Blood Group Antibodies & Haemolytic Disease of the Newborn

Blood group antibodies may cause haemolysis

Many maternal antibodies are transported across the placenta and may react with paternally derived blood groups on fetal red cells. Red cells coated with antibodies are destroyed faster than normal.

Accelerated destruction of red cells is called haemolysis. Rapid haemolysis will cause anaemia and production of large amounts of bilirubin. A high titre maternal antibody will cause severe anaemia and in very severe cases, fetal death. High and moderate titre antibodies cause neonatal anaemia and are a cause of high bilirubin levels after birth. Intrauterine transfusion of red cells and top-up transfusions in the first 3-4 weeks after birth may be needed.

Bilirubin is not cleared efficiently by newborn infants. High levels of bilirubin produced by haemolysis may cause irreversible brain damage called kernicterus. Postnatal phototherapy and sometimes exchange transfusion are used to help clear excess bilirubin.

Blood group serology & other tests used to detect and manage problems caused by blood group antibodies

- **ABO and D grouping**
- **Antibody screen:** Detects unexpected blood group antibodies (i.e. other than anti-A and anti-B)

Perform these tests at the start of pregnancy and repeat the tests in D-negative women at 27 and 34 weeks. These tests are repeated whenever blood group antibody titres are assessed.

- **Antibody specificity:** Identifies the type of antibody (the blood group target of the antibody)
- **Antibody titre:** A titre is an estimate of the amount of antibody. Some antibodies are more likely to reach a high titre, eg anti-D. Higher titres usually result in more severe haemolysis.

Titres provide a guide to when more specific tests such as fetal ultrasound assessment, and umbilical cord blood sampling, should be used. Serial titre measurements are needed – often monthly in the second trimester, fortnightly in the third trimester but more often after a boost in titre has occurred.

- **Tests on neonates who may have haemolytic disease of the newborn (HDN):** If the mother has a clinically significant blood group antibody (not anti-A or anti B) send cord blood samples for: full blood count; bilirubin; ABO, D and any other relevant blood group tests and DAT.
- The **direct antiglobulin test (DAT)** detects antibodies on red cells. It is carried out on the same sample used for blood grouping tests.
- **Crossmatching red cells for neonatal transfusion:** A maternal blood sample is normally used as it provides best access to any maternal antibody causing haemolysis.

**Testing for Fetal Red Cells in Maternal Blood**

The standard dose of anti-D injection (600-625IU) will clear up to 6 ml of D-positive red cells from maternal blood. If a feto-maternal haemorrhage is larger than 6 ml further doses of anti-D injection will be indicated.

The **Kleihauer test** is carried out on D-negative women to detect fetal red cells where an infant is D-positive or the D group is unknown (e.g. unborn fetus or miscarriage). It is used to detect a large fetomaternal haemorrhage where additional anti-D is needed. A negative Kleihauer test does not mean anti-D is not needed as the test cannot detect trace amounts of fetal red cells.

Further Sources of Advice or Information

- Anti-D Information Leaflet (for use when obtaining informed consent)
- Transfusion Medicine Specialists – contact your local Blood Bank for access details
- Transfusion Nurse Specialists – main Centres
- NZBS Transfusion Medicine Handbook
- Blood Groups, Antibodies and Immunology: A Resource Book for Lead Maternity Providers

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**What are Blood Groups?**

Blood groups are present on the surface of blood cells. They are passed from parents to children. They are inherited differences between people. Most blood groups occur on red cells but some special blood groups are also found on platelets and white blood cells.

Blood groups are important because individuals who do not have a particular blood group may make an antibody against that blood group. Antibodies may cause rapid destruction of red blood cells. This is important when:

- a woman makes an antibody that could react with a blood group in her fetus.
- red cells are selected for transfusion.

Blood groups on red blood cells differ between people

Blood groups occur in related families called Blood Group Systems. The two most important blood group systems are ABO and Rh (previously called Rhesus).

### Important Blood Group Systems

**ABO**

ABO is important because A and B are strong blood group factors and anti-A and, or anti-B are present in 97% of people. The four ABO blood groups are shown in the table below.

<table>
<thead>
<tr>
<th>The ABO blood groups</th>
<th>Genes present</th>
<th>ABO antibodies normally present in plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>AA or AO</td>
<td>anti-B</td>
</tr>
<tr>
<td>B</td>
<td>BB or BO</td>
<td>anti-A</td>
</tr>
<tr>
<td>AB</td>
<td>AB</td>
<td>anti-A &amp; anti-B</td>
</tr>
<tr>
<td>O</td>
<td>OO</td>
<td></td>
</tr>
</tbody>
</table>

Antibodies are produced by the immune system against foreign substances. Anti-A and anti-B are produced soon after birth by everyone who does not have A or B. They appear to be induced by A-like and B-like substances present on some bacteria. Group O people make both anti-A and anti-B as they lack both A and B blood group factors. In contrast, people who are group AB cannot make anti-A or anti-B as the A and B blood group factors are a normal part of their blood cells.

**Rh**

The Rh blood group system has three pairs of blood groups: D or d, C or c and E or e. Rh D is shown in the table below.

<table>
<thead>
<tr>
<th>Rh D group</th>
<th>Genes present</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-positive</td>
<td>DD or Dd</td>
<td>85%</td>
</tr>
<tr>
<td>D-negative</td>
<td>dd</td>
<td>15%</td>
</tr>
</tbody>
</table>

Key points about Rh D are:

- D is a strong blood group factor.
- D-negative is identified as ‘d’ and refers to absence of D; it is not a blood group factor.
- A D-negative person who is exposed to D positive red cells may be immunised and start to make anti-D. Once started, anti-D production is permanent; it will continue for life.
- If a D-negative woman has a D-positive infant the chance for anti-D immunisation is about 16% unless treatment is given.

The Rh blood group factors: C, c; and E, e are all weak blood group factors.

- This means that antibodies against these blood group factors are not often produced.

### Names of Other Blood Group Systems

The following blood group factors are all relatively weak.

<table>
<thead>
<tr>
<th>Name of System</th>
<th>Main blood group factors</th>
<th>Most common antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kell</td>
<td>K (Kell), k (Cellano)</td>
<td>anti-K</td>
</tr>
<tr>
<td>Duffy</td>
<td>Fy(a), Fy(b)</td>
<td>anti-Fy(a), anti-Fy(b)</td>
</tr>
<tr>
<td>Kidd</td>
<td>Jk(a), Jk(b)</td>
<td>anti-Jk(a), anti-Jk(b)</td>
</tr>
<tr>
<td>Ss</td>
<td>S, s</td>
<td>Anti-S, anti-s</td>
</tr>
<tr>
<td>MN</td>
<td>M, N</td>
<td>anti-M</td>
</tr>
</tbody>
</table>

- An antibody produced against a weak blood group factor may create an important clinical issue. Advice on appropriate action is available from NZBS Transfusion Medicine Specialists.
- If a D-negative woman has an antibody other than anti-D and if her baby is D-positive she will still need anti-D Immunoglobulin.

### Blood groups are inherited – passed from parents to children

Where a woman has an unexpected blood group antibody the Blood Bank will often request blood samples from both parents. The samples are used to determine the relevant blood groups and help estimate the risk of the fetus developing red cell haemolysis.

A D positive person: may be either DD (double dose of the D gene) or Dd (single dose of D and d). A person who is DD will only produce D-positive infants; a person who is Dd may produce D-positive or D-negative infants.

Blood groups are possible in the children born to each set of parents.