Blood Groups and Antibodies, Transfusion and Pregnancy

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To cover:

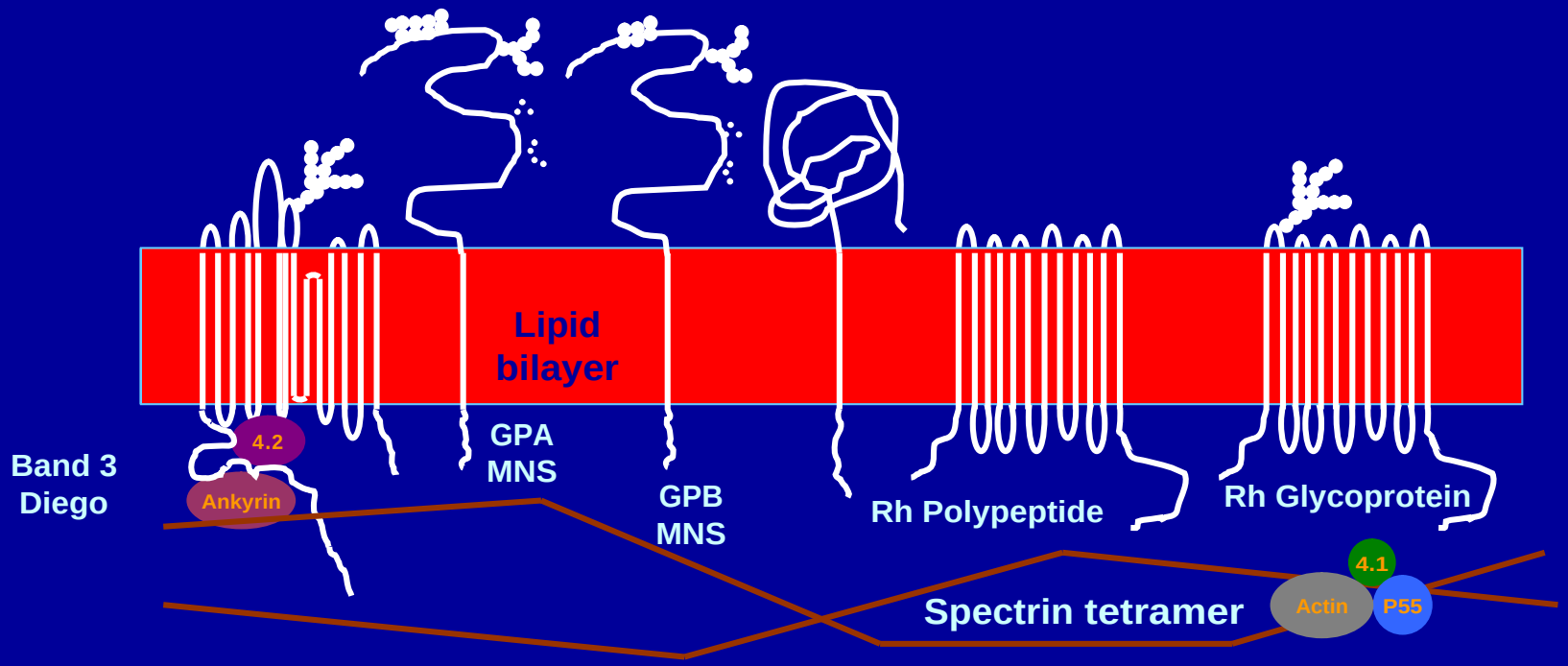
- What is a red cell antigen?
- What is a red cell antibody?
- Haemolytic Disease of the Newborn
  - Monitoring pregnancies
  - Preventing HDN, particularly through antenatal anti-D prophylaxis
  - Predicting outcomes
  - Difficult interpretations and working together
- The Direct Antiglobulin Test (DAT/DCT)

An Antigen

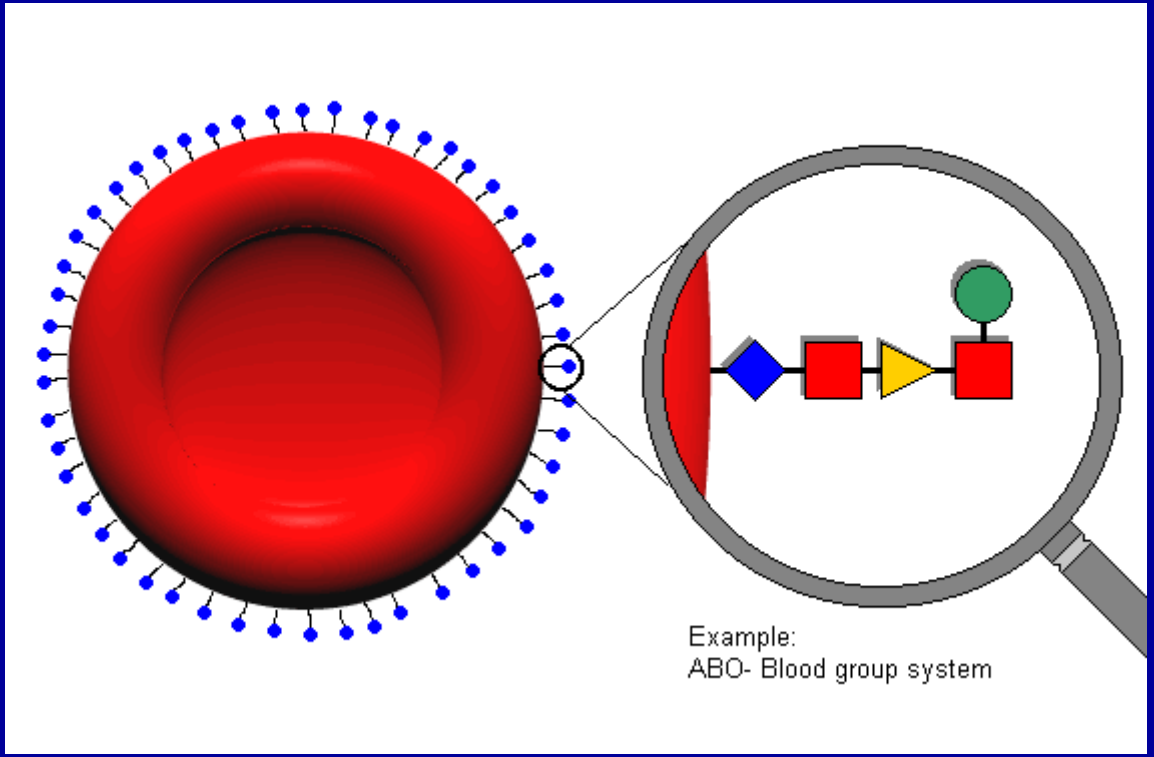
- An antigen can be defined as **a substance** that, when introduced into the circulation of an individual lacking that antigen, can **stimulate the production of a specific antibody**.

- Red cell antigens

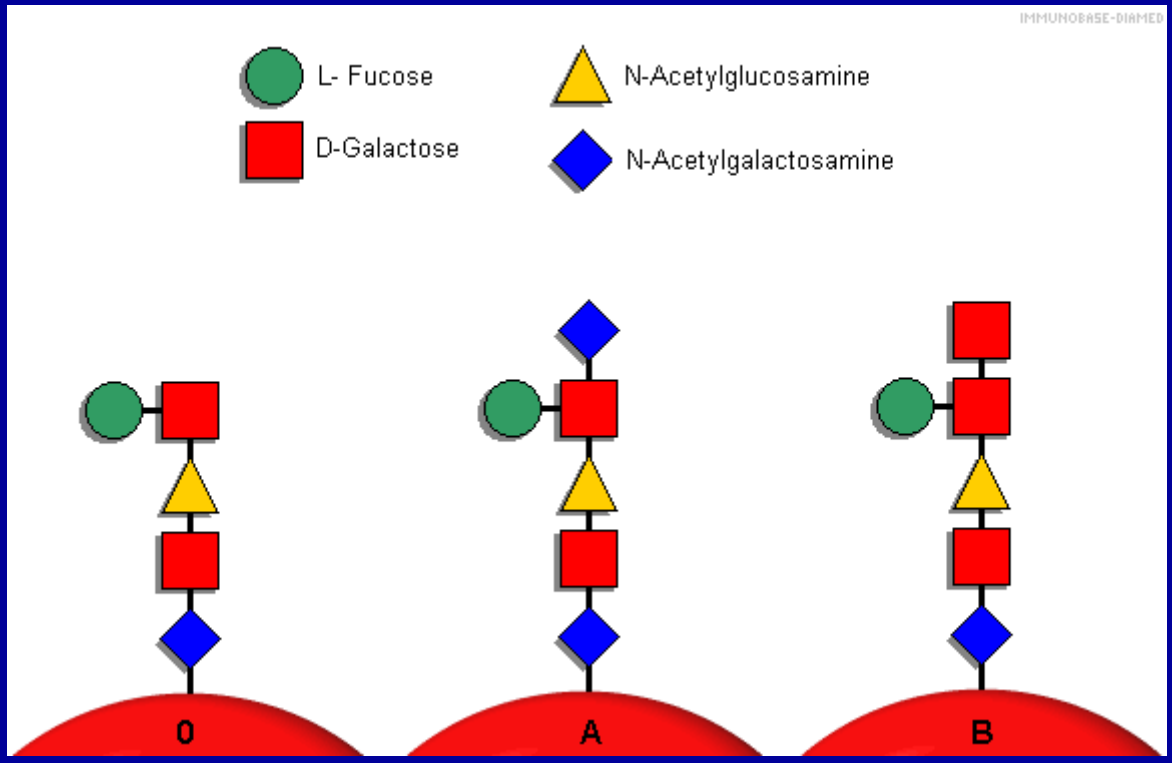
Blood Group Antigens



ABO Antigens



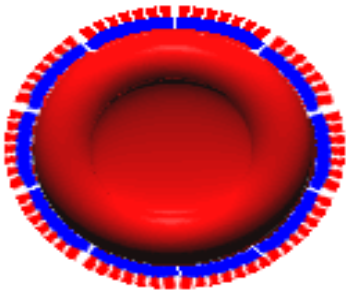
A Close Up

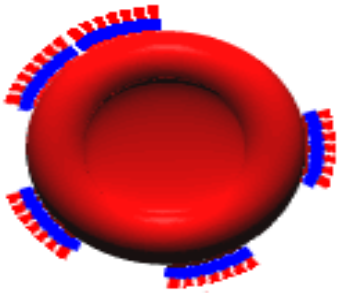

L- Fucose
D-Galactose
N-Acetylglucosamine
N-Acetylgalactosamine
0
A
B

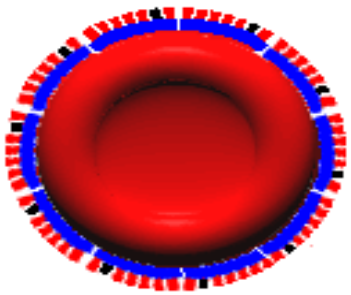
The D Antigen

- Most individuals are D positive or D negative
- An individual may have a weak D antigen (previously known as D^{u}).
- An individual may have a partial D antigen (previously known as a $D^{variant}$).

RhD

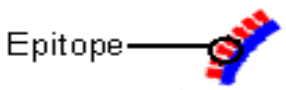


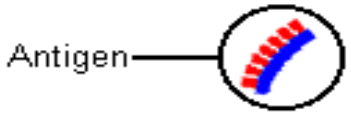




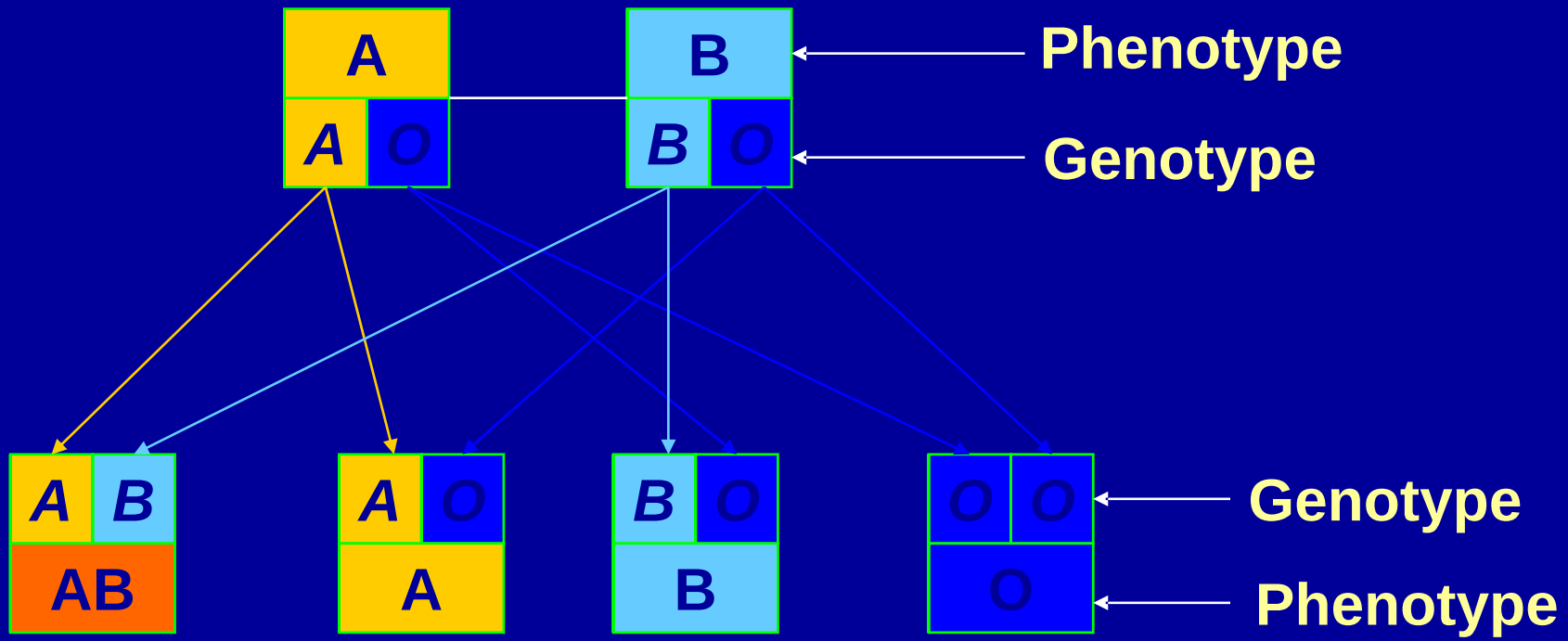
	Normal D-Antigen	D-weak	D-Variant
Epitope:	Normal	Normal	Mutated
Antigen frequency:	Normal	Reduced	Normal or reduced

Legend:

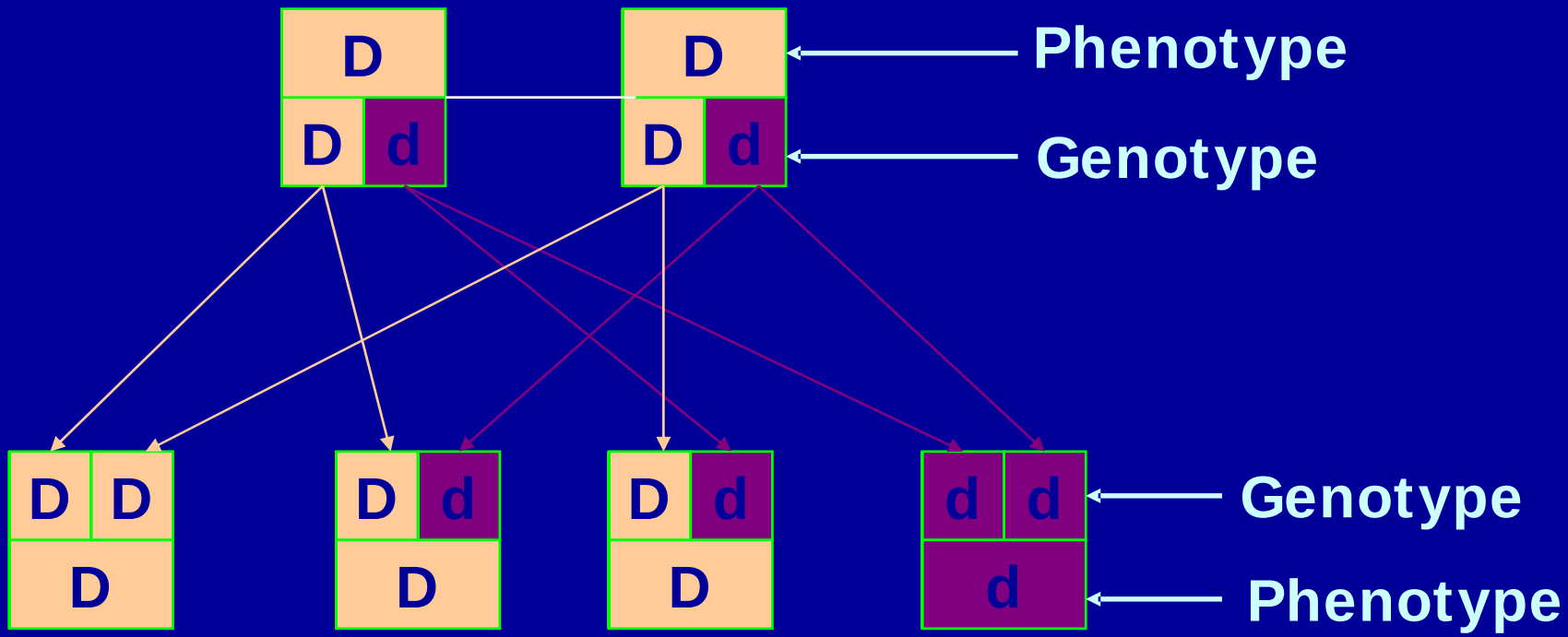




Inheritance



Genetics


D
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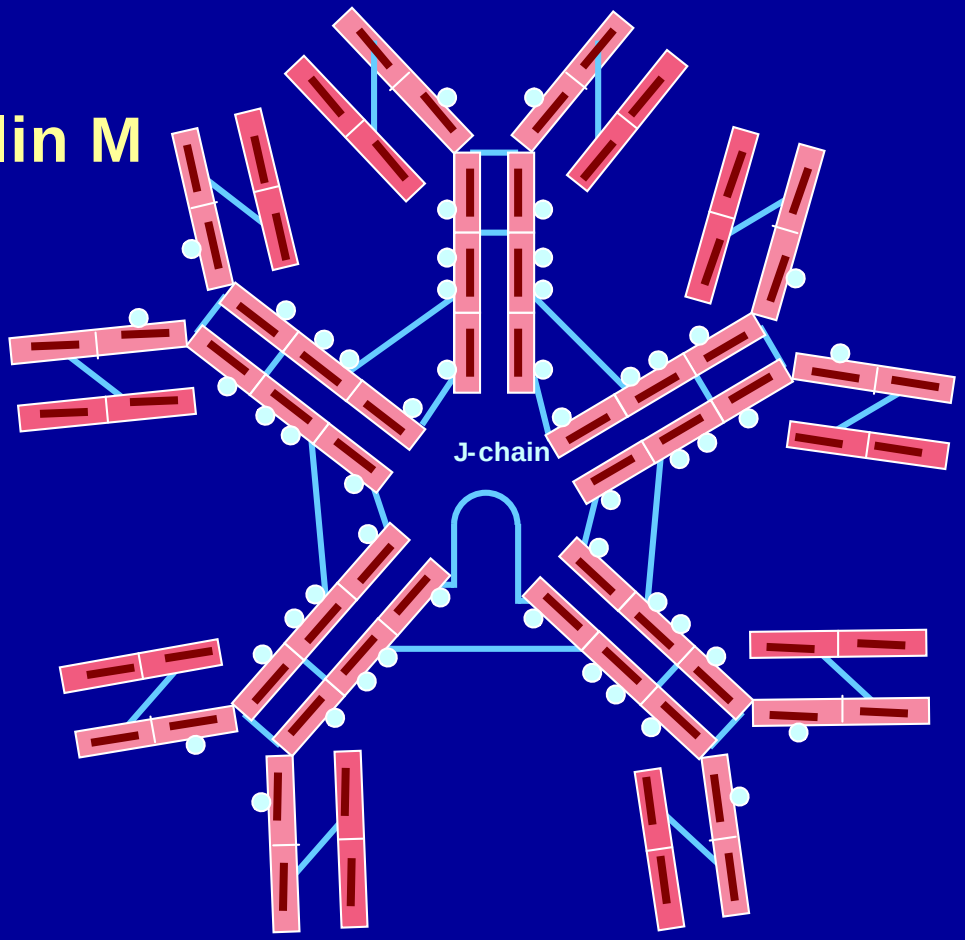
d
Genotype
Phenotype

An Antibody

- An antibody can be defined as a **serum protein** (*i.e.* an immunoglobulin with **specific antigen binding sites**) produced as a result of the introduction of a **foreign antigen**, that has the ability to combine with (and, in many cases, destroy) the cells carrying the antigen that stimulated its production

Antibodies - IgM

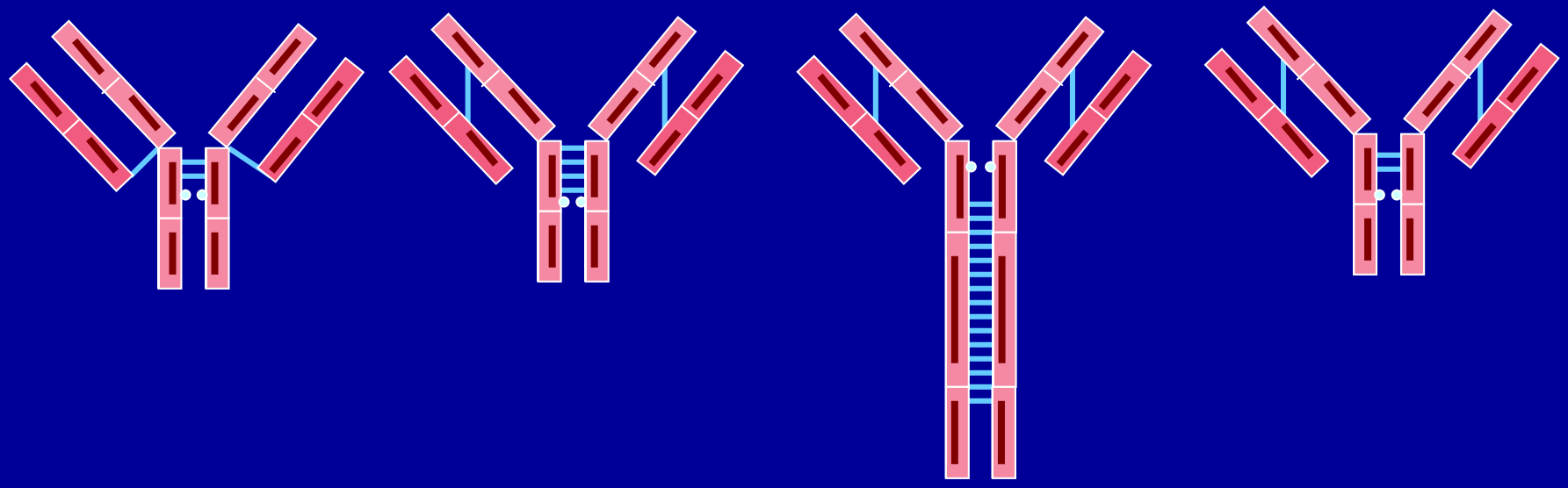
Immunoglobulin M



Carbohydrate unit

Antibodies - IgG

Immunoglobulin IgG subclasses



IgG1 IgG2 IgG3 IgG4

Red Cell Antibodies

Produced when exposed to foreign **blood**:

- Previous transfusion of blood/components
- Fetal maternal haemorrhage

ABO System

Red Cells (Antigens)	Plasma (Antibodies)
• A	• Anti-B
• B	• Anti-A
• O	• Anti-A,B
• AB	• None

Haemolytic Disease of the Fetus and Newborn

- Is a condition in which the lifespan of the infant's red cells is shortened by the action of specific antibodies derived from the mother by placental transfer.
- Anaemia, jaundice, liver damage, kernicterus, IUD

Serological Testing During Pregnancy

Purpose:

- To identify those at risk of HDN
- Identify RhD negative individuals so that appropriate anti-D prophylaxis can be given to prevent HDN due to anti-D
- To predict the severity of the HDN to plan treatment

Maternal Monitoring

- Booking bloods
  - ABO, D type and antibody screen
- Repeat test at 28 weeks
  - Confirm ABO and D type, repeat antibody screen
- If antibodies detected
  - Identify and monitor, regime dependent upon antibody

The Big Three

- Anti-D, anti-c and anti-K
- Test monthly up to 28 weeks
- Test every 2 weeks up to delivery
- Anti-D and anti-c are quantitated against a National Standard with results in IU/mL
- Anti-K is titrated
- Current sample is tested in parallel with previous sample to accurately identify changes in antibody level

The Others

- Tested at booking and 28 weeks
- In general a titre of >32 may possibly cause HDN
- A steep increase in titre between the two samples is worrying and may lead to further monitoring

Paternal Testing

- Determining paternal phenotype and likelihood of fetal genotype may be useful particularly when anti-D, anti-c or anti-K have been detected

- Misidentification of the father needs to be acknowledged

Fetal Genotyping

- Historically fetal DNA obtained by amniocentesis – invasive
- Fetal DNA can now be extracted from maternal peripheral plasma

Preventing HDN

- Give anti-D prophylaxis
- Prevent production of red cell antibodies in females of child-bearing potential
  - conservative transfusion regimes
  - transfuse D negative blood to D negative females of child bearing potential
  - and K negative blood to females of child bearing potential

Prophylaxis Regime

Following an event:

- <20 weeks gestation 250iu
- >20 weeks gestation at least 500iu followed by a test to measure the size of the FMH

Routine antenatal anti-D prophylaxis:

- 1500iu at 28 weeks or
- 2x500iu at 28 and 34 weeks

Following delivery of a D positive baby:

- At least 500iu followed by a test to measure the size of the FMH

Difficult Interpretations

Midwives:

- Maintain a clear record of prophylactic anti-D given: dose and date.
- Inform laboratory
- Vital to take 28 week samples for group and antibody screen BEFORE giving routine prophylaxis

Laboratory:

- Identify and quantitate antibody
- Give advice on anti-D prophylaxis based on history provided and results obtained
- Request further samples at stated times to monitor the level of antibody

Actions

Midwives:

- If immune anti-D is present do NOT give prophylactic/passive anti-D
  - failed to prevent anti-D formation
  - must not give an unnecessary blood product
- If interpretation of results is in doubt give anti-D as
  - may prevent HDN
  - anti-D is a blood product with a good safety record
- If further samples are requested send them
  - could miss catching an immune anti-D that is increasing to a dangerous level.

Direct Antiglobulin Test (Direct Coombs Test)

- A test performed on the cord/baby's sample soon after birth
- The test to see whether an antibody is attached to an antigen on red cells
- Under what circumstances should a DAT be tested?