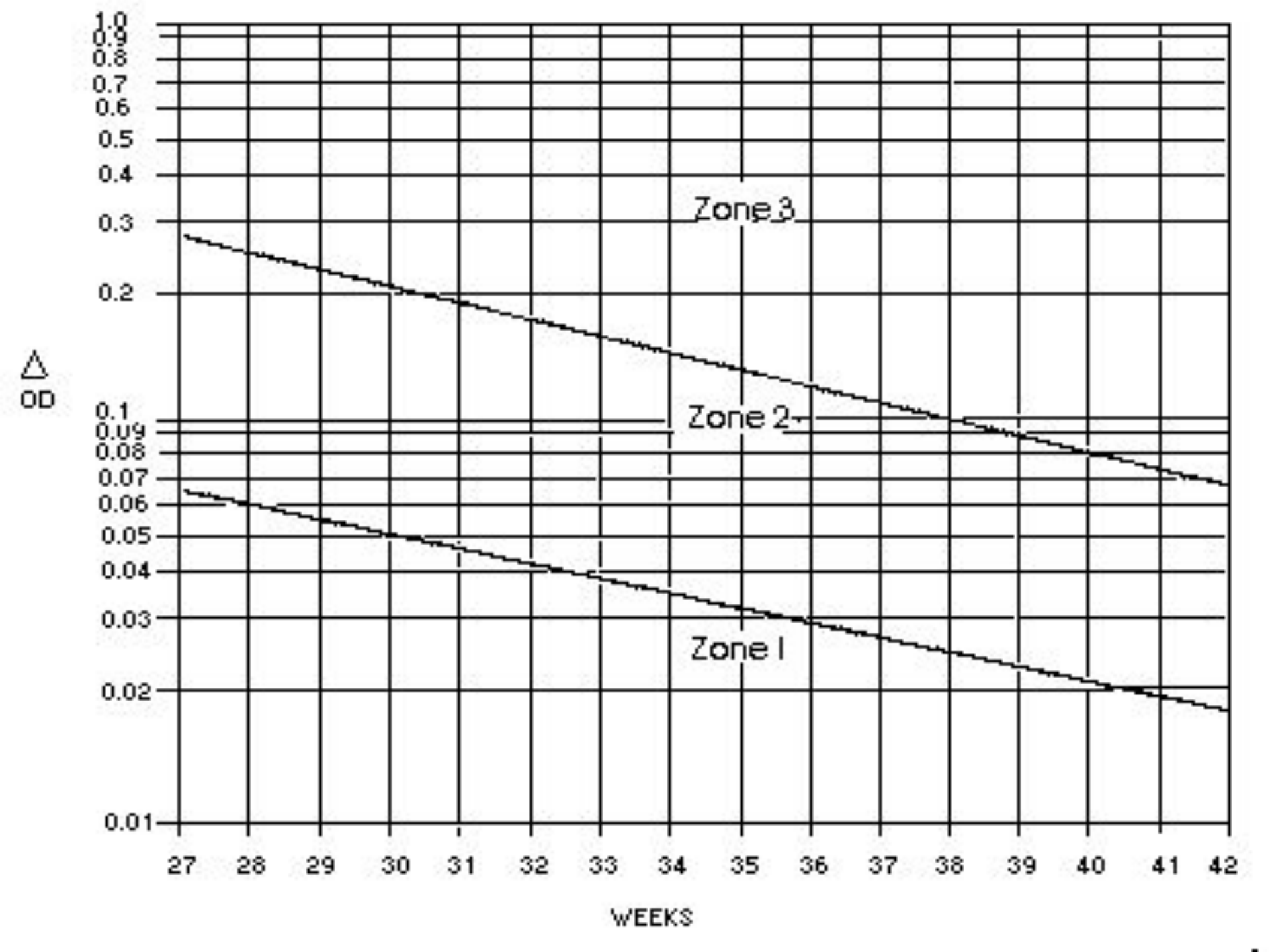
U/S Parameters

- Non Reliable Parameters:
  - Placental thickness
  - Umbilical vein diameter
  - Hepatic size
  - Splenic size
  - Polyhydramnios
- Visualization of walls of fetal bowel from small amounts intraabdominal fluid may be 1st sign of impending hydrops
- U/S reliable for hydrops (ascites, pleural effusions, skin edema) – Hgb < 70


nowlan,jennifer
IWK FETAL ASSESSMENT
28-12-2005
K00447515
AB 2-7/Obstetric
22.3cm
34Hz
2:29:13 PM
Fet.Cardio
Har-mid
Pwr 1
Gn -8
C6 / M7
P2 / E1
MI 1.0
B
Cine 49
Cine/pos

Amniocentesis

- Critical titre/previous affected infant
- Avoid transplacental needle passage
- Bilirubin correlates with fetal hemolysis
- Δ optical density of amniotic fluid @ 450nm on spectral absorption curve
- Data plotted on Liley curve


1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
Δ OD
Zone 3
Zone 2
Zone I
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
WEEKS

Liley Curve

- Zone I – fetus very low risk of severe fetal anemia
- Zone II – mild to moderate fetal hemolysis
- Zone III – severe fetal anemia with high probability of fetal death 7-10 days

- Liley good after 27 weeks
- 98% sensitive for detecting anemia in upper zone 2/ zone 3

