MELBOURNE PATHOLOGY
Quality is in our DNA

# RhD Immunisation – being positive about being negative

Insight – November 2017

A great medical achievement of the last 50 years has been the introduction of preventative strategies for haemolytic disease of the newborn, in particular prophylaxis against Rh(D) immunisation.

## Haemolytic disease of the newborn (HDN)

Haemolytic disease of the newborn may be caused by a number of different red cell antigens/antibodies including those of the ABO group, Kell and other Rhesus antigens (including c and E). The D antigen of the Rhesus group is by far the most immunogenic and associated with the greatest likelihood of adverse outcomes for mother and foetus. Immunisation leads to intra-uterine haemolysis with consequent anaemia, heart failure and hyperbilirubinemia post delivery. In contrast anti-Kell, the next most important antibody, causes earlier foetal loss and suppression of foetal erythropoiesis with anaemia, but fewer complications from neonatal jaundice.

Fetomaternal haemorrhage leading to active immunisation most commonly occurs by complications of pregnancy, invasive procedures or traumatic events (Table 1).

A proportion of episodes are silent so despite adherence to guidelines a background incidence of anti-D formation continues and is probably unavoidable. Failure of provision of either prophylaxis or therapy when indicated, inadequate dosage of Rh(D) immunoglobulin for the size of the bleed (including due to difficulties calculating the bleed size by laboratory techniques) and variant D phenotypes may also contribute. Much less commonly, immunisation may occur outside of pregnancy by transfusion of Rhesus incompatible red cell or platelet concentrates.

**Figure 1. Phototherapy for HDN**

## Causes of Immunisation

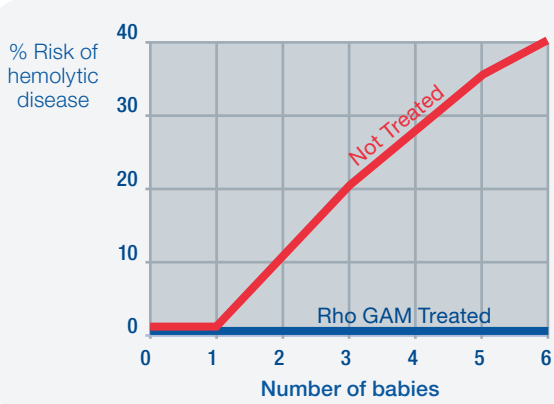
- Miscarriage
- Termination
- CVS
- Abdominal trauma
- External cephalic version
- Intrauterine death
- Ectopic pregnancy
- Amniocentesis/cordocentesis
- APH (covert and overt)
- Intrauterine surgery

**Table 1**

## Rhesus group negative and pregnancy

17 percent of Caucasian mothers are Rh(D) negative but not all of them have Rh(D) negative partners. Of Rh(D) positive partners a little more than half are heterozygotes (one D allele) rather than homozygote, ie. not every woman is at equal risk when the partner is Rhesus positive. The risk of HDN increases with each subsequent pregnancy to the same partner. Interestingly, concurrent ABO incompatibility actually reduces the likelihood of Rhesus immunisation as foetal cells have shorter survival in the maternal circulation. Prior to the introduction of preventative therapy, the risk of immunisation of an Rh(D) negative mother carrying an Rh(D) positive infant was in the order of 13 percent. Simple provision of post-partum immunisation with RhoGam almost 40 years ago reduced the incidence to 1.3% (Figure 1). The rate of immunisation with full antenatal prophylaxis is now <0.2%.

## Risk to Rh negative mother with Rh positive partner



# RhD Immunisation – being positive about being negative cont...

MELBOURNE PATHOLOGY
Quality is in our DNA

## Prophylaxis Regimens

In 1999 the NHMRC declared routine antenatal prophylaxis standard of care. NBA guidelines followed in 2003. Staged implementation of prophylaxis of firstly primigravid women, then all rhesus negative women, was supported initially by use of imported product (WinRho®), and eventually by ARCBS through the recruitment of immunised donors and active immunisation of volunteers. Stage 3, national self-sufficiency, was achieved in 2006 with Australian Rh(D) immunoglobulin supplied by CSL. The schedule and dosage for administration is illustrated in figure 2.

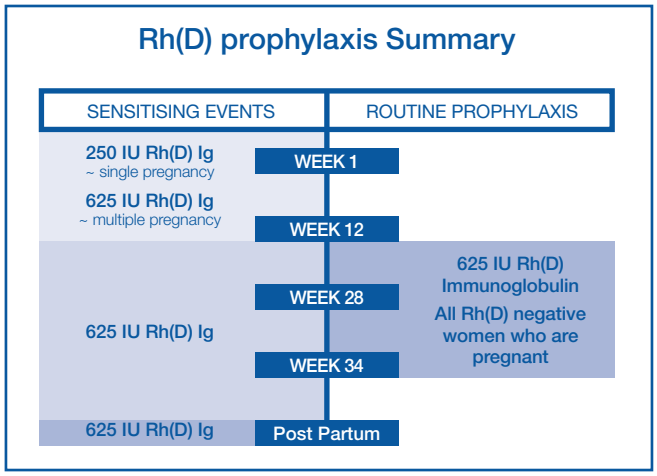


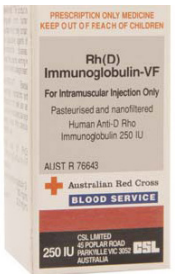

**Figure 2. Prophylaxis summary**

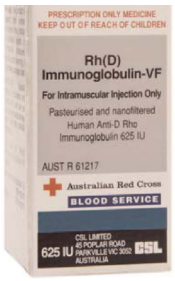
Please note: the prophylactic dosage schedule reflects the half-life of the immunoglobulin. We strongly recommend strict adherence to the described regimen for maximal benefit.

For immunosensitising events the dose should be delivered within 72 hours. Some benefit is still likely to be gained up to nine days post event, therefore Rh(D) immunoglobulin should not be withheld should an unavoidable delay occur. The dosage appropriate after first trimester should be determined by a quantitative measure of fetomaternal haemorrhage (FMH), either by Kleihauer or flow cytometry. Large FMH may need to be supported by intravenous prophylaxis due to a prohibitive number of IM injections that would otherwise be indicated. CSL Rh(D) Immunoglobulin-VF is not suitable for administration by this route. Our laboratory haematologists can advise on provision and dosing of the correct product.

Introduction of prophylaxis has increased the complexity of both antenatal and postnatal antibody screening. New guidelines from the Australian and New Zealand Society of Blood Transfusion assist a reporting schema which you will see illustrated on your current patient reports. Correct interpretation and clinical guidance needs to be informed by details about recent administration of Rh(D) immunoglobulin. Please consider inclusion of this information on referrals to assist the laboratory.

CSL Rh(D) Immunoglobulin is derived from Australian volunteer donