Haemolytic disease of the newborn

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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

Maternal red cell antibodies (IgG)

Haemolysis

↑ Bilirubin

Jaundice

Anaemia

Heart Failure

Hydrop
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.
<table>
<thead>
<tr>
<th>Blood Type</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>O</th>
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<tbody>
<tr>
<td><strong>Red Blood Cell Type</strong></td>
<td><img src="image" alt="A antigen" /></td>
<td><img src="image" alt="B antigen" /></td>
<td><img src="image" alt="A and B antigens" /></td>
<td><img src="image" alt="None" /></td>
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<tr>
<td><strong>Antibodies in Plasma</strong></td>
<td>Anti-B</td>
<td>Anti-A</td>
<td>None</td>
<td>Anti-A and Anti-B</td>
</tr>
<tr>
<td><strong>Antigens in Red Blood Cell</strong></td>
<td>A antigen</td>
<td>B antigen</td>
<td>A and B antigens</td>
<td>None</td>
</tr>
<tr>
<td><strong>Blood Types Compatible in an Emergency</strong></td>
<td>A, O</td>
<td>B, O</td>
<td>A, B, AB, O (AB⁺ is the universal recipient)</td>
<td>O (O is the universal donor)</td>
</tr>
</tbody>
</table>
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?
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+ / strongly positive 4+ (degree of haemolysis)

• 23% of DAT+ required phototherapy

• 100% of DAT 4+ required phototherapy

• 15% DAT+ from prophylactic anti-D

• 94% DAT+ 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 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, IV IG
Any Questions