Haemolytic disease of the newborn

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PaNDR

Paediatric & Neonatal Decision
Support & Retrieval Service

Contents

- History
- Pathophysiology
- Diagnosis
- Management

History of HDN

- HDN used to be a major cause of fetal loss and death among newborn babies

- 1609 French midwife – twins.
  - One baby being swollen and died soon after birth, the other baby developed jaundice and died several days later.

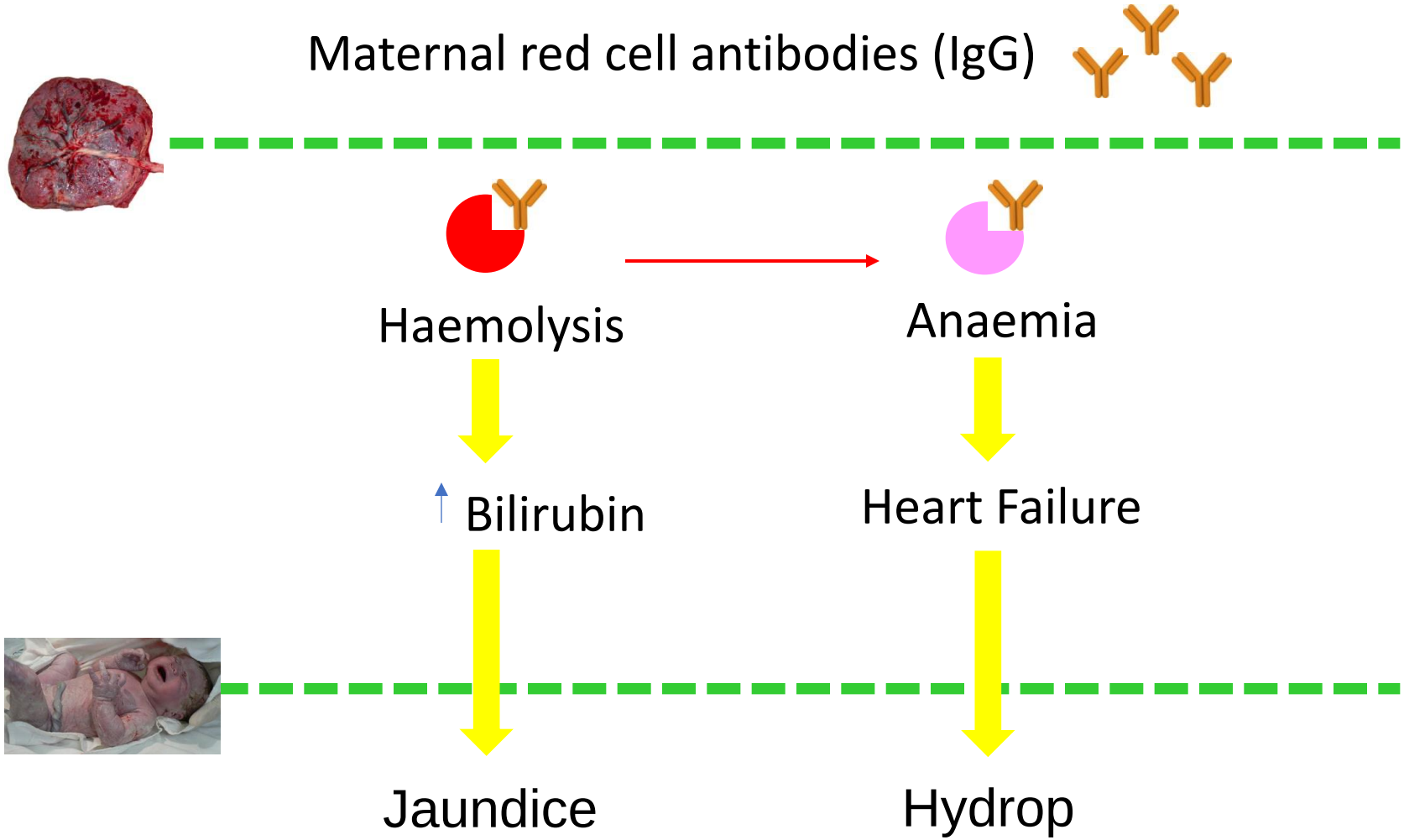
- 1950 the underlying cause was defined
  - Newborn's red blood cells (RBCs) are being attacked by antibodies from the mother.

