HAEMOLYTIC DISEASE OF THE NEWBORN

Blood and immunology module

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OBJECTIVES

What is haemolytic disease of the newborn (HDN)?

What are the causes?

How does it happen?

What are the clinical features?

How is haemolytic disease of the newborn diagnosed?

How is it managed? – antenatally, postnatally

Rh incompaitibility vs. ABO incompatibility

HAEMOLYTIC DISEASE OF THE NEWBORN

Condition occurring in newborns where,

- red blood cells breakdown faster than usual resulting in
- anaemia (neonatal and / or fetal)
- hyperbilirubinaemia

CAUSES FOR HAEMOLYTIC DISEASE OF THE NEWBORN (HDN)

- Immune haemolysis
  - Rh isoimmunization (traditional commonest cause; HDN was = Rhesus incompatibility)
  - ABO incompatibility
  - Other minor blood group incompatibilities
- Red blood cell membrane defects
  - Hereditary spherocytosis
- Red blood cell enzyme defects
  - G6PD deficiency
- α Thalassaemia major (very rarely)

HDN DUE TO IMMUNE HAEMOLYSIS

Transplacental passage of maternal IgG alloantibodies to red cell antigens

↓

React with fetal / neonatal specific antigens on red cells

↓

Haemolysis

↓

Fetal / neonatal anaemia and neonatal hyperbilirubinaemia

HOW DOES HDN OCCUR?

HDN can occur due to

- Rhesus or
- ABO incompatibility between mother and baby or
- Other maternal antibodies - anti- Kell, anti Kidd, anti-Duffy

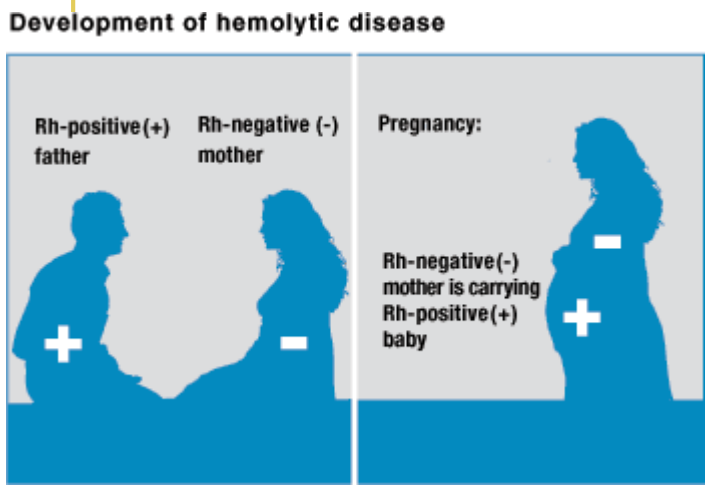
Rhesus incompatibility

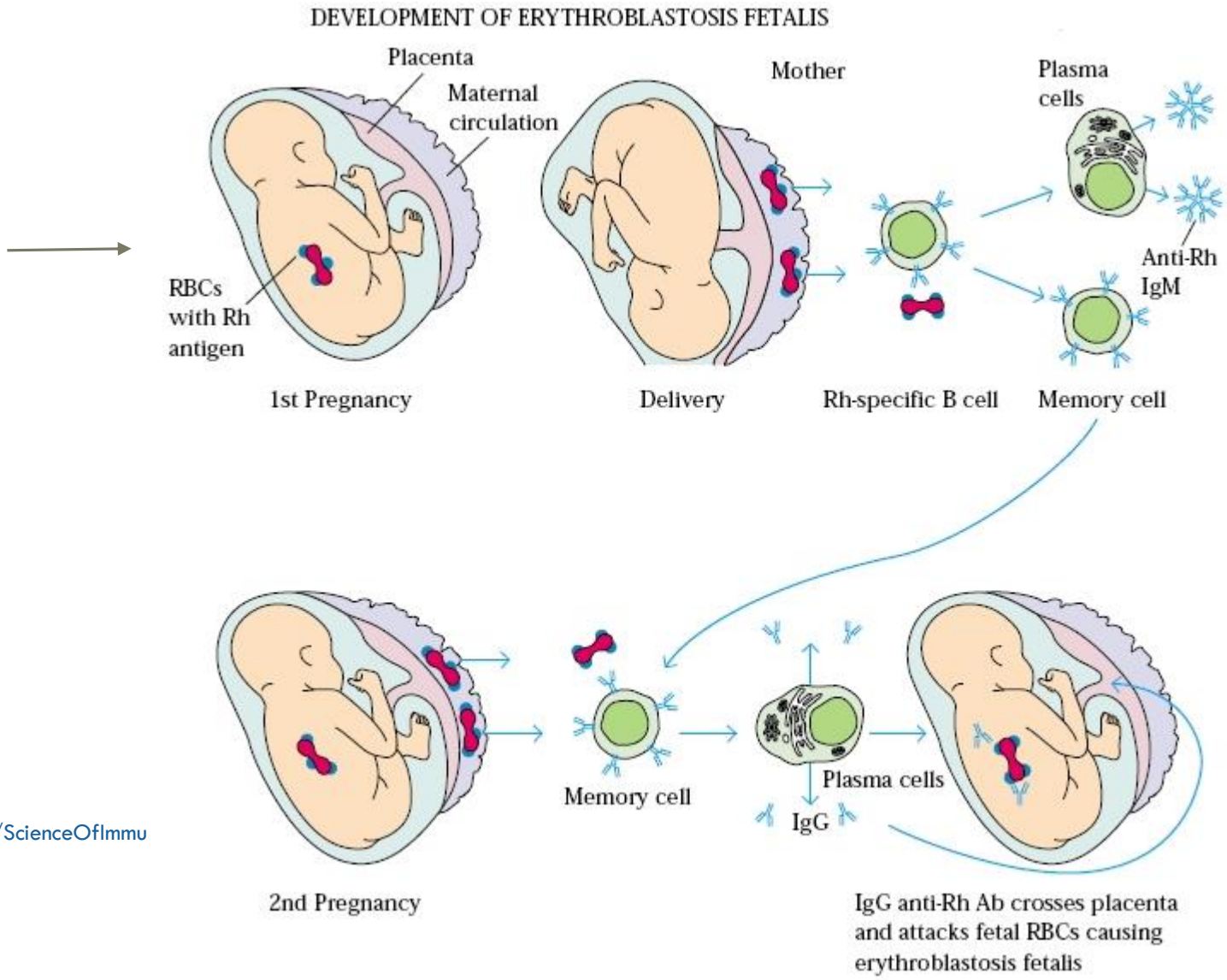
- Mother Rhesus negative and baby rhesus positive
- Mother previously exposed to rhesus positive blood

ABO incompatibility

- Mother blood group O
- Preformed anti-A and anti-B present in maternal blood

HOW DOES RH INCOMPATIBILITY CAUSE HDN?





Courtesy:
http://wenliang.myweb.uga.edu/mystudy/immunology/ScienceOfImmunology/NotesImages/Topic745NotesImage4.jpg

HOW DOES ABO INCOMPATIBILITY CAUSE HDN?

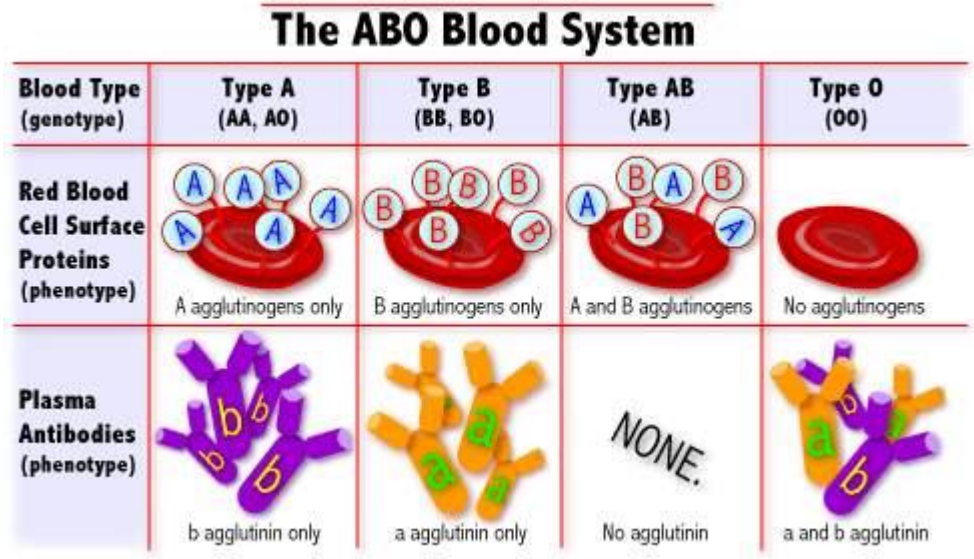
10-15% of pregnancies have ABO incompatibility set-up

Very few newborns however develop HDN

Anti-A and Anti –B usually IgM antibodies

Some produce IgG – can cross placenta to

React with baby's RBC and haemolyse them



CLINICAL FEATURES OF HDN - FETAL

Erythroblastosis fetalis

- Accelerated red cell destruction
- Increased production of RBC
- Increased nucleated RBC, reticulocytes
- Hepatosplenomegaly

Severe anaemia

Hydrops fetalis (generalised oedema)

CLINICAL FEATURES OF HDN – NEONATAL

Hyperbilirubinaemia

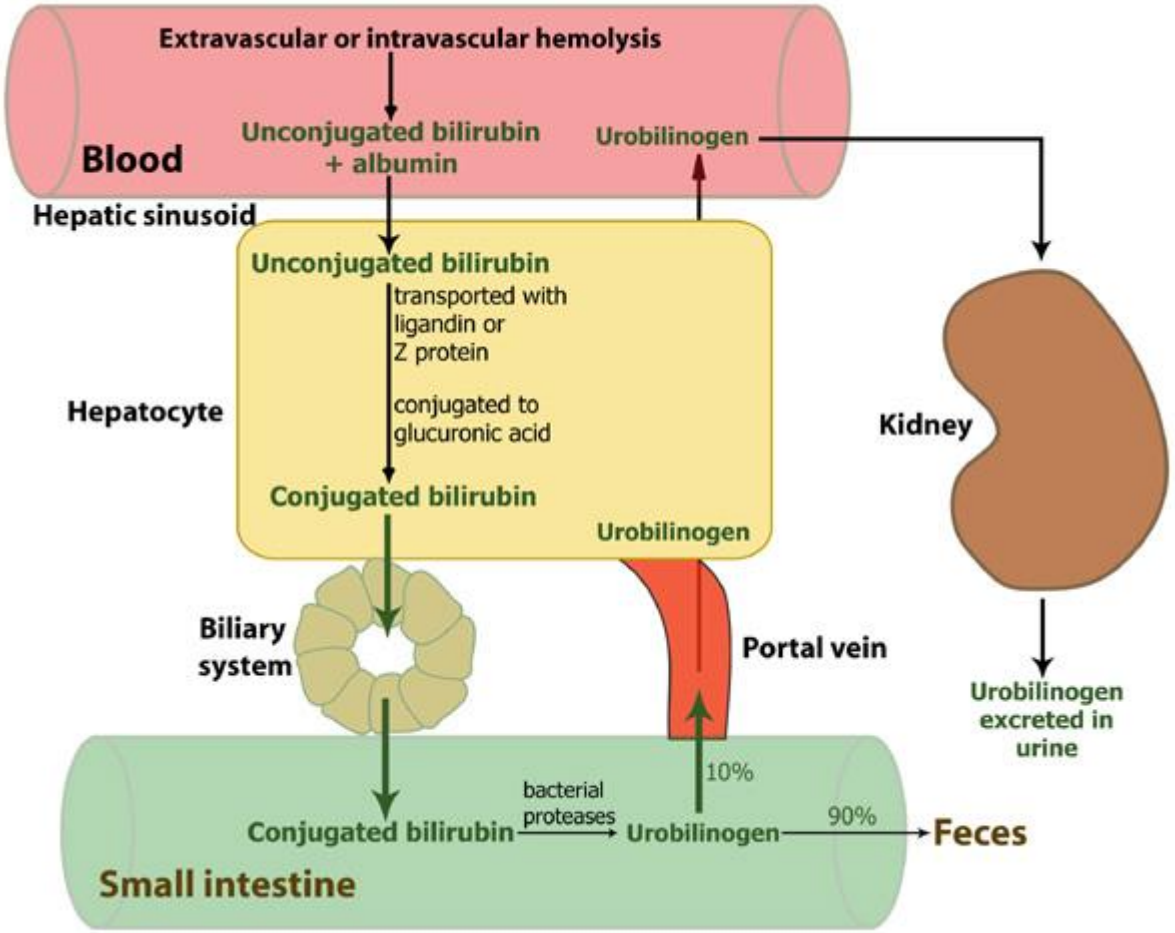
- Due to increased RBC destruction
- In-utero – cleared by conjugation in maternal liver
- Newborn – immature liver unable to cope
- Results in early neonatal jaundice (unconjugated hyperbilirubinaemia)

Bilirubin encephalopathy (Kernicterus)

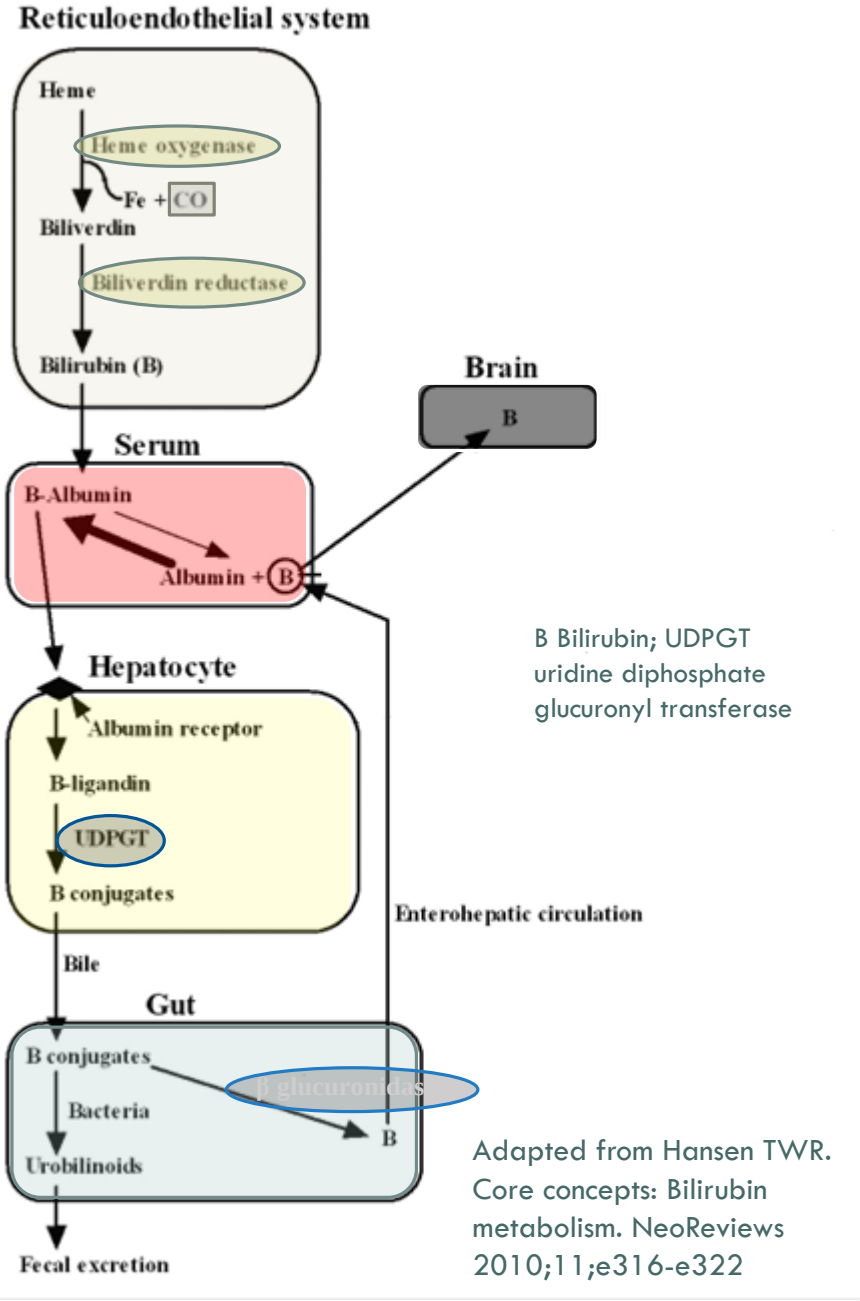
- Maturity of blood brain barrier
- Level of bilirubin
- Duration of hyperbilirubinaemia above a threshold level
- Factors displacing bilirubin from albumin

Anaemia

BILIRUBIN METABOLISM



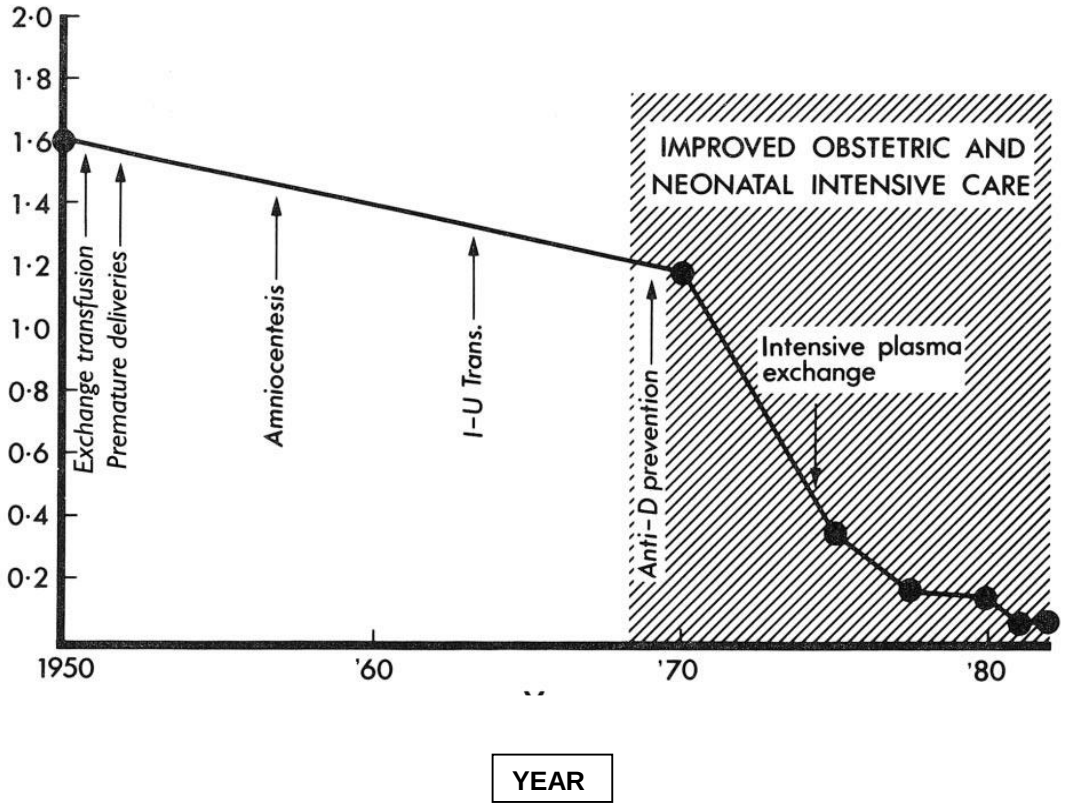
Courtesy
http://nursingcrib.com/wp-content/uploads/bilirubin-metabolism.jpg?9d7bd4



B Bilirubin; UDPGT uridine diphosphate glucuronyl transferase

Adapted from Hansen TWR. Core concepts: Bilirubin metabolism. NeoReviews 2010;11;e316-e322

HISTORY : MANAGEMENT OF Rh ISOIMMUNISATION



Perinatal deaths due to anti-D haemolytic disease of the newborn per 1000 births.
Adapted from Tovey (1984): 100.

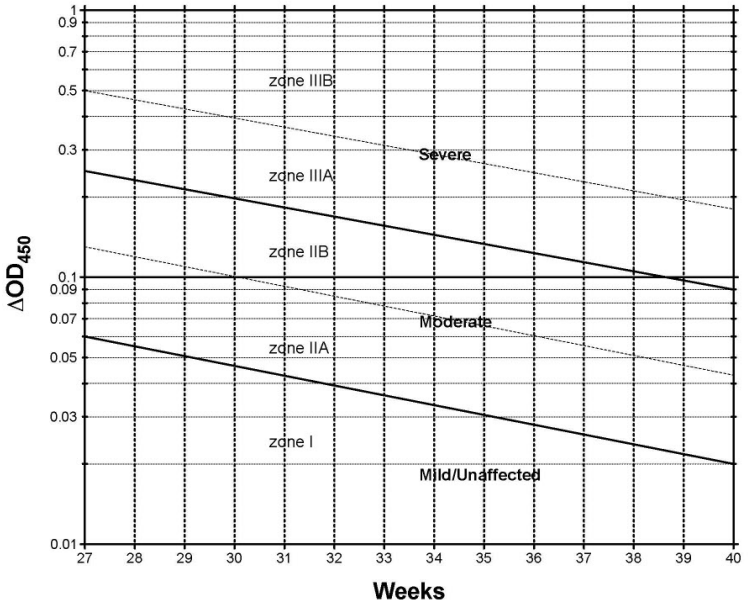
ANTENATAL MANAGEMENT OF Rh ISOIMMUNISATION

Antenatal screening

Blood group and Rh (pregnant females)

History

- which pregnancy? Rhogam given for miscarriages? Any previous transfusions
- known antibody status



Antenatal care

Administration of Anti D IgG (Rhogam) to unsensitised mothers

If sensitised - monitor antibody titres (>4IU/ml), fetal anaemia

- intrauterine transfusions

ANTENATAL MANAGEMENT OF Rh ISOIMMUNISATION

Anti D (Rhogam): prevention of isoimmunisation in Rh negative unsensitised mothers

Usage and dosing depends on unit policy, availability / cost

Ideally at 28 and 34 weeks of gestation

After delivery within 72 hours if baby is Rh positive

Intramuscular to deltoid

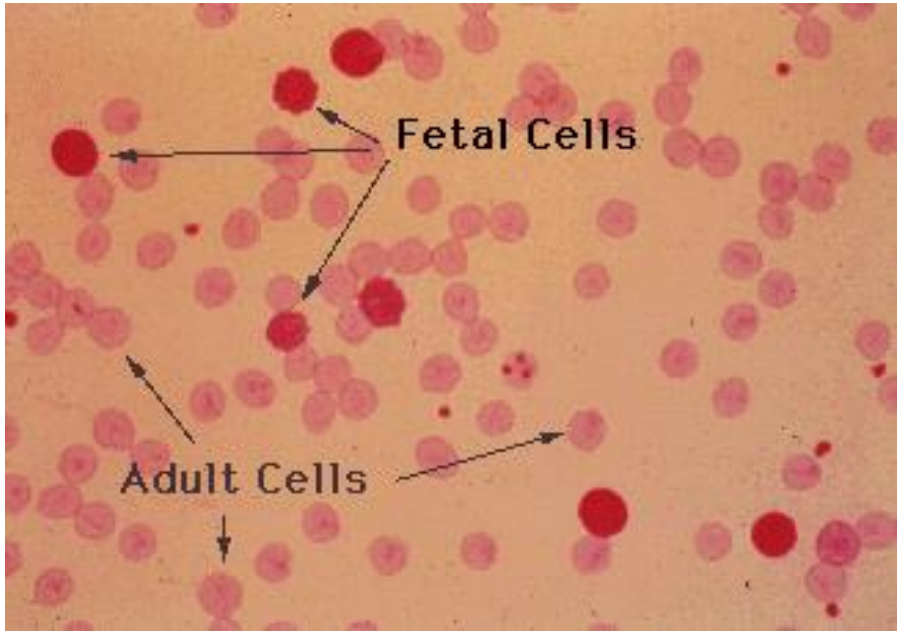
Kleihauer test – identify volume of fetomaternal haemorrhage (for additional Anti D)

After potential sensitising events: miscarriages, external cephalic version of babies in breech presentation, intrauterine death, chorionic villus sampling etc

MANAGEMENT OF Rh ISOIMMUNISATION

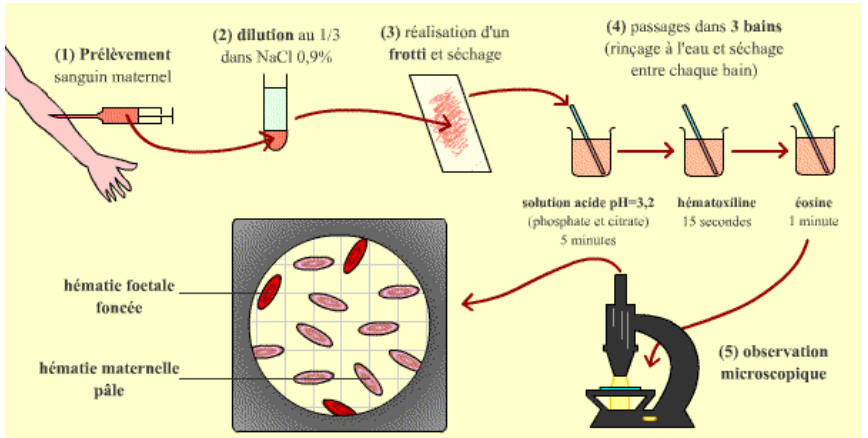
Kleihauer test

- Post-partum maternal blood sample (EDTA)



Kleihauer- Betke test

- The adult hemoglobin is more readily acid eluted through the cell membrane than fetal hemoglobin.
- Maternal blood is fixed on a slide with ethanol 80%, treated with citrate phosphate buffer.
- After staining with hematoxylin and eosin the fetal cells will be stained while the adult cells appear like ghost cells.
- No. of fetal cells/ No. of adult cells is equal to fetal blood volume/ maternal blood volume.



MANAGEMENT OF HAEMOLYTIC DISEASE OF THE NEWBORN

INVESTIGATIONS

Baby

- Blood group, Rh, Direct Coomb's test
- Full Blood Count (FBC) with RBC indices and reticulocyte count (NRBC)
- Blood picture
- Serum bilirubin

Mother

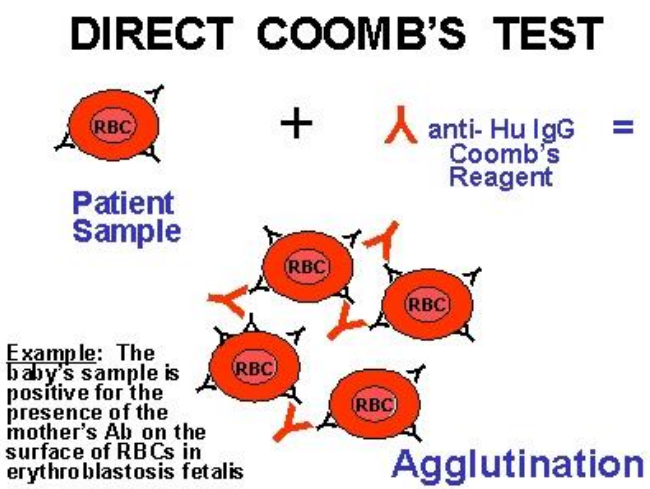
- Antibody screen
- Antihaemolysin titres A or B

Cord blood (when mother Rh negative)

- Blood group , Rh and Direct Coomb's test
- (FBC, SBR)

MANAGEMENT OF HAEMOLYTIC DISEASE OF THE NEWBORN

INVESTIGATIONS



Courtesy:
1. http://newborns.stanford.edu/images/directcoombs.jpg
2. http://www.med-ed.virginia.edu/courses/path/innes/images/rcdjpegs/rcd%20dat%20b.jpeg

MANAGEMENT OF HAEMOLYTIC DISEASE OF THE NEWBORN

SPECIFIC

- Phototherapy
- Exchange transfusion
- IV immunoglobulin

GENERAL

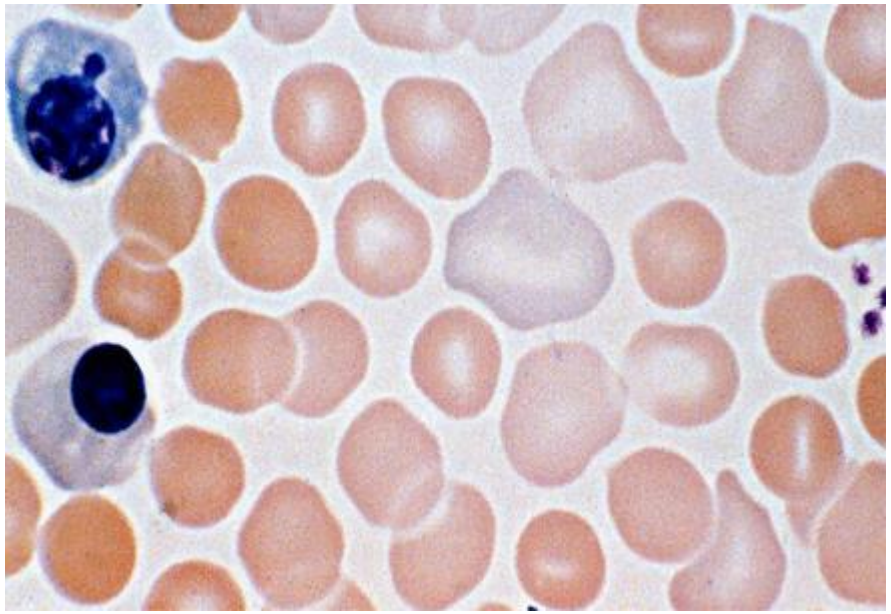
- Hydration, blood pressure
- Investigate and treat for sepsis (if clinically indicated)

FOLLOW-UP

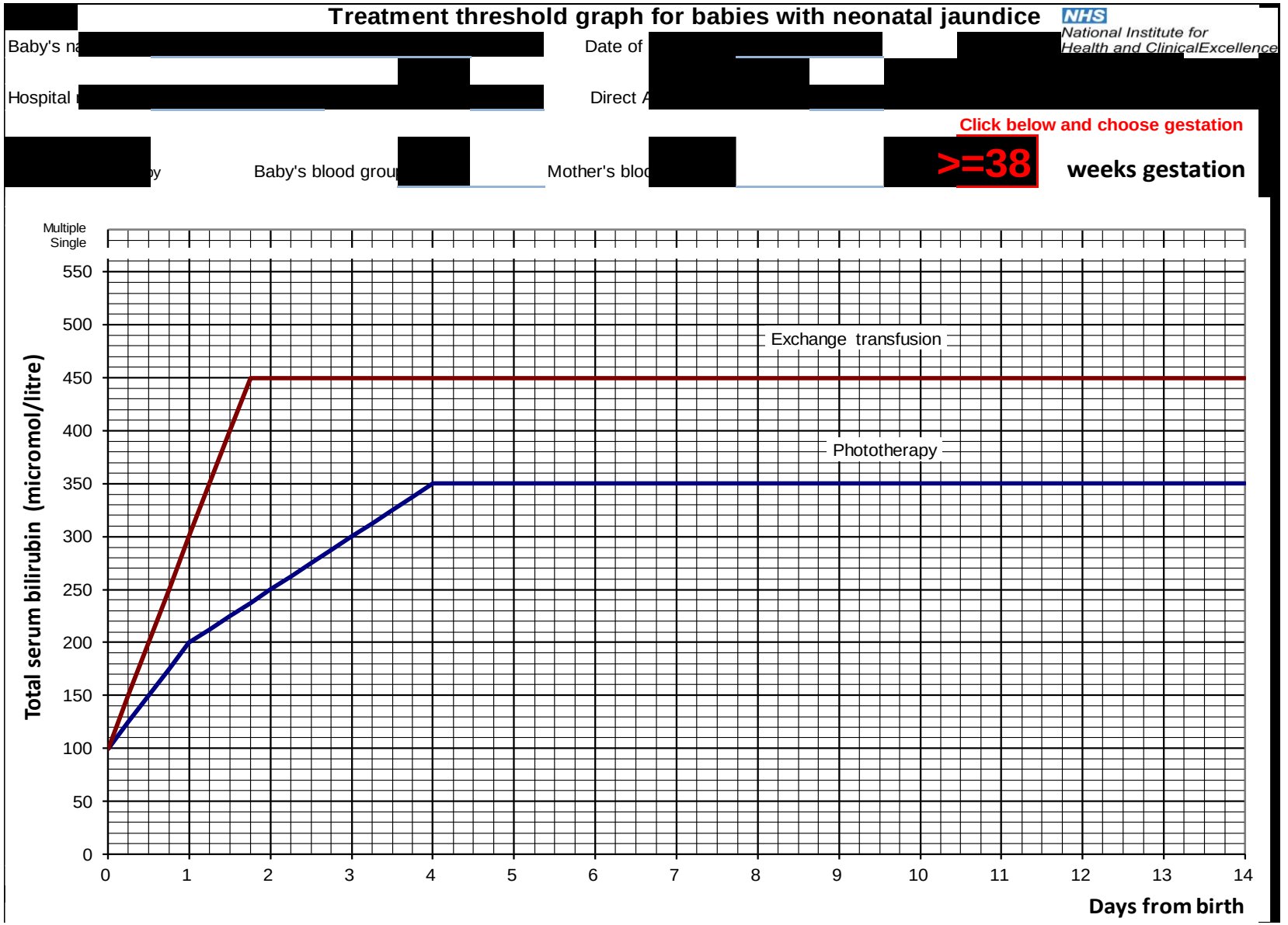
- Anaemia (upto 2-3 months)
- Folic acid

HEREDITARY SPHEROCYTOSIS

- Due to defects in erythrocyte membrane proteins: ankyrin-1, band 3, spectrin
- Commonest reason for DAT negative anaemia requiring blood transfusion in neonates
- Hyperbilirubinaemia : neonatal presentation
- Diagnosis
  - Family history (AD), blood picture and red cell indices (MCHC and MCV)
  - Osmotic fragility – unreliable in neonates
  - Eosin-5-maleimide (EMA) binding – a flow cytometry test



NICE (UK) GUIDELINE THRESHOLD CHARTS



http://guidance.nice.org.uk/CG98/treatmentthresholdgraph/xls/English

PHOTOTHERAPY

How does it work?

- Converts serum bilirubin to lumirubin
- Lumirubin water soluble

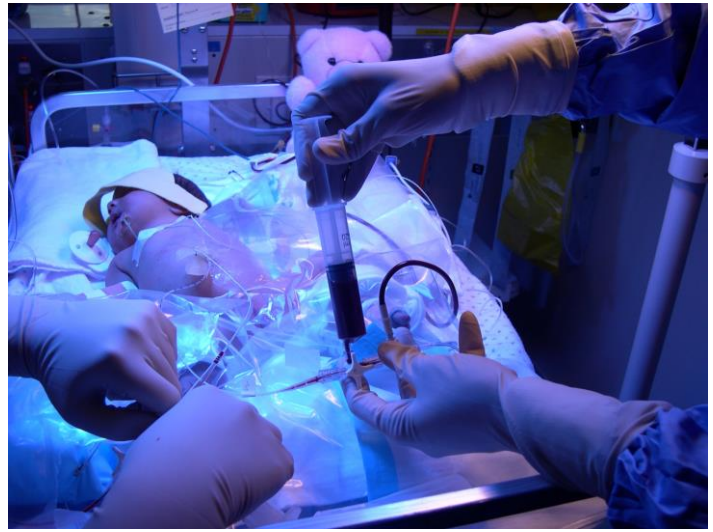
Features

- Spectral output of light source (blue 430-490nm)
- Correct distance between light source and baby to be maintained
- Adequate skin exposure required
- Biliblankets available

EXCHANGE TRANSFUSION

Mechanism of action

- Removes maternal antibodies & antibody coated red blood cells from circulation
- Corrects anaemia
- Removes unconjugated bilirubin from circulation



Volume

- Total volume : 2 x 80ml/kg [blood volume 80ml/kg]

Complications (Reported mortality 1-5%)

- Thromobosis / embolism / acute necrotising enterocolitis
- Thrombocytopaenia
- Infection
- Metabolic disturbances – Ca, Mg, hypoglycaemia, acidosis; leading to arrhythmias

Rh incompatibility vs. ABO incompatibility

	Rh incompatibility	ABO incompatibility
Mother	Rh Negative	Group O
Infant	Rh Positive	Group A or B (AB)
Occurrence in first born	5%	40-50%
Stillbirth and or hydrops	Frequent	Rare
Severe Anaemia	Frequent	Rare
Direct Coomb's Test (DAT/DCT)	Positive	Positive or Negative
Spherocytes	None	Present
Exchange Transfusion	Frequent	Infrequent
Phototherapy	Adjunct to exchange	Often only treatment

ANY QUESTIONS?

SUMMARY

HDN is the immune destruction of fetal/neonatal RBC due to maternal antibodies

Rh and ABO incompatibility are the 2 common types

Rh isoimmunisation is preventable

Consequences of HDN can be devastating

Management of HDN: intrauterine transfusions, phototherapy, exchange transfusions, IV immunoglobulin