# *Neonatal Jaundice*
# *Hemolytic disease of the newborn*

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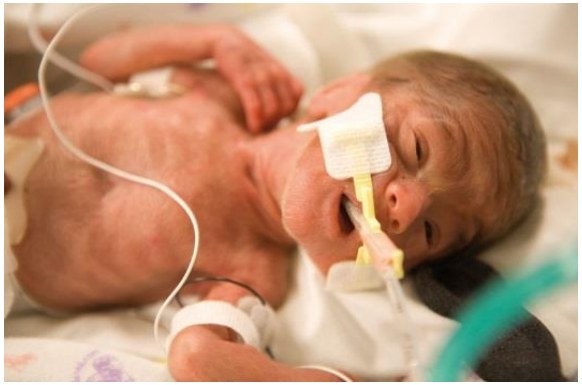
# What Is **Neonatology** anyway?

- Neonatology is the medical specialty of taking care of newborn babies, sick babies, and premature babies.

- The word "neonatology" is stuck together from several root words and basically means "science of the newborn" :"neo" (Greek) = new, "natal"(Latin "natus") = to be born, "ology"(Greek) = science of.

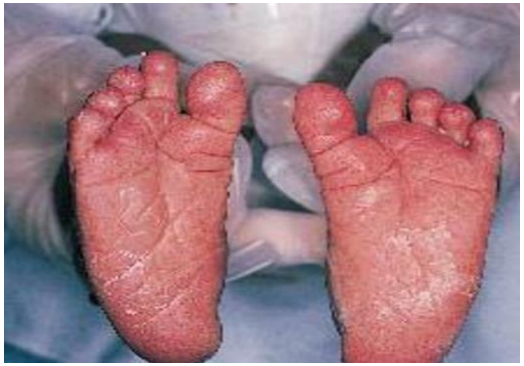
# Newborn babies?

an infant from the time of birth through the 28th day of life.



***Preterm (premature) newborn***
Infants born between 22 and 37 weeks (154-258 d.) of pregnancy

***Term babies*** are born from 37 to 42 weeks (259-294 d.) of the estimated date of birth.



***Postterm (postmature) newborn***
babies born after 42 weeks of gestation.

# Introduction

During the first week of life all newborns have increased bilirubin levels by adult standards, with approximately 60% of term babies and 85% of preterm babies having visible jaundice. Most of these cases are benign but it is important to identify those babies at risk (although rare) of acute bilirubin encephalopathy and kernicterus/chronic encephalopathy. Jaundice may also be a sign of a serious underlying illness.

# Definition

***Jaundice (Hyperbilirubinemia)*** **-** the yellow coloration of the skin and sclera as a result of accumulation of bilirubin

## Visible bilirubin level

*(Bilirubin higher than normal blood)*

- In adults: >34 μmol/l
- In term infants: >85 μmol/l
- In preterm infants: >120 μmol/l

## Occurrence

**~60%** of full-term infants

**~85%** of preterm infants.

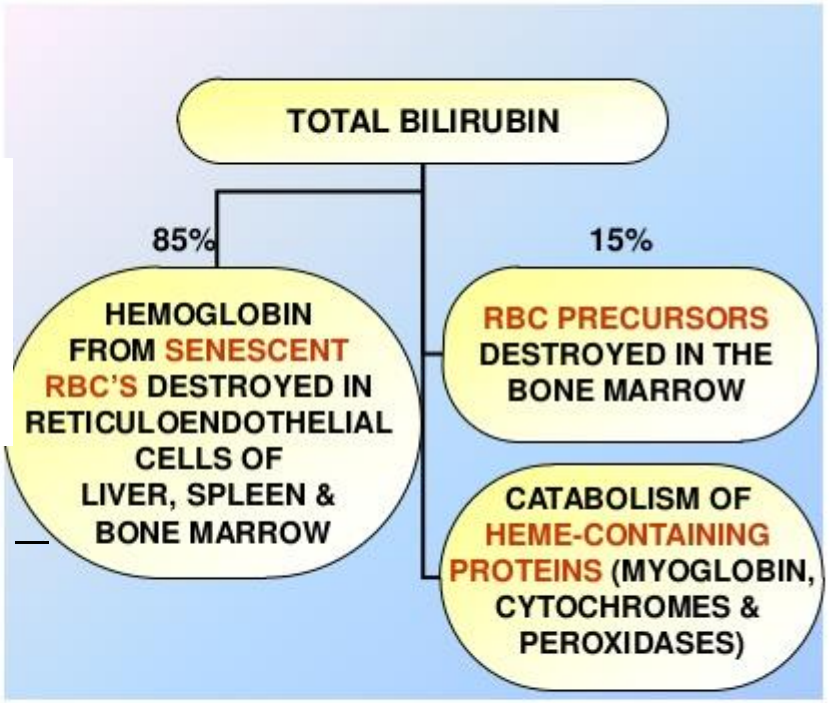

***Visual assessment of jaundice does not permit a reliable conclusion about the level of bilirubin***

# Sources of Bilirubin

## Haem containing proteins:

- **RBC Hb – Major source**

1g Hg=34mg bilirubin

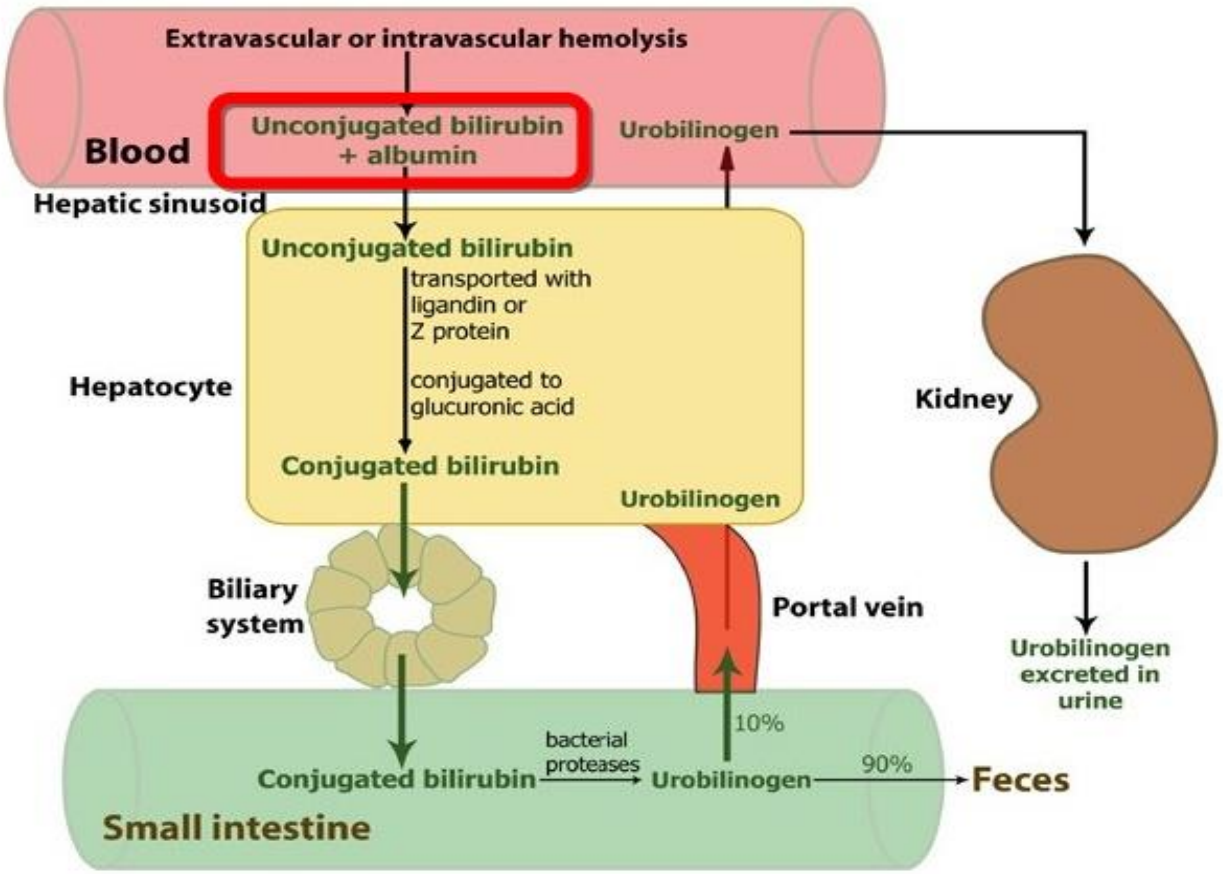



•Haem from ineffective erythropoiesis in bone marrow

•Other haem containing proteins – myoglobin, cytochromes, catalase, peroxidase

•Free haem

# Bilirubin Metabolism



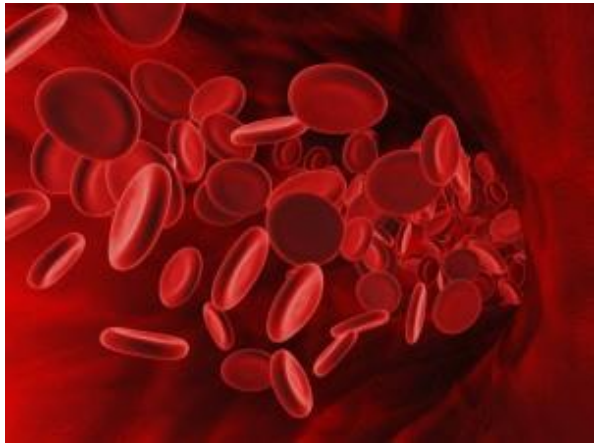

***1g albumin binds 14, 4 mkmol bilirubin***

Unconjugated bilirubin = *Indirect bilirubin* (**fat soluble**).
Unconjugated bilirubin+albumin= protein-bound unconjugated bilirubin *(Indirect bilirubin)*.
Conjugated bilirubin = *Direct bilirubin* (**water soluble**).