- 1960s, trials in the US and the UK
  - Showed that giving therapeutic antibodies to women during their pregnancy largely prevented HDN from developing

- 1970s, routine antenatal care included screening of all expectant mothers to find those whose pregnancy may be at risk of HDN and giving preventative treatment.

- Currently, dramatic decrease in the incidence of HDN, particularly severe cases that were responsible for stillbirth and neonatal death.

Pathophysiology of HDN

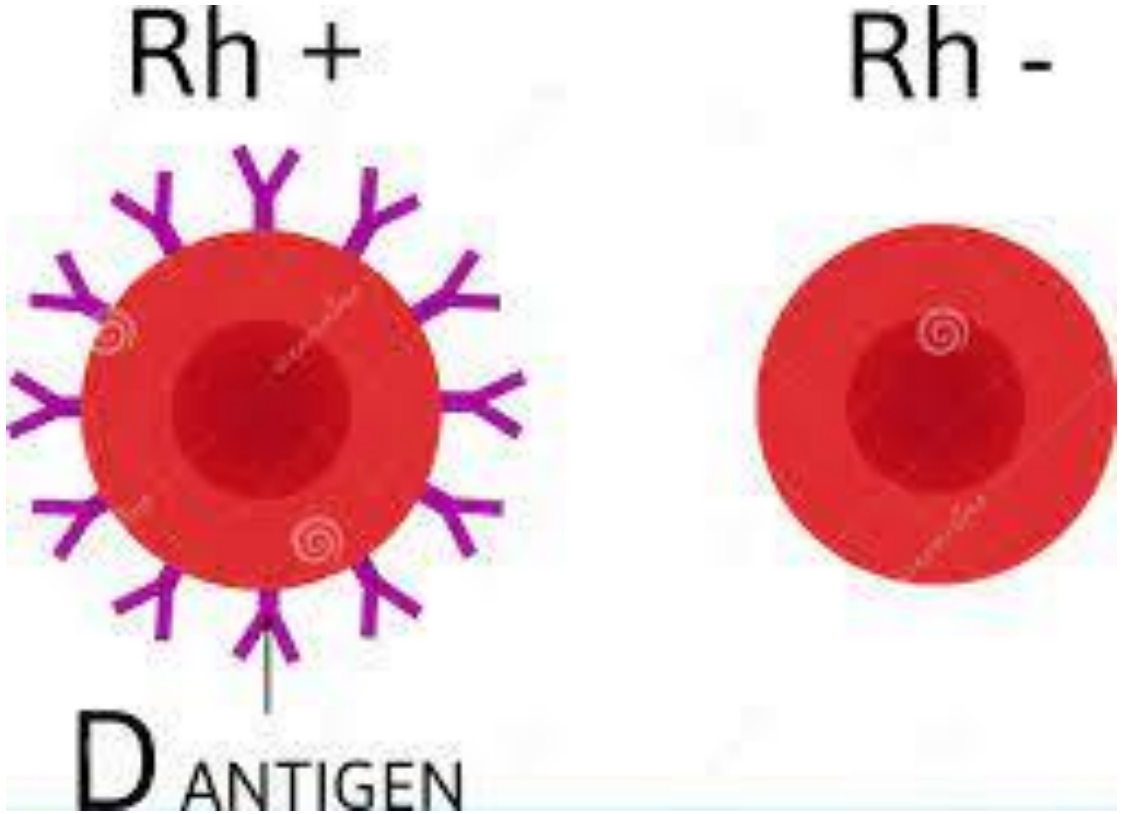


Causes of HDN – Rhesus incompatibility

- Incompatibility of the Rh blood group between the mother and fetus.
- D antigen on rbc surface
- Other Rh antigens as c, C, E, and e

Rh D-negative mother and an Rh D-positive child

- Mother is exposed to babies blood and produces **anti-D antibodies (**sensitization)
- Antibodies cross the placenta > haemolysis of foetal rbc
- HDN worsens in subsequent pregnancies
- Anti-D antibody injection after sensitization event

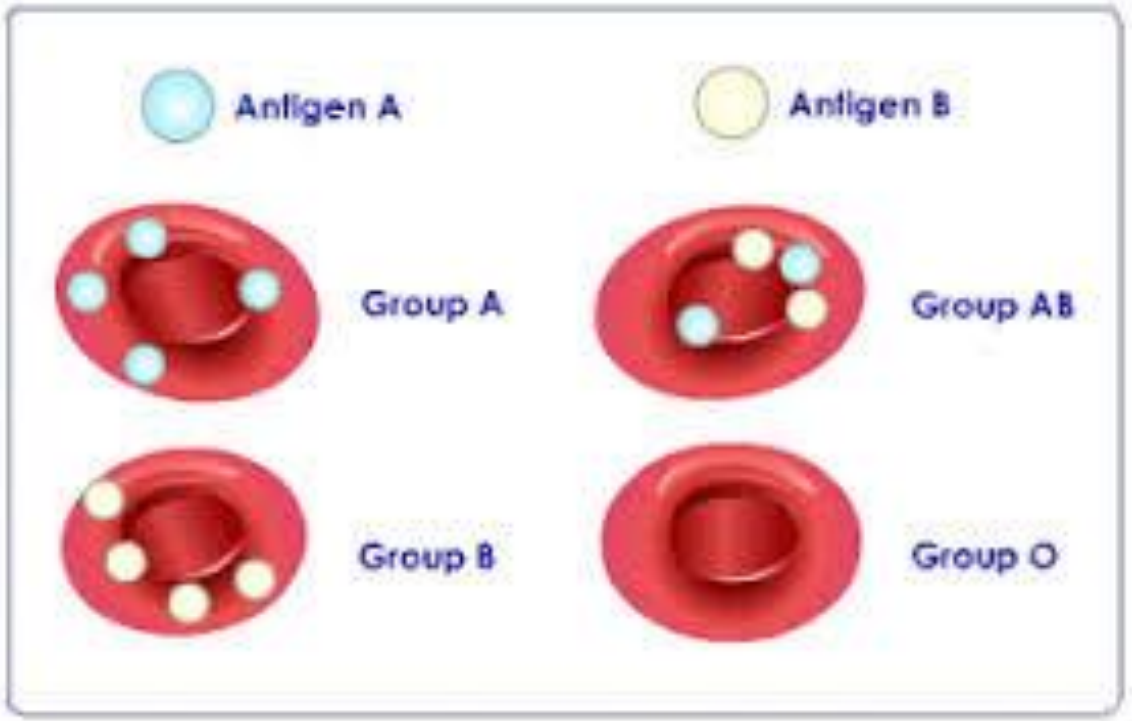


Causes of HDN – ABO incompatibility

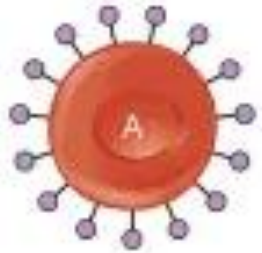
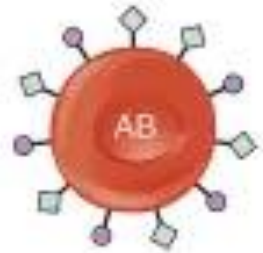
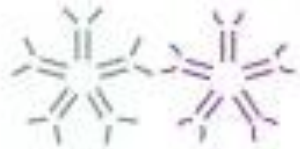
- **Mother O type blood**, foetus AB, A or B type (A most common)
- O type serum contains naturally occurring

  anti-A and anti-B antibodies

- HDN due to ABO incompatibility is usually less severe than Rh incompatibility.
  - foetal RBCs express less of the ABO blood group antigens compared with adult levels.
  - The ABO blood group antigens are expressed by a variety of fetal tissues, reducing chance of anti-A and anti-B binding their target antigens on the fetal RBCs.



Blood Type

	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red blood Cell	 A antigen	 B antigen	 A and B antigens	None
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

Diagnosis of HDN

- **Antenatal** - Positive maternal antenatal antibody screening and/or anaemic/hydropic foetus

- **Postnatal** - Rapidly developing or significant hyperbilirubinaemia not predicted by maternal antenatal antibody screening

- **Laboratory findings**- Positive direct anti-globulin test (DAT), Haemolysis on blood film

Antenatal-maternal antibody screening

Rh antigens: anti-D (1 in 1,200), anti-c, anti-E

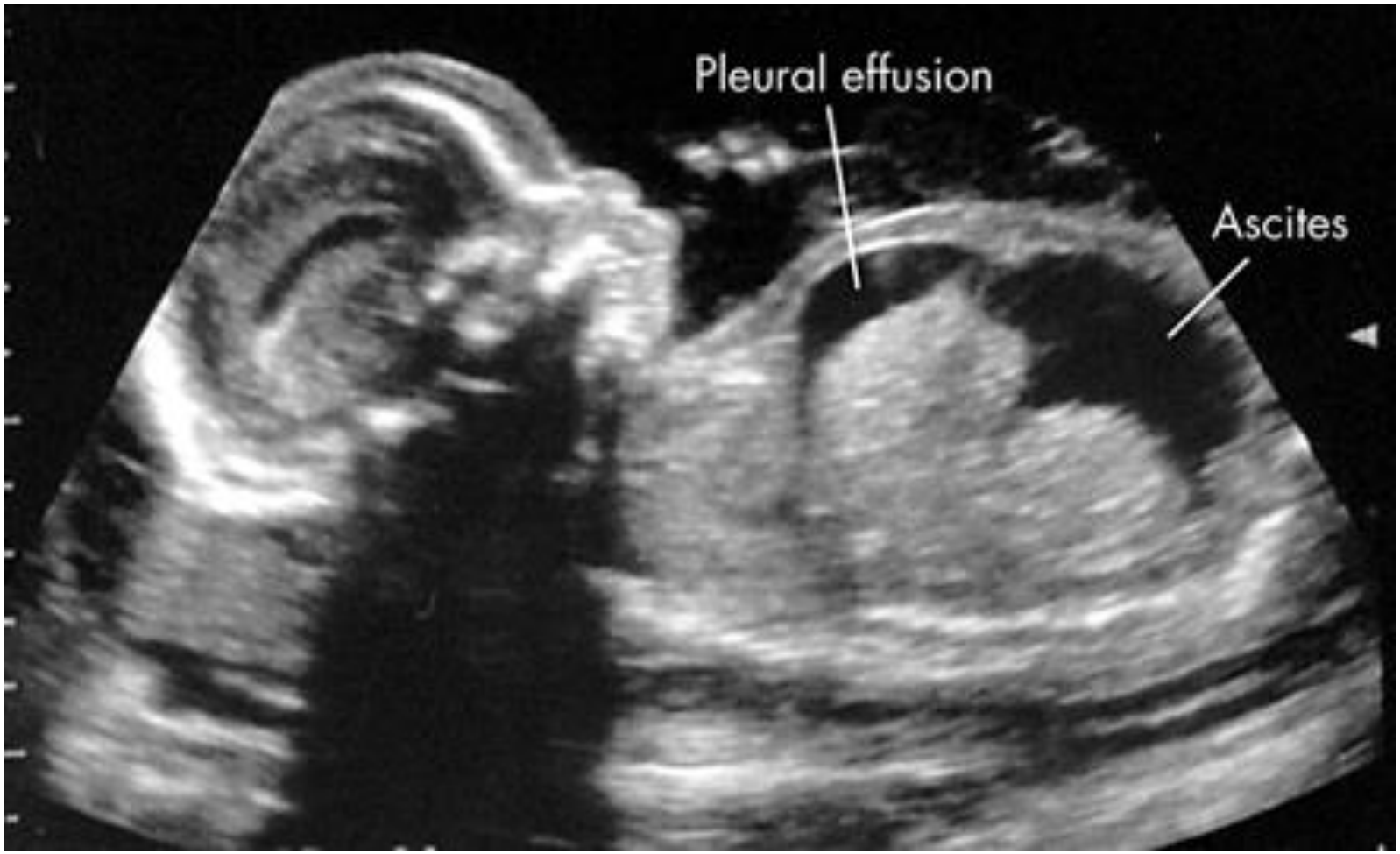
anti-Kell

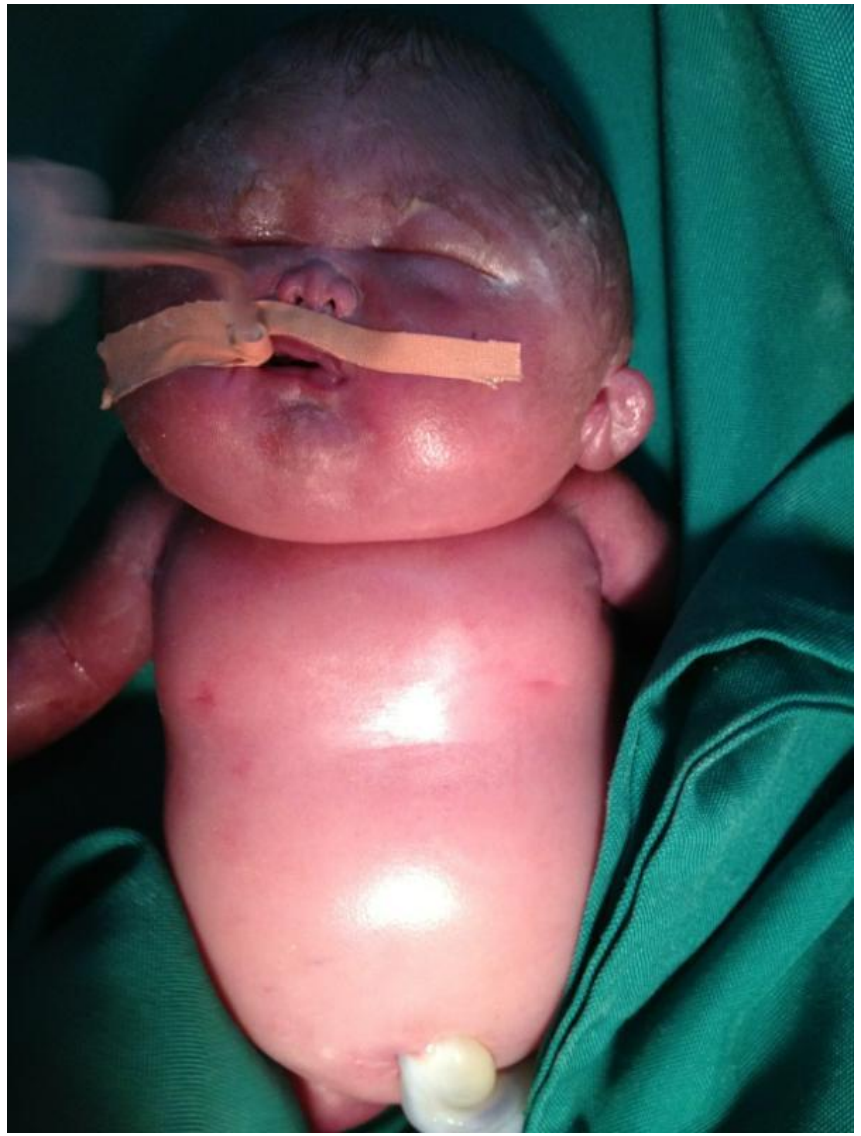
anti-Kidd (Jk)

anti-Duffy (Fy)

anti-MNS antigens

Antenatal scan - Hydrops





Postnatal - Jaundice in first 24 hrs

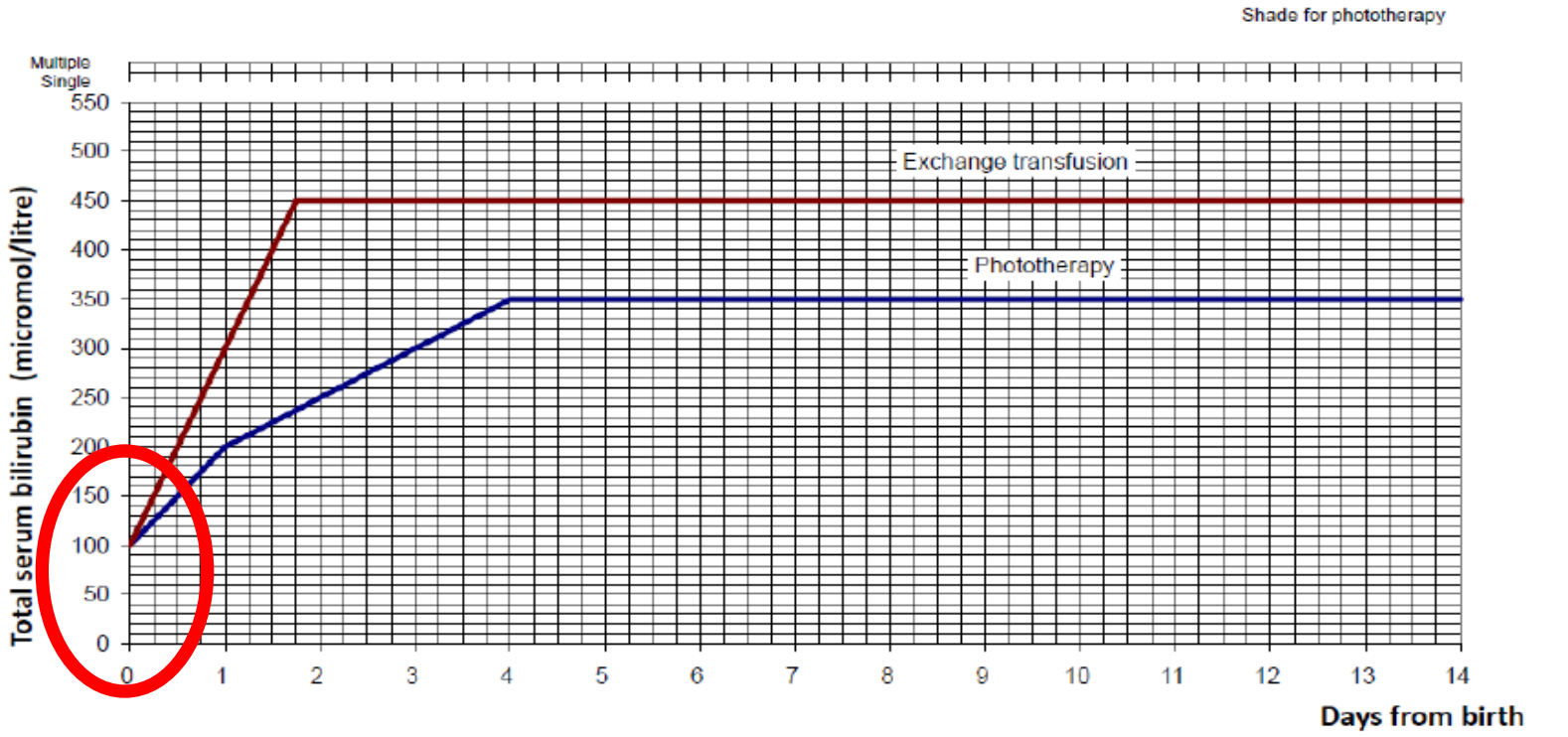
- Jaundice – physiological / pathological
- Jaundice is always pathological if develops in first 24 hrs of life
- THINK SEPSIS
- LOOK FOR EVIDENCE HAEMOLYSIS