Middle Cerebral Artery Dopplers

- Measures peak velocity of blood flow
- Anemic fetus preserves O2 delivery to brain by increasing flow
- Sensitivity of detecting severe anemia when MCA >1.5 MoM approaches 100%
- Not reliable > 35 weeks GA

Fetus at Risk

- Fetal anemia diagnosed by:
  - *amniocentesis*
  - *cordocentesis*
  - *ultrasound*
    - *hydrops*
    - *middle cerebral artery Doppler*

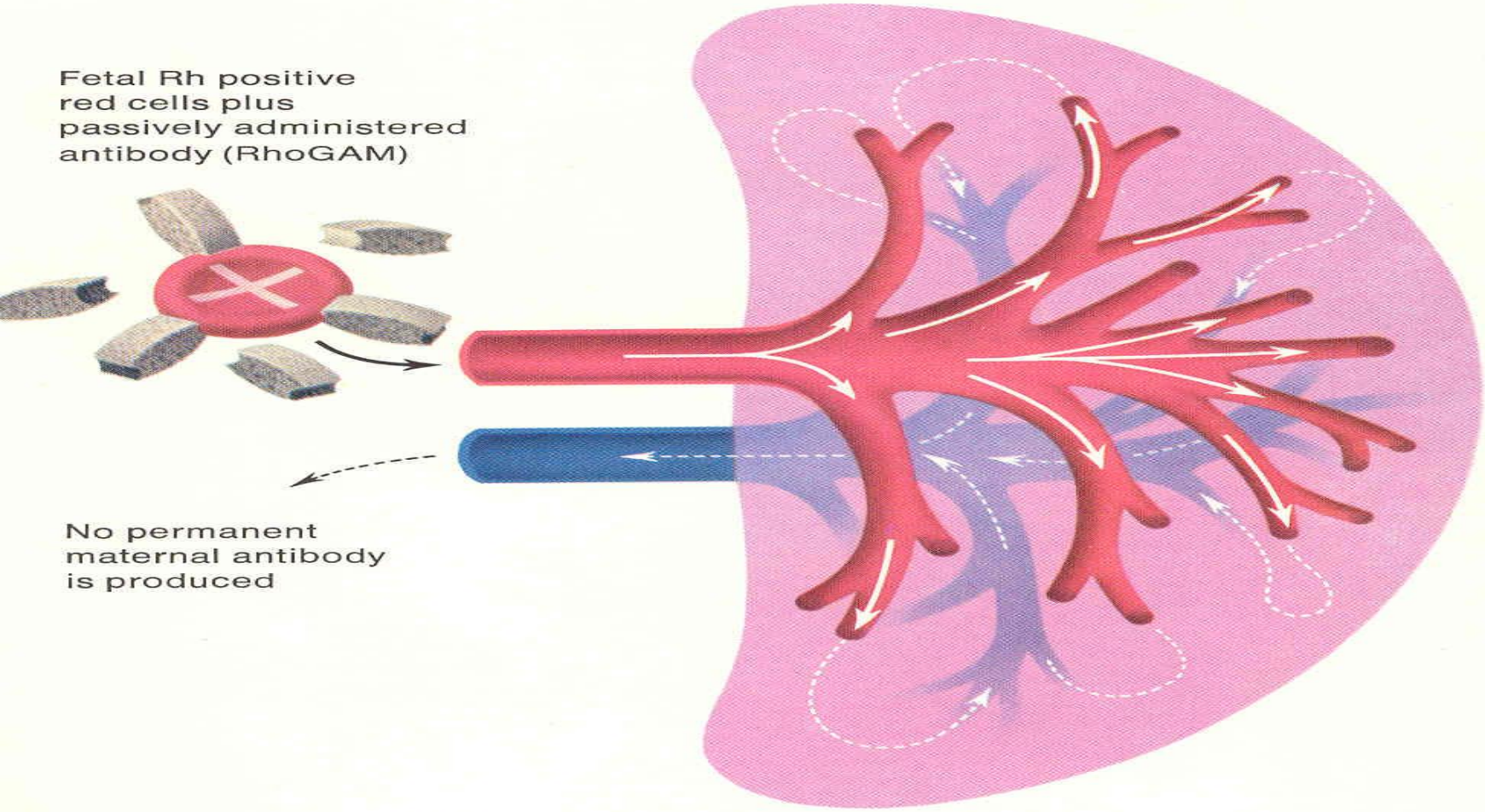
- Treatment:
  - *intravascular fetal transfusion*
  - *preterm birth*

Infant at Risk

- **Diagnosis:**
  - *history of HDN antibodies?*
  - *early jaundice < 24 hours*
  - *cord DAT ("Coomb's") **positive** (due to HDN or ABO antibodies)*
- **Treatment:**
  - *Phototherapy*
  - *Exchange or Direct blood transfusion*

Prevention of Primary Immune Response to Rh_o (D) at Delivery of an Incompatible Fetus

RhoGAM Rh_o (D) Immune Globulin (Human) is injected into the mother within 72 hours of delivery and the immune globulin enters the spleen and lymph nodes. Incompatible Rh_o (D) positive fetal cells are not capable of initiating a primary response in the presence of adequate antibody of the same specificity.



Prevention

- RhoGAM (120mcg or 300mcg)
- Anti-D immune globulin
- Previously 16% Rh(D)- women became alloimmunized after 2 pregnancies, 2% with routine PP dose, and 0.1% with added dose @ 28 wks