Haemolytic disease of the newborn

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Haemolytic disease of the newborn...

...used to be synonymous with Rhesus D allo-immunisation

<table>
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<tr>
<th>Rh - ve</th>
<th>Rh + ve</th>
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<tbody>
<tr>
<td>Mother</td>
<td>Fetus (Second exposure)</td>
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Mother's immune system rapidly recognizes the new antigen and produces large number of IgG antibodies.

Rh antibody attaches to fetal RBCs and marks them for destruction.

IgG antibodies can cross the placenta. Fetal red cells are susceptible to destruction.
Haemolytic disease of the newborn...

...used to and still can be an emergency

Fetal haemolysis

Neonatal haemolysis

Neonatal hyperbilirubinaemia

Neonatal anaemia
Pathophysiology

Incompatible blood transfusion or feto-maternal ‘haemorrhage’

Maternal red cell antibodies: IgG

Haemolysis $\rightarrow$ Anaemia with erythroblastosis

$\uparrow$Bilirubin

Liver & heart failure $\rightarrow$ Hyrdrops

Jaundice $\rightarrow$ Kernicterus

Intra-uterine blood transfusions

Postnatal management
In contemporary neonatal clinical practice...
When you say...

Haemolytic Disease of the Newborn
...we think *** High-risk Neonates ***
Consider haemolytic disease if ≥1 of...

- Positive maternal antenatal antibody screening and/or anaemic/hydropic fetus
- Rapidly developing or significant hyperbilirubinaemia not predicted by maternal antenatal antibody screening
- Prolonged postnatal hyperbilirubinaemia
- Haemolysis on postnatal blood film
- Positive postnatal direct anti-globulin test (DAT)
How common is “significant” jaundice?

Jaundice is always significant
How common is jaundice?

• 6 in 10 babies develop jaundice

• 8 in 10 premature babies develop jaundice

• 1 in 20 babies need treatment

• <1 in 100,000 develop kernicterus (England 2013-14)
When is it significant jaundice?

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

37 weeks gestation

Shade for phototherapy

Exchange transfusion

Phototherapy

Total serum bilirubin (micromol/litre)

Days from birth

Baby's blood group

Mother's blood group

NHS National Institute for Health and Clinical Excellence
When is it significant jaundice at 38+ weeks?
When is it significant *early* jaundice?

Bilirubin
Haemoglobin
Consider haemolytic disease if ≥1 of...

• Positive maternal antenatal antibody screening and/or anaemic/hydropic fetus

• Rapidly developing or significant hyperbilirubinaemia not predicted by maternal antenatal antibody screening

• Prolonged postnatal hyperbilirubinaemia

• Haemolysis on postnatal blood film

• Positive postnatal direct anti-globulin test (DAT)
DAT: Please help us record the result

Billirubin 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

Shade for phototherapy

Exchange transfusion

Phototherapy

Total serum bilirubin (micro/mole/litre)

Days from birth

Baby's blood group ________________ Mother's blood group ________________
DAT
The “problems” with DAT

- 23% of DAT+ required phototherapy
- 100% of DAT 4+ required phototherapy
- 94% DAT+ in ABO-incompatible mother/neonate
- 15% DAT+ from prophylactic anti-D
Consider haemolytic disease if ≥1 of...

- Positive maternal antenatal antibody screening and/or anaemic/hydropic fetus
- Rapidly developing or significant hyperbilirubinaemia not predicted by maternal antenatal antibody screening
- Prolonged postnatal hyperbilirubinaemia
- Haemolysis on postnatal blood film
- Positive postnatal direct anti-globulin test (DAT)
Don’t forget about this cause for haemolysis

SEPSIS
Positive 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

*Same attention – no matter ‘how positive’*

1. Maternal antibody screening +
2. DAT +
3. Jaundice
4. Anaemia
Intrinsic causes of haemolytic disease

• ABO incompatibility

• Red blood cell membrane defect

• Red blood cell enzyme defect

• Haemoglobinopathy: α-thalassaemia major
ABO incompatibility

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name

Date of birth

Hospital number

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Direct Antiglobulin Test

>=38 weeks gestation

Shade for phototherapy

Exchange transfusion

Phototherapy

Baby's blood group

Mother's blood group

NHS National Institute for Health and Clinical Excellence
ABO incompatibility

15-25% mat/neo ABO incompatibility

O  --- Anti-A IgG --- A

A  --- High titre Anti-B IgG --- B
ABO incompatibility: DAT+ jaundice (+ anaemia)
RBC membrane defects: **DAT- jaundice** (+ anaemia)

**Hereditary spherocytosis** (1 in 5000 births in northern Eur.)
Red blood cell enzyme defects: Jaundice +

X-linked G6PD deficiency (high prev. central Africa & Med.)

G6PD DEFICIENCY

X-LINKED RECESSIVE DISORDER CHARACTERIZED BY RED BLOOD CELL HEMOLYSIS AFTER EXPOSURE TO OXIDATIVE DRUGS (E.G., ASPIRIN, SULFONAMIDES, NITROFURANTOIN, DAPSONE, PRIMAQUINE, QUINIDINE), FAVA BEANS, OR INFECTION

BITE CELLS AND HEINZ BODIES

MOST CASES ARE SELF-LIMITED AS RED BLOOD CELLS ARE REPLACED; OXIDATIVE DRUGS SHOULD BE AVOIDED
α-thalassaemia major (pred. south east Asian families)

2nd trimester fetal anaemia & hydrops
Postnatal management

1. Cooperation: let us know – again & again
2. A-B-C-D
3. (Cord) blood test: bilirubin, Hb, group, DAT, blood film
4. Maternal blood sample
5. Transcutaneous bilirubin
6. Appropriate hydration & nutrition
7. Screen and treat for infection
8. Early and effective phototheraphy
9. Comfort incl. body temperature control
10. Folic acid 0.5 mg daily
Effective phototherapy...
Postnatal management

1. Cooperation: let us know – again & again
2. A-B-C-D
3. (Cord) blood test: bilirubin, Hb, group, DAT, blood film
4. Maternal blood sample
5. Transcutaneous bilirubin
6. Appropriate hydration & nutrition
7. Screen and treat for infection
8. Early and effective phototherapy
9. Comfort incl. body temperature control
10. Folic acid 0.5 mg daily
11. May need NICU Ax, Iv Ig, exchange transfusion
Follow-up

- Anaemia, part. after intra-uterine & exchange transfusions
- 1-2 weekly for 6-8 weeks
- Top-up transfusions may be needed
- Folic acid till weaning