When is it significant jaundice at 38+ weeks?

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ >=38 **weeks gestation**



Baby's blood group _____ Mother's blood group _____

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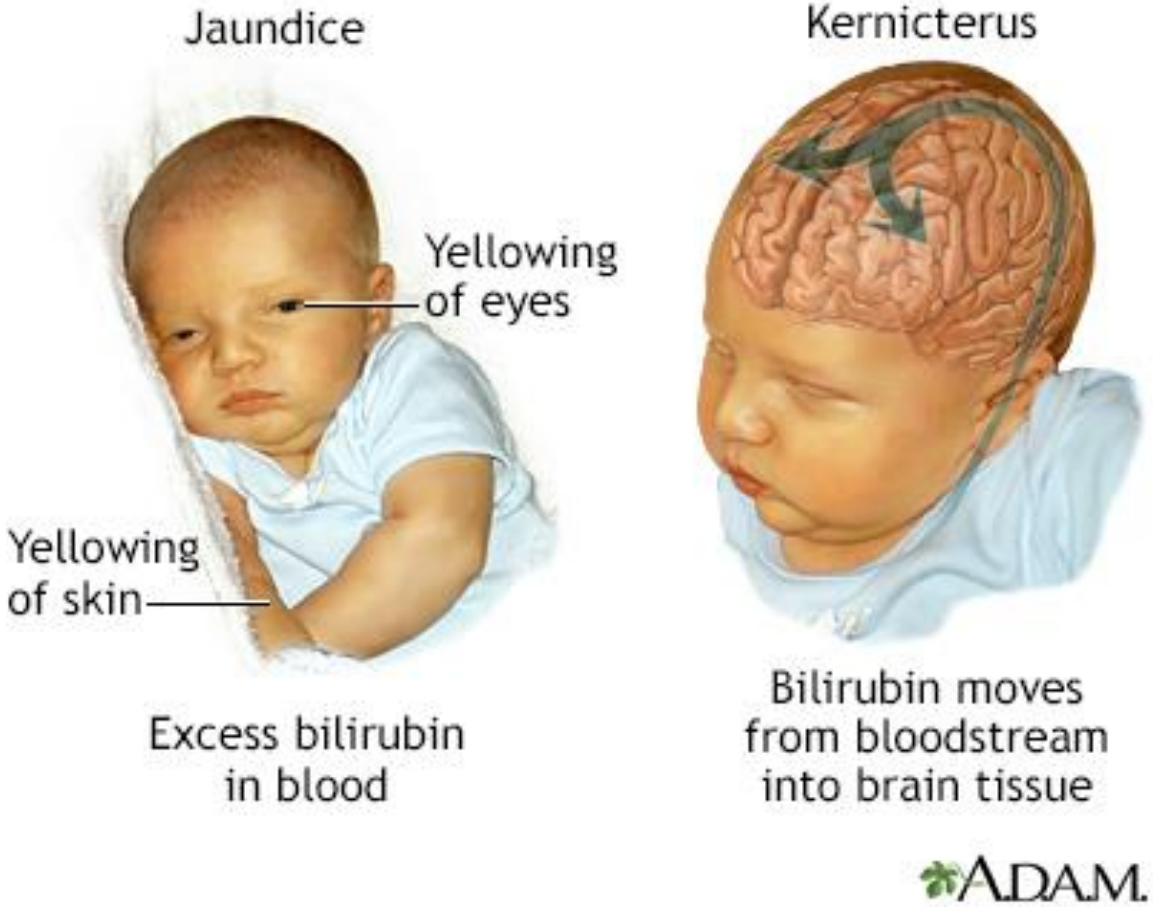
Why are we worried about jaundice

- Unconjugated Bilirubin (water insoluable)
- Crosses blood brain barrier
- Toxic to brain at high levels
- Bilirubin encephalopathy (Kinicterus)

- Kernicterus is now very rare in

the UK, affecting less than 1 in every 100,000 babies.

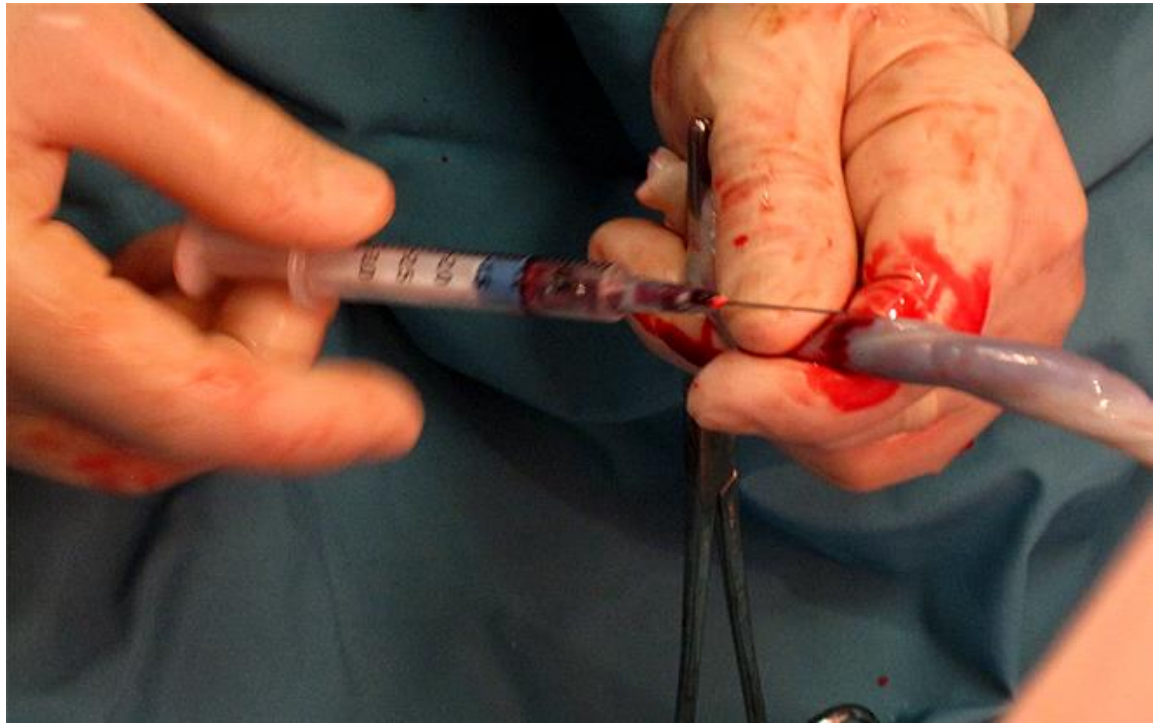


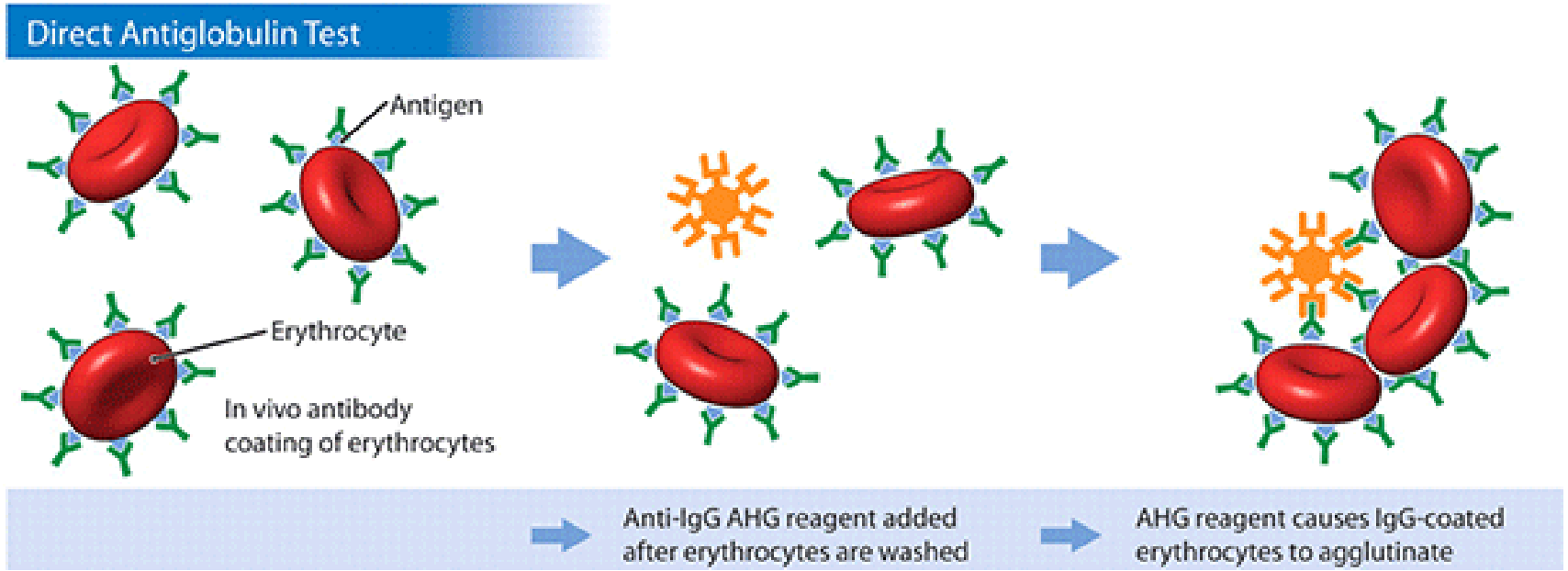
Postnatal - Laboratory tests

Cord gas – known high risk pregnancies (Rh –ve mother)

Or Infants blood

- Hb
- Blood film (spherocytes ABO incompatibility)
- Bilirubin
- Direct coombs test (DCT) / Direct antibody test (DAT)




Direct Antiglobulin Test
Antigen
Erythrocyte
In vivo antibody
coating of erythrocytes
Anti-IgG AHG reagent added
after erythrocytes are washed
AHG reagent causes IgG-coated
erythrocytes to agglutinate

DAT - **weakly 1+** to **strongly positive 4+** (degree of haemolysis)

- 23% of DAT 1+ required phototherapy
- 100% of DAT **4+** required phototherapy
- 15% DAT 1+ from prophylactic anti-D
- 94% DAT 1+ in ABO-incompatible mother/baby

Other causes of haemolytic disease

- Red blood cell membrane defect
- Red blood cell enzyme defect
- Haemoglobinopathy: α-thalassaemia major

Treatments

- Phototherapy
- Exchange Transfusion
- IV immunoglobulin

Phototherapy

Native bilirubin (water **Insoluble**)

450-460nm of light

`Photo isomers of bilirubin (water **Soluble**)

Urine

Exchange transfusion

- Removing the infant's blood in small aliquots and it replacing with donor blood

- Physically removing bilirubin & antibodies

Risks:
Cardiovascular and respiratory instability
Electrolyte imbalance
NEC
Mortality

IV immunoglobulin
Attached to antigen on babies rbc to prevent the maternal antibodies attaching and causing the rbc to break down

Summary HDN

- History
- Pathophysiology – Rhesus / ABO incompatibility
- ABO more common and less severe
- Maternal IgG antibodies crossing placenta and causing breakdown of infants rbc
- Diagnosis – antenatal, postnatal, laboratory
- Jaundice in first 24 hrs pathological
- Treatments – phototherapy, exchange transfusion, IVIg

Any Questions