# Special characteristic of bilirubin metabolism in neonates

**1. Increased production of bilirubin**

- Physiological Polycythemia
- Shorter life span of HbF (90 days)



**2. The low capability of albumin on unconjugated bilirubin transportation**

- Less albumin in neonates

**3. Decreased uptake and binding by liver cells**

- Transient deficiency of Y & Z acceptor proteins

# Special characteristic in neonates

**4. Decreased conjugation (most important)**

• Reduced UDPG enzymes
(UDP-glucuronosyltransferase)

**5. Increased enterohepatic circulation of bilirubin.**

- High levels of beta-glucuronidase

**6. Decreased excretion**

- Less bacterial
- Low enzymatic activity in intestine

***Jaundice of newborns could be of the following types***

- **Physiological jaundice**
- **Pathological jaundice**

# Physiological jaundice

## Characteristics

- **Appears after 24 hours**
- **Maximum intensity by 4th-5th day in term**, 7th day in preterm
- Maximum serum bilirubin level less than **256 µmol/l**
- Umbilical cord bilirubin levels less than **35 µmol/l**
- **Direct bilirubin 10-15%** of total bilirubin
- Clinically not detectable **after 14 days**
- Disappears **without any treatment**

**Note:**

***Treatment usually is not required***

***Baby should, however, be watched for worsening jaundice.***

# Pathological jaundice

## Characteristics

• Clinical jaundice detected **before 24 hours of age (after 72 hours of age)**
• Umbilical cord bilirubin levels more than **42 µmol/l (2,5 mg/dl)**
• Serum bilirubin more than **256 µmol/l** in term **(150 µmol/l** in preterm) at any time
• Clinical jaundice **persisting beyond 14 days** of life
• Clay/white colored stool and/or dark urine
• Direct bilirubin more then **10-15% of total bilirubin** at any time

**Note:**

***Treatment must be initiated as soon as possible***

# Classification

- **Physiological jaundice**
- **Pathological jaundice**

***Indirect Hyperbilirubinemia:***

•**Disorders of Production** (*HDN*, drug hemolysis: menadione, oxytocin, penicillin, RBC biochemical defects and structural abnormalities, infection, polycythemia, hemoglobinopathy, Glucose-6-phosphate dehydrogenase (G6PD) deficiency)

•**Disorders of Hepatic Uptake** (Gilbert Syndrome)

•**Disorders of Conjugation** (Crigler-Najjar Syndrome Type I&II, Lucey-Driscoll Syndrome, hypothyroidism)

•**Other Causes** (Breastfeeding jaundice - lack of volume, Breast milk jaundice, Infant of diabetic mother

***Direct Hyperbilirubinemia:***

*More common causes:*

•Hepatitis: Idiopathic, Infectious, Toxic
•Infection: Sepsis, TORCH
•Biliary atresia
•Inspissated bile plug
•Choledochal cyst
•Alpha-1-antitrypsin deficiency, Galactosemia

*Less common causes:*

•Cholelithiasis
•Rotor's Syndrome, Dubin-Johnson Syndrome
•Storage diseases (Niemann-Pick, Gaucher's)
•Metabolic disorders (tyrosinemia, fructosemia)
•Alagille Syndrome, Zellweger Syndrome

# Day 1 – Always pathological

- Usually due to **hemolysis:**

Hemolytic disease of newborn: Rh, ABO incompatibility

- Exclude **sepsis**
- Rarer causes may include:

-other blood group incompatibilities (Kell, Duffy, anti – E)

-red cell enzyme defects (glucose-6-phosphate dehydrogenase deficiency (G6PD))

-red cell membrane defects (hereditary spherocytosis)

- Obstructive jaundice in neonatal hepatitis due to rubella, CMV and syphilis is occasionally present (conjugated)

***Investigations:*** Mother and baby`s blood group, direct Coomb`s test, reticulocyte count, haematocrit, haemoglobin and blood film. Must repeat serum bilirubin. Serological tests for TORCH infections if indicated

# Day 2-9

- Sepsis
- Polycythemia
- Breakdown of extravasated blood due to:

-cephalhaematoma

-central nervous system haemorrhage

- Increased enterohepatic circulation which may be due to gut obstruction
- ***Physiological jaundice (mostly)***

***Investigation:*** Full blood count, urine for microscopy and culture, investigation for bacterial infections, glucose-6 phosphate dehydrogenase screen, blood groups, direct Coomb`s test.

# Day 10 – 4 weeks

- Sepsis
- Pyloric stenosis (especially greater than 2 weeks)
- Conjugated hyperbilirubinaemia due to:

-idiopathic neonatal hepatitis
-infections (Hepatitis B, TORCH, sepsis)
-congenital malformations (biliary atresia, choledochal cyst, bile duct stenosis)
-metabolic disorders (galactosaemia, hereditary fructose intolerance, Alpha-1 antitrypsin deficiency, tyrosinaemia, hypothyroidism)

- Breast milk jaundice

***Investigations***: Full blood count, investigation for bacterial infections, thyroid function tests, urine for reducing substances to exclude galactosaemia.

# Workup for pathological jaundice

1. ***Review maternal and perinatal history***

family history of jaundice, liver disease, previous sibling with jaundice for blood group incompatibility, maternal illness during pregnancy, traumatic delivery, delayed cord clamping, oxytocin use, birth asphyxia, delayed feeding, delay in meconium passage, breast feeding

2. ***Physical examination***

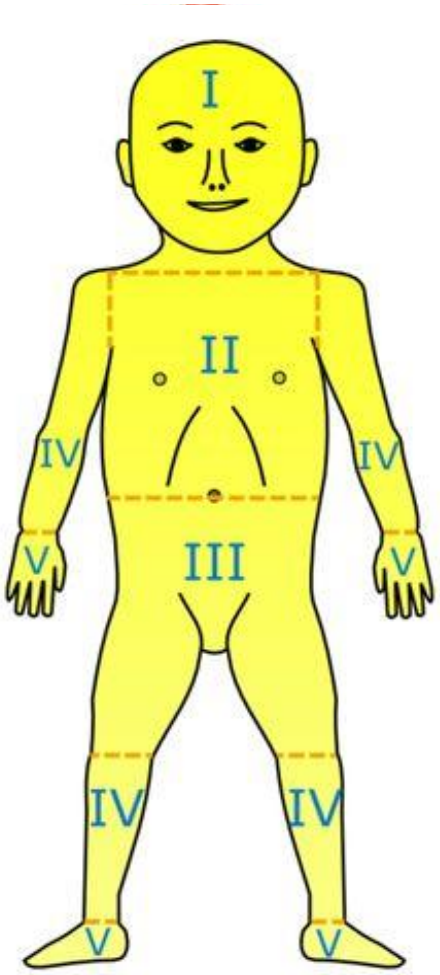
Extent of jaundice, prematurity, small for gestation (polycythemia, hepato-splenomegaly, cataract, rash), extravascular bleed (cephalhematoma); pallor (hemolysis, blood loss); petechiae (sepsis, TORCH infections); hepatosplenomegaly (Rh-isoimmunization, sepsis, TORCH infections)

3**. *Laboratory tests***

Serum bilirubin total and direct, blood group and Rh for mother and baby, Direct Coomb's test on infant, hematocrit, RBC morphology, evidence of hemolysis, reticulocyte count, sepsis screen, liver and thyroid function tests in cases with prolonged jaundice, TORCH titres

# Physical examination

## Extent of jaundice

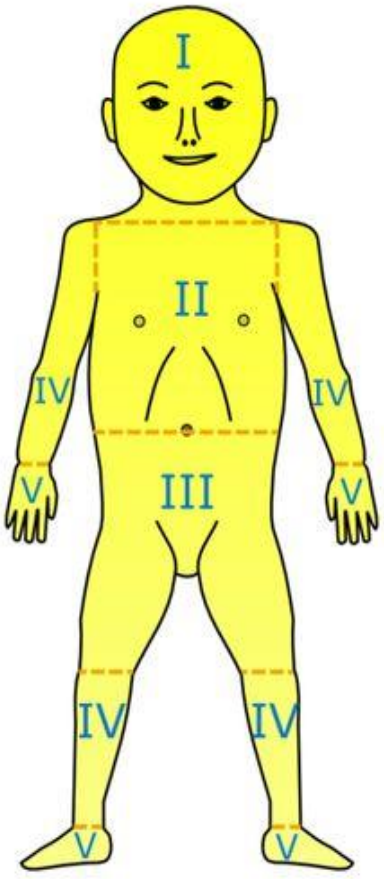



### Kramer's index

| Grade | Extent of jaundice |
|---|---|
| 0 | None |
| 1 | Face and neck only |
| 2 | Chest and back |
| 3 | Abdomen below umbilicus to knees |
| 4 | Arms and legs below knees |
| 5 | Hands and feet |

# Physical examination

## Extent of jaundice




The bilirubin range associated with each zone is:

| Zone | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| SBR (micromol/L) | 100 | 150 | 200 | 250 | >250 |

# Physical examination

## Transcutaneous bilirubinometry

- ✓ Since 2006 transcutaneous bilirubinometry has been dopted as the first-line screening tool for jaundice in well, full-term babies.
- ✓ This leads to about 50% of blood test previously required being avoided.
- ✓ To take a measurement, the device is calibrated prior to each measurement; the disposable probe is applied on the forehead level below the hairline (figure 1) or on the chest (figure 2) and five readings are used to generate one measurement.
- ✓ The correlation between bilirubin concentration in derma and bilirubin concentration in blood is caused by existing dynamical balance between bilirubin concentration in blood and subcutaneous tissues due to reversible diffusion of a bilirubin between blood and tissues

*figure 1*

*figure 2*

# Physical examination

**Assess each jaundiced baby to see whether the following danger signs are present:**

- family history of significant haemolytic disease
- pallor, bruising, petechiae
- lethargy
- poor feeding
- fever
- vomiting
- dark urine and light stools
- hepatosplenomegaly
- high pitched cry

# Laboratory tests

- **The total SBR** continues to be the "gold standard" for deciding if a baby's jaundice requires intervention.

- In the case of preterm infants, greater caution should be exercised. These babies are at risk of kernicterus at lower SBR levels.

# Laboratory tests

- Hematocrit
- Examination of a blood sample under a microscope to look for signs of red blood cell breakdown
- Reticulocyte count
- Coombs test (which checks for certain antibodies attached to red blood cells)
- Measurement of different types of bilirubin
- Blood type and Rh status (positive or negative) of the newborn and mother

# Management

1. Prevention of hyperbilirubinemia:
- Early and frequent feeding
- Adequate hydration

2. Reduction of bilirubin:
- phototherapy or/and
- exchange transfusion

# Breast milk jaundice (BMJ)

**Causes**:

•not completely understood
•associated with nonesterified *long-chain fatty acids*, *metabolite of progesterone* in breast milk that competitively inhibit glucuronyl transferase, also *glucoronidase* which will increase deconjugation and enterohepatic recirculation of bilirubin

- In 2-4 % EBF (exclusivley breast feeding) babies
- Appears after the fourth day of life
- SBr>**170 µmol/l** beyond 3rd-4th week

**Management:**

- Some babies may require therapy
- Should be differentiated from hemolytic jaundice, hypothyroidism, G6PD deficiency, *breastfeeding jaundice*
- Continue breast feeding
- Usually declines over a period of time

# Breastfeeding jaundice

## Case #1

- A 3.2-kg female infant was born at 40 weeks' gestation.
- Apgar scores was 8 and 9 at 1 and 5 minutes
- Pregnancy and delivery without complications
- Mother and baby are both B positive.
- **No** known **risk factors**.
- Currently 48h of life.Weight is 2850 g (**about 11% less than BW**). Jaundice. **Insufficient intake of breast milk**
- Total/direct bilirubin is 308/17μmol/l

## Management:

- Initiate phototherapy
- Monitor serial bilirubin levels
- Encourage increased frequency of feedings
- Consider additional feeding
- Request lactation consultant

# Disorders of hepatic uptake

## Gilbert syndrome

- Gilbert's syndrome is due to a mutation in the UGT1A1 gene which results in decreased activity of the glucuronosyltransferase enzyme, the capture of bilirubin by hepatocytes is disturbed.
- Gilbert syndrome affects ~9% of the population
- Usually not diagnosed in the neonatal period and occurs as physiological jaundice.
- Conjugated bilirubin is usually within the normal range and is less than 20% of the total.
- Although Gilbert syndrome is most commonly diagnosed in young adulthood, this disorder might contribute to **indirect hyperbilirubinemia** in the newborn period
- Newborns with Gilbert syndrome may have severe hyperbilirubinemia and even kernicterus, if they have a concurrent hemolytic disorder such as ABO incompatibility or glucose-6-phosphate dehydrogenase deficiency.

# Disorders of Conjugation

## Crigler-Najjar Syndrome Type I&II

- Crigler-Najjar syndrome type I, characterized by a nearly complete lack of glucuronosyltransferase enzyme activity and severe symptoms
- Crigler-Najjar syndrome type II (Arias syndrome), characterized by partial enzyme activity and milder symptoms.
- Both forms are inherited as autosomal recessive traits and are caused by errors or disruptions (mutations) of the UGT1A1 gene.
- Type 1 is characterised by a serum bilirubin usually above 345 μmol/L
- therapy includes: exchange transfusions in the immediate neonatal period
- 12 hours/day phototherapy
- heme oxygenase inhibitors, oral calcium phosphate and carbonate
- liver transplantation

# Remember that

- The age of appearance may overlap and the above mentioned grouping is only a general classification
- Infection must be ruled out in jaundice appearing any time after third day of life.
- Even after extensive investigations, cause remains uncertain in over one third of cases.
- Neonatal jaundice may be multifactorial in origin.

# Remember that

- Never discharge a baby with conjugated hyperbilirubinaemia without attempting to find the cause.
- Assess all babies for risk of developing severe hyperbilirubinaemia at hospital discharge.
- Visual estimation of bilirubin levels can lead to errors, especially in darkly pigmented babies and in infants who have received phototherapy.
- Parents should be advised to contact a healthcare professional if: *their baby becomes jaundiced, baby's jaundice is worsening, jaundice is persisting beyond 14 days, their baby is passing pale stools*

# Hemolytic Disease of the fetus and newborn

## (HDN, erythroblastosis fetalis, isoimmunization)

**HDN** is a blood disorder that occurs when the blood types of a mother and baby are incompatible.

- The first description of HDN is thought to be in *1609*
- The underlying cause of HDN was clarified in *1950*

- **The frequency of HDN – 3-6%**

- **Mortality – 0,01-0,02‰**

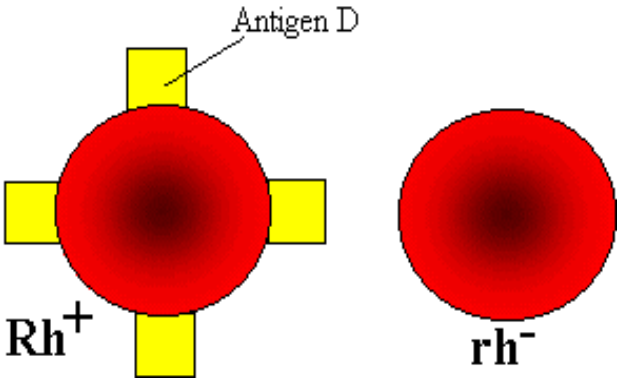
# Hemolytic Disease of the newborn

## CAUSES OF HDN

- Rh (D) Incompatibility
- ABO Incompatibility
- Minor Blood Group Incompatibility

**50 known membrane proteins → 25 proteins carry the various antigens**

# Rh Incompatibility




**Rh positive (+)** denotes presence of **D antigen**. The number of antigenic sites on RBCs varies with genotype.

D/D – Rh positive (+)
D/d – Rh positive (+)
d/d – Rh negative (-)

| mother \ father | D | D |
|---|---|---|
| d | Dd | Dd |
| d | Dd | Dd |

100% Rh+ children

| mother \ father | D | d |
|---|---|---|
| D | DD | Dd |
| d | Dd | dd |

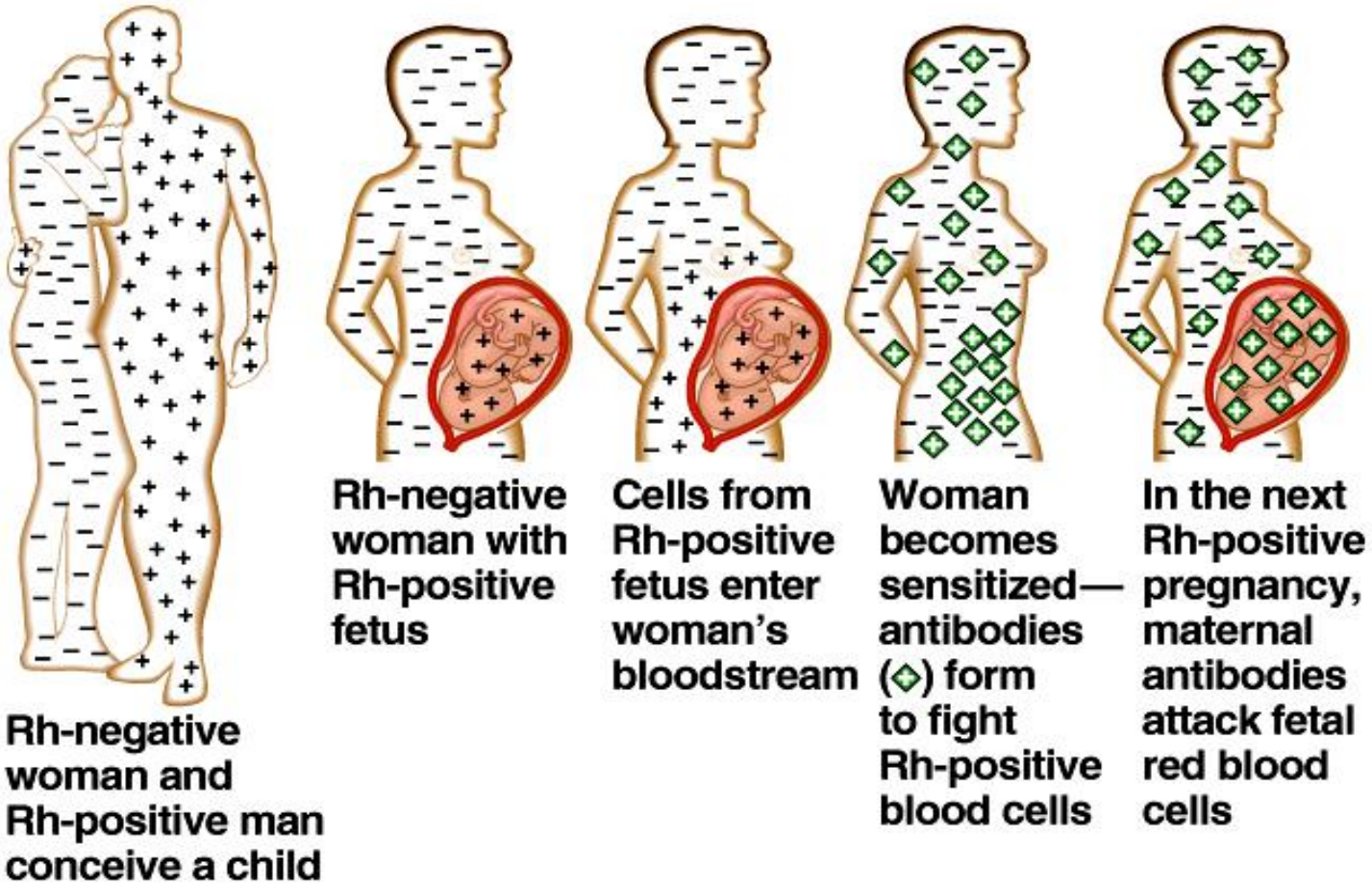
75% Rh+ children

| mother \ father | D | d |
|---|---|---|
| d | Dd | dd |
| d | Dd | dd |

50% Rh+ children

# Rh Incompatibility

## Pathophysiology of HDN




The process of antibody formation is called ***maternal sensitization.***

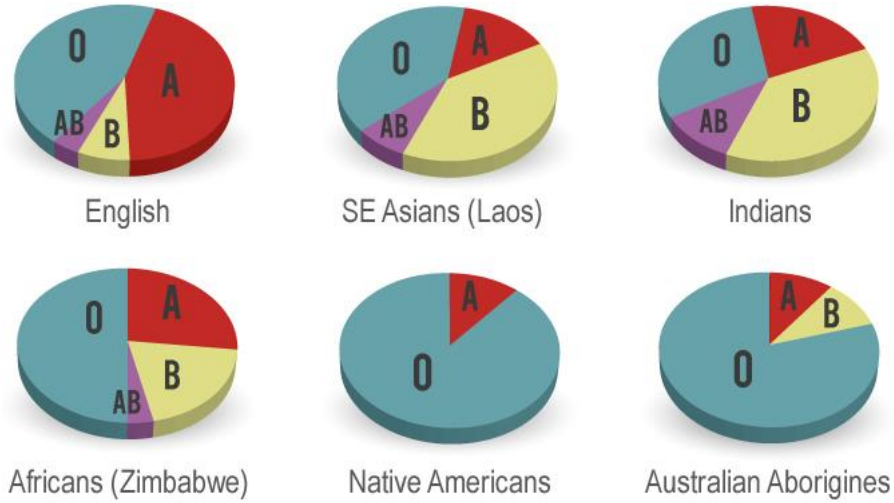
# ABO INCOMPATIBILITY

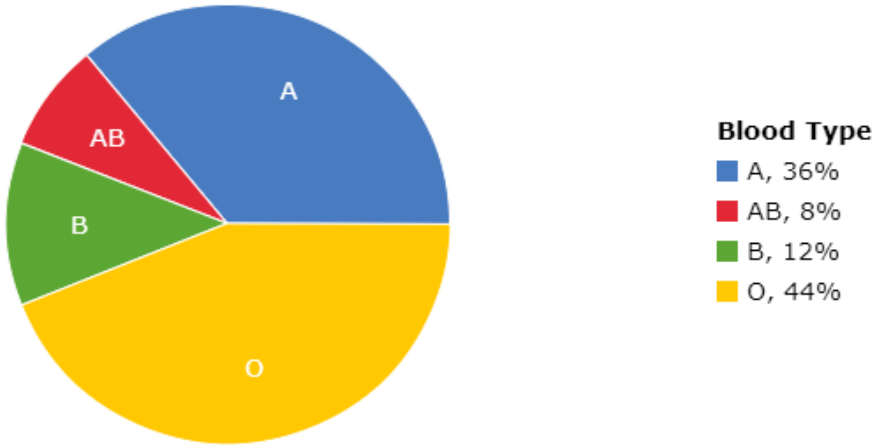
| | Antigen A | Antigen B | Antigens A and B | Neither antigen A nor B |
|---|---|---|---|---|
| Erythrocytes |  |  |  |  |
| Plasma | Anti-B antibodies  | Anti-A antibodies  | Neither anti-A nor anti-B antibodies | Both anti-A and anti-B antibodies  |
| Blood type | **Type A** Erythrocytes with type A surface antigens and plasma with anti-B antibodies | **Type B** Erythrocytes with type B surface antigens and plasma with anti-A antibodies | **Type AB** Erythrocytes with both type A and type B surface antigens, and plasma with neither anti-A nor anti-B antibodies | **Type O** Erythrocytes with neither type A nor type B surface antigens, but plasma with both anti-A and anti-B antibodies |

(a)

| Mother's Blood Type | Father's Blood Type: A | B | AB | O | Baby's Blood Type |
|---|---|---|---|---|---|
| A | A or O | A, B, AB or O | A, B, or AB | A or O | |
| B | A, B, AB or O | B or O | A, B or AB | B or O | |
| AB | A, B or AB | A, B or AB | A, B or AB | A or B | |
| O | A or O | B or O | A or B | O | |

# ABO INCOMPATIBILITY



# ABO INCOMPATIBILITY

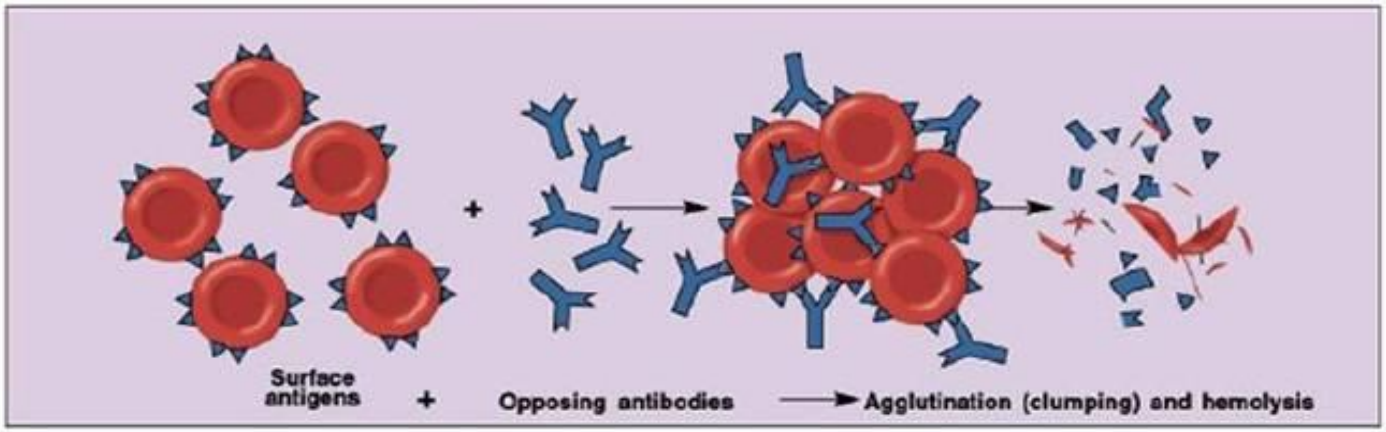
•ABO disease **can occur in first pregnancies** without any transfusion

•The mechanism of ABO HDN is similar to the RH HDN

• In contrast to the Rh antigens, the ABO blood group antigens are **expressed by a variety of fetal tissues**, reducing the chances of anti-A and anti-B binding their target antigens on the fetal RBCs.

•Generally **less severe** than Rh disease

•The risk of sensitization to the Rh D antigen is decreased if the fetus is ABO incompatible.

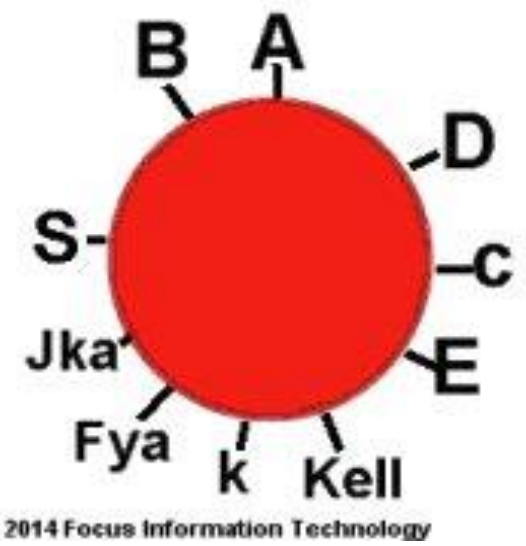


# Minor Blood Group Incompatibility

•Uncommon, occurs in ~0.8% of pregnant women

•Others unexpected immune antibody :
-Other Rh antibodies:
- anti-E (second most common, mild disease)
- anti–c (third most common, mild to severe)
- anti-C and anti-e (rare)
- antibody combination (anti-c and anti-E occurring together, can be severe)

-Other antibodies:
- Kell system antibodies (uncommon causes)
- Duffy, MNSs and Kidd system antibodies (rare causes)




•Clinical presentation is similar to Rh (D) disease

# Hemolytic Disease of the fetus and newborn

## Clinical symptoms

Varies from mild **jaundice** and anemia to **hydrops fetalis** (with ascites, pleural and pericardial effusions)

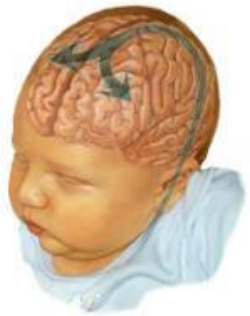
- Chief risk to the fetus is **anemia**
- Extramedullary hematopoiesis due to anemia results in **hepatosplenomegaly**
- Risks during labor and delivery include: **asphyxia** and **splenic rupture**

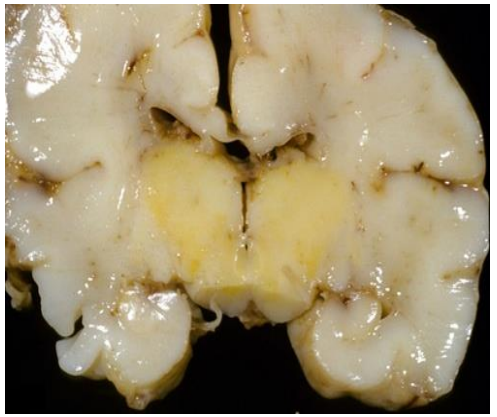
*Postnatal problems include:*

- Asphyxia
- Pulmonary hypertension
- **Pallor** (due to anemia)
- **Edema** (hydrops, due to low serum albumin)
- Respiratory distress
- Coagulopathies (↓ platelets & clotting factors)
- **Jaundice**
- **Kernicterus** (from hyperbilirubinemia)
- Hypoglycemia (due to hyperinsulinemnia from islet cell hyperplasia)

# Kernicterus (Acute Bilirubin Encephalopathy)

- Kernicterus or bilirubin encephalopathy results from high levels of unconjugated bilirubin in the blood which is more than **342µmol/l**
- Because unconjugated **bilirubin** are lipid soluble and toxic, it can crosses the blood-brain barrier and it will **penetrates neuronal and glial membrane** thus cause neurotoxicity
- Patients surviving kernicterus have severe permanent neurologic symptoms such as a) choreoathetosis b) spasticity c) muscular rigidity d) ataxia e) deafness f) mental retardation





**Affected structures have a bright yellow color due to bilirubin stained**

# Hydrops fetalis

•If Rh isoimmunization occurs early greater rapid and prolonged destruction of RBCs leads to **severe anemia in the fetus.**
•The liver, spleen, and other organs increase their production of RBCs to compensate for their loss.
•The drive to produce RBCs causes the liver and spleen to increase in size (**hepatosplenomegaly**) and liver dysfunction can occur.
• A complication of severe HDN is hydrops fetalis, in which the fetal tissues become swollen (edematous).
•This condition **is usually fatal**

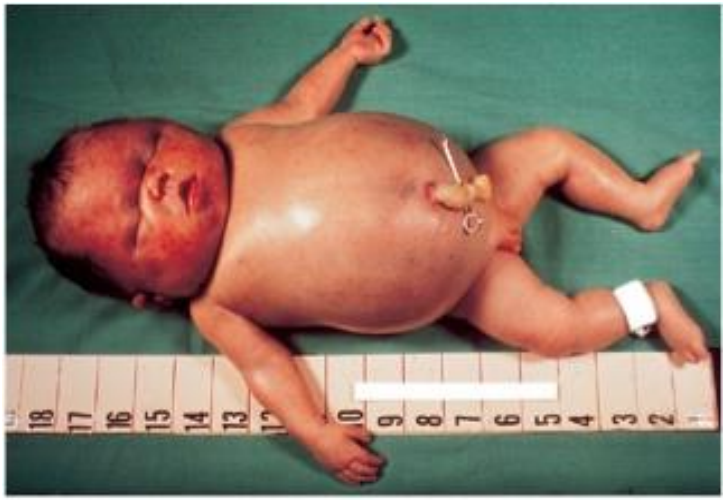
# Hydrops fetalis

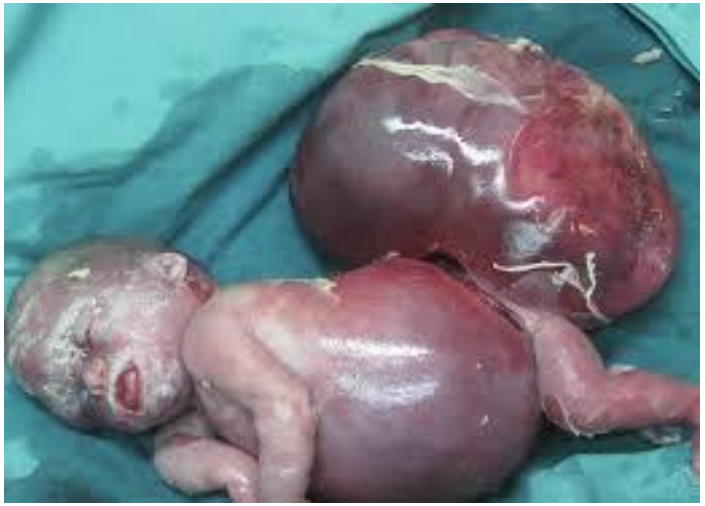
condition in the fetus characterized by an abnormal collection of fluid with at least two of the following:

- **Edema** (fluid beneath the skin, more than 5 mm).
- **Ascites** (fluid in abdomen)
- **Pleural effusion** (fluid in the pleural cavity, the fluid-filled space that surrounds the lungs)
- **Pericardial effusion**

(fluid in the pericardial sac, covering that surrounds the heart)

In addition, hydrops fetalis is frequently associated with polyhydramnios and a thickened placenta (>6 cm).





# Management of HDN

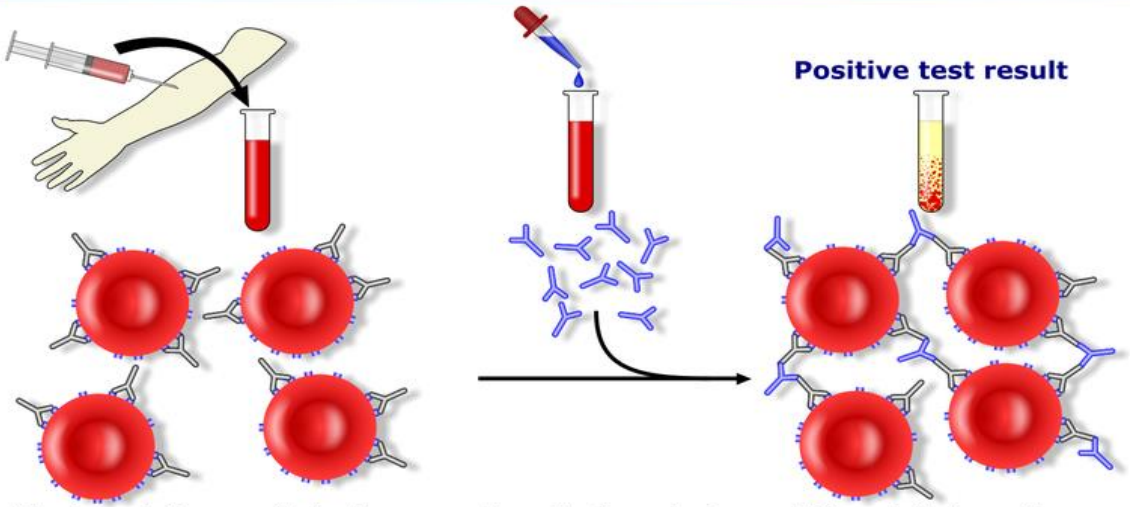
1. **Determine Rh, ABO status of the mother**. All D-negative pregnant women should undergo an antibody screen (an increase of antibodies represents **sensitize**) at the first prenatal visit then routine repeat screen at 28 weeks
2. **If the mother is not sensitized, reduce the risk of future sensitization.**
   **Rh D-negative mothers receive on injection of anti-D Ig** at 28 weeks gestation, another dose at about 34 weeks, a few weeks before labor begins. A final dose of anti-D Ig is given after the baby (D-positive) has been delivered (300 micrograms within 72 hours of delivery) .
3. **If the mother is sensitized, determine whether the fetus is at risk and monitor accordingly.**
   Monitoring includes regular ultrasound scans of the fetus and monitoring of the amount of anti-D in the mother's serum, fetal blood test.

# Diagnostics

**Laboratory Findings vary with severity of HDN and include:**

- Anemia
- Hyperbilirubinemia
- Reticulocytosis (6 to 40%)
- ↑ nucleated RBC count
- Thrombocytopenia
- Leucopenia
- + Antiglobulin Test (Coombs test)
- Hypoalbuminemia
- Rh negative blood type
- Smear: polychromasia, anisocytosis, no spherocytes
- Cord blood bilirubin >68 μmol/l indicates severe isoimmunization

# Direct Coombs test / Direct antiglobulin test

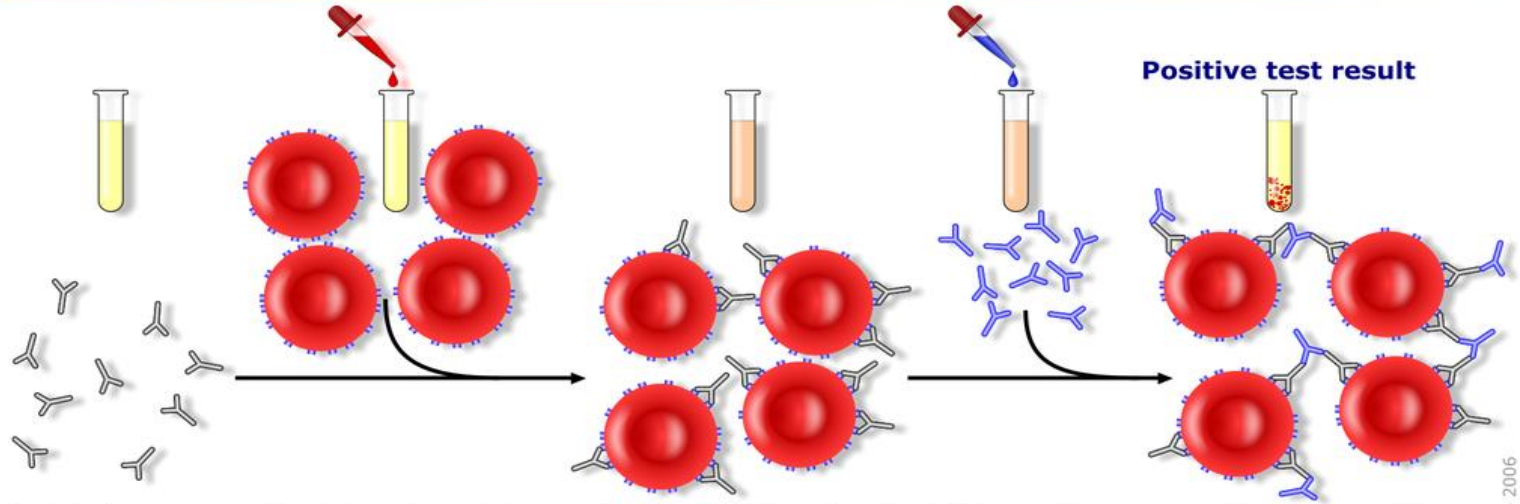



Blood sample from a patient with immune mediated haemolytic anaemia: antibodies are shown attached to antigens on the RBC surface.

The patient's washed RBCs are incubated with antihuman antibodies (*Coombs reagent*).

RBCs agglutinate: antihuman antibodies form links between RBCs by binding to the human antibodies on the RBCs.

# Indirect Coombs test / Indirect antiglobulin test




Recipient's serum is obtained, containing antibodies (Ig's).

Donor's blood sample is added to the tube with serum.

Recipient's Ig's that target the donor's red blood cells form antibody-antigen complexes.

Anti-human Ig's (*Coombs antibodies*) are added to the solution.

Agglutination of red blood cells occurs, because human Ig's are attached to red blood cells.

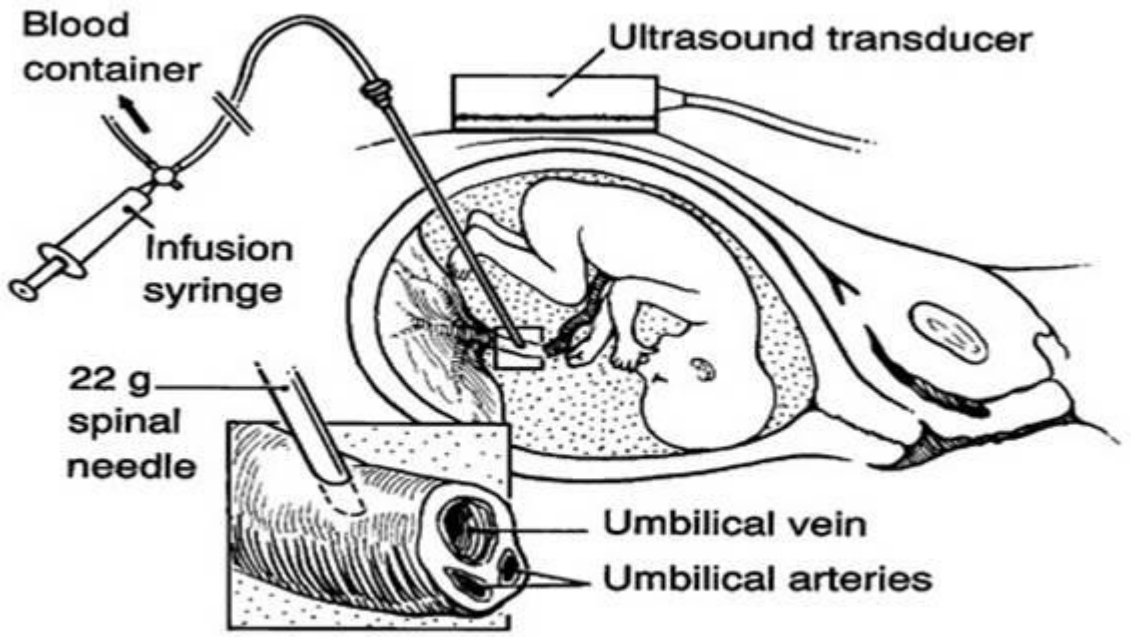
# Treatment of HDN (unconjugated hyperbilirubinemia)

•Intrauterine therapy
•If the infant is hydropic, intubate immediately and begin assisted ventilation with oxygen. If ventilation is difficult, drain pleural and ascitic fluid
•Insert umbilical arterial (UAC) and venous catheters (UVC) immediately measure blood pressures, arterial pH and blood gas tensions, hematocrit (Hct) and blood sugar
•**Exchange transfusions**
•Correct metabolic acidosis
•Correct anemia
•**Use Intravenous Immune Globulin**
•Follow platelet counts; consider platelet transfusion for counts <50,000.
•**Phototherapy**

# **Fetal Blood Transfusion (**Intrauterine Therapy)

This procedure is done when a baby that is still in the womb suffers from severe anemia caused by Rh incompatibility

Usually, between 30-200 ml RBC is transfused during a single procedure (transfusion volume is calculated by the fetal medicine specialist using a formula based on the haematocrits of the donor blood and fetus, the estimated feto-placental blood volume and the target haematocrit).



# **Fetal Blood Transfusion (**Intrauterine Therapy)

High-risk pregnancies are monitored by:

- weekly fetal Doppler ultrasound scans to measure middle cerebral artery peak systolic velocity
- an indication of the severity of fetal anaemia, and regular ultrasound monitoring of fetal growth

Monitoring is indicated if severe anaemia before 24 weeks gestation is suspected, if there has been a previous intrauterine death.

# Phototherapy

This involves exposure of the naked baby to blue, cool white or green light of wave length 450-460 nm The light waves convert the bilirubin to water soluble nontoxic forms which are then easily excreted.

•The advantages of phototherapy are that it is noninvasive, effective, inexpensive and easy to use.

• Eye shades should be fixed, external genitalia may be covered

# Treatment threshold graph for babies with neonatal jaundice

NHS
National Institute for Health and ClinicalExcellence

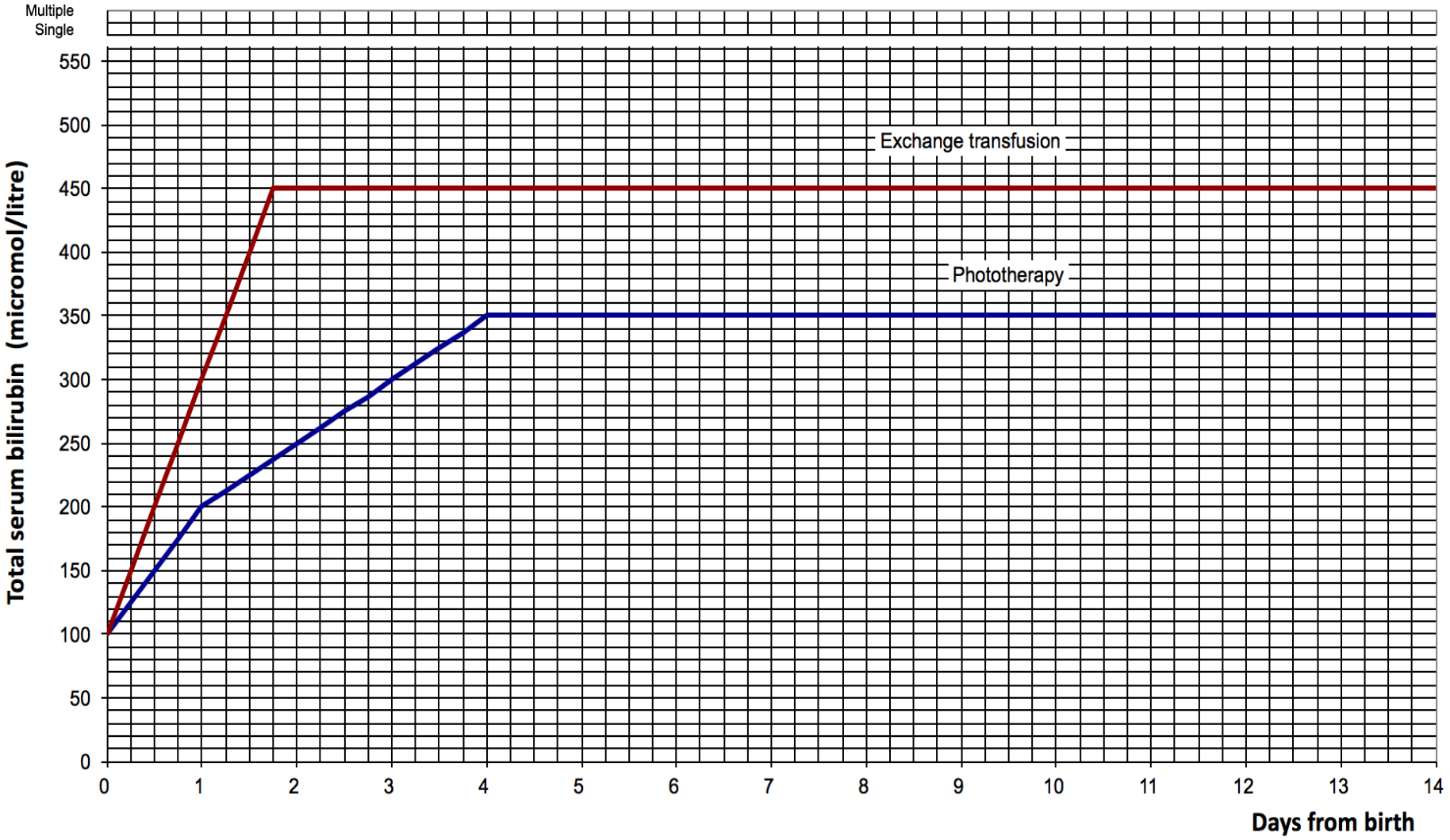
Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____

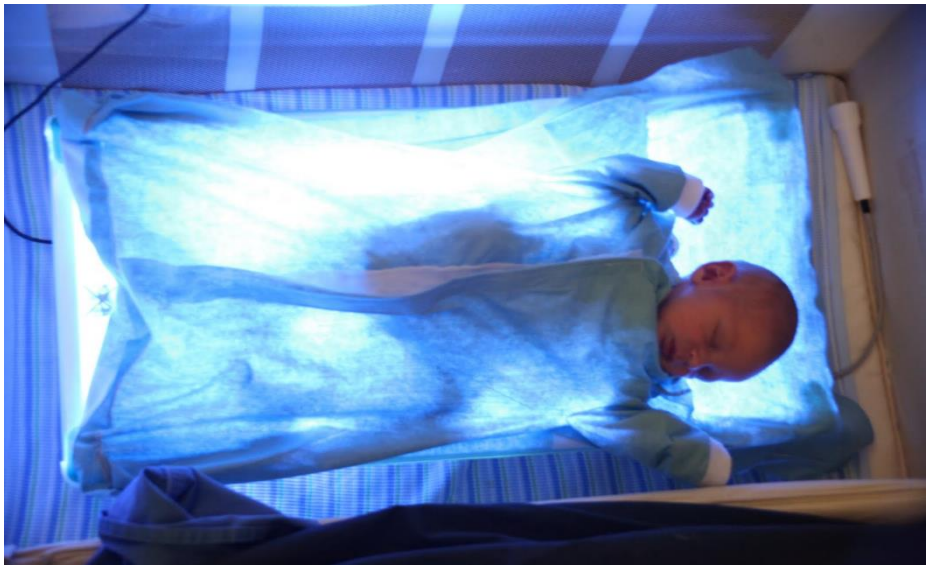
Click below and choose gestation

Shade for phototherapy Baby's blood group _____ Mother's blood group _____

>=38 weeks gestation



# Phototherapy



# Complications of phototherapy

• Babies with congenital erythropoietic porphyria can develop severe blistering and photosensitivity during phototherapy
• Intestinal **hypermotility, diarrhoea**
• Separation of mother and baby causing interference of mother baby interaction
• Changes in the baby's thermal environment lead to increased **peripheral blood flow and water loss**
• Babies with cholestatic jaundice may development **«bronze baby syndrome»** and rarely purpura and bullous eruptions
• Concomitant use of certain drugs or agents may cause **photosensitivity**

# Treatment of HDN (unconjugated hyperbilirubinemia)

## Exchange Transfusions

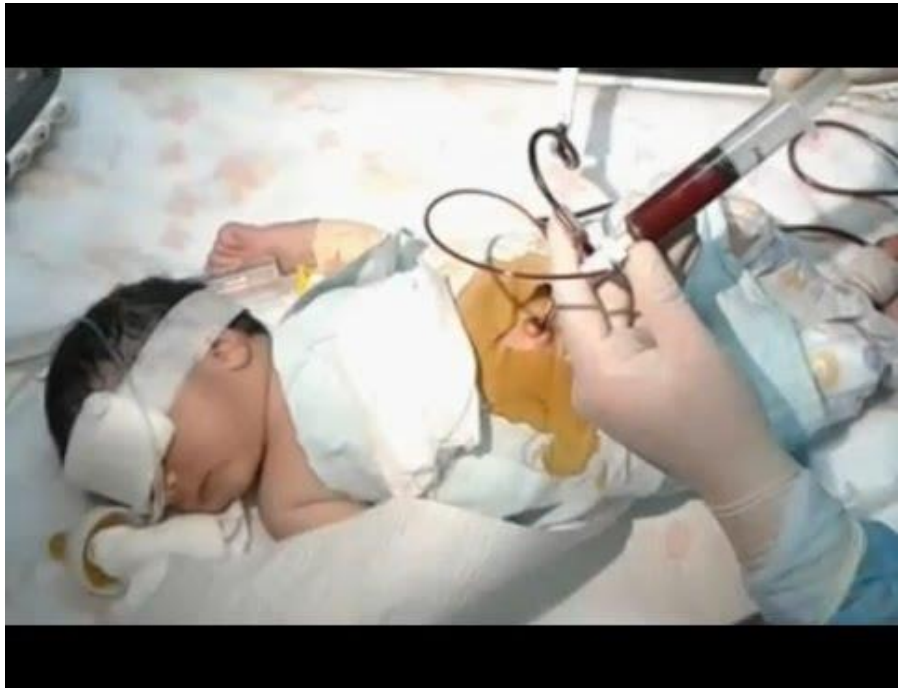
**Objective**:

1.To decrease the level of bilirubin and prevent kernicterus.
2.To remove baby's sensitized red blood cells.
3.To provide compatible red blood cells adequate oxygen carrying capacity.
4.To decrease the level of incompatible antibody in the baby.
5.The exchange transfusion is done if the total bilirubin level is aprroaching 342μmol/l and continues to rise despite the baby undergo the phototherapy.
6.The blood should be reconstituted from fresh, O negative packed RBCs cross-matched against the mother and typespecific fresh frozen plasma.
7. 30 min before the exchange transfusion, give albumin 1g/kg to increase the bilirubin bound to albumin in the circulation and make the exchange transfusion more effective.
8. Exchange 2-3 times the blood volume (85mL/kg)

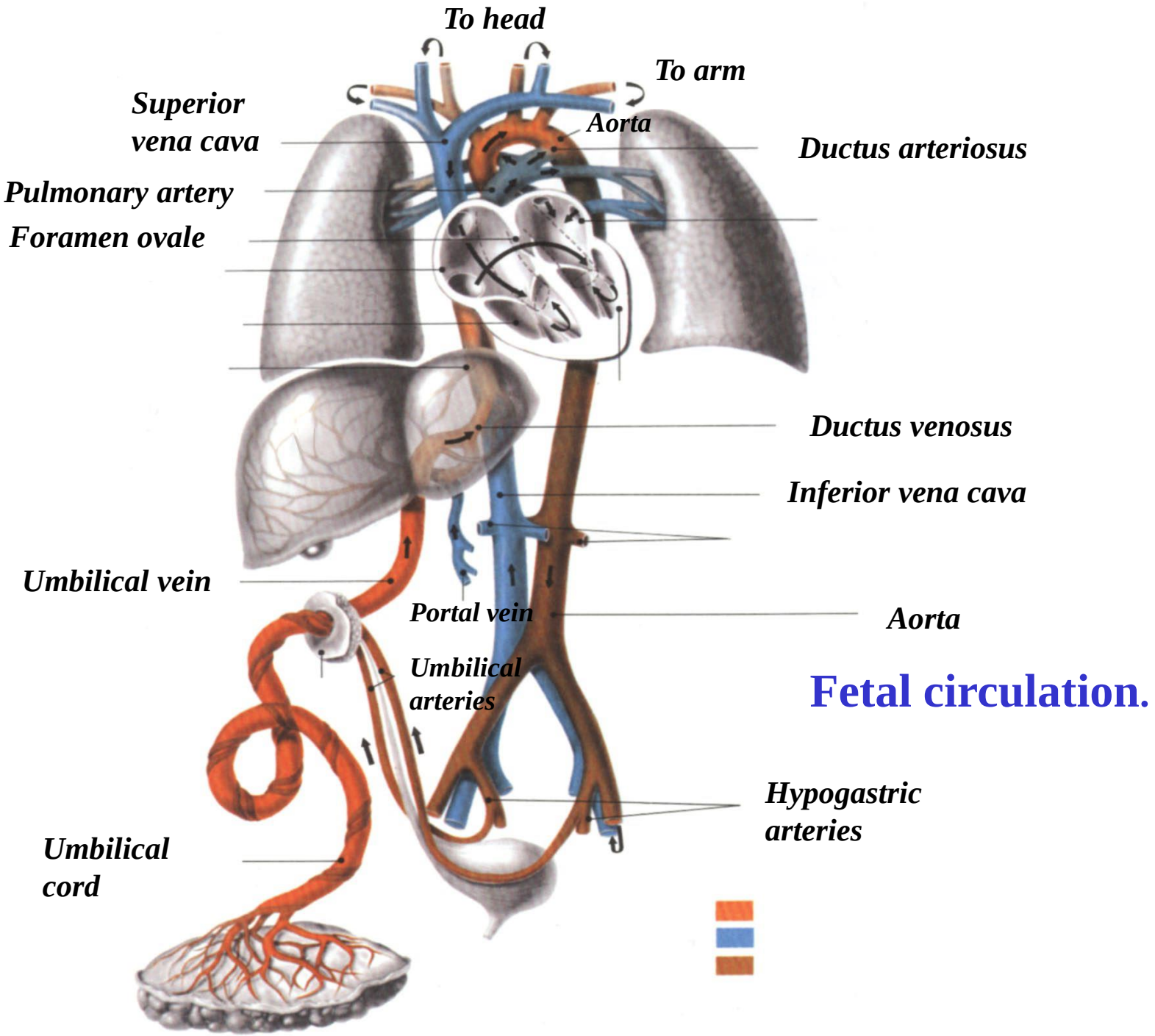
# Treatment of HDN (unconjugated hyperbilirubinemia)

## Exchange Transfusions

- Exchange transfusions are performed using either one catheter or two catheter push-pull method.
- ***Two Catheter Push-pull Technique***: Blood is removed from the artery while infusing fresh blood through a vein at the same rate.



| | In | Out |
|---|---|---|
| | Umbilical vein | Peripheral artery |
| or | Umbilical vein | Umbilical artery |
| or | Peripheral vein | Peripheral artery |
| or | Peripheral vein | Umbilical artery |




# Fetal circulation.

# Treatment of HDN (unconjugated hyperbilirubinemia)

## Intravenous Immune Globulin

- Intravenous immune globulin (IVIG) is made up from plasma isolated.
- This treatment use strengthen body immune system beside to treat immune deficiency.
- Intravenous Immunoglobulins were found to decrease hemolysis leading to reduction in serum bilirubin level.
- The immunoglobulin could act by occupying the FC receptors of reticulo-endothelial cells preventing them from taking up and lysing antibody coated RBCs. This subsequently leads to decrease in the need for exchange transfusion.
- The required dose of immune globulin is 1 g / kg for 1-3 days

# Treatment of HDN (unconjugated hyperbilirubinemia)

**Feeding**

•Increase feeding frequency to 8 - 12 feeds in 24 hours to meet the increased fluid needs due to insensible water

•Check the baby's weight to gauge his/her hydration. Supplementation with expressed breast milk and/or formula is appropriate if weight loss is excessive despite frequent feeds

**Intravenous therapy may be indicated in severe cases**

**Ursodeoxycholic acid**

May improve bile flow and lower bilirubin concentrations

**Phenobarbitone (Phenobarbital)**

May improve bile flow but is not recommended for treatment of hyperbilirubinaemia

# Treatment of conjugated hyperbilirubinemia

**Treat underlying cause:**

•TPN-associated cholestasis:
-Stop TPN or at least reduce (especially lipid) and advance feeds, “TPN-Cholestasis protocol” (remove trace elements certain days), Ursodiol (Actigall), Phenobarbital use controversial
-Biliary atresia with Kasai procedure +/- liver transplant
-Alpha-1-antitrypsin with liver transplant
- Choledochal cyst with surgical removal
- Galactosemia with dietary elimination

•Supportive care if no treatment possible

# Approach to a jaundiced baby

## Ask 4 questions

-What is the birth weight?

-What is the gestation?

-What is the postnatal age in hours?

-Is the jaundice physiological or pathological?

**If jaundice is physiological and baby is well** – only observe
**If deep jaundice** – Assess for bilirubin toxicity (kernicterus)

# References


- **Examination of the Newborn**

  An Evidence-Based Guide edited by Anne Lomax
- **Neonatology**

  **A Practical Approach to Neonatal Diseases**

  Giuseppe Buonocore, Rodolfo Bracci, Michael Weindling
- **Neonatal jaundice: prevention, assessment and management**

  Queensland Maternity and Neonatal Clinical Guidelines Program

# *Thank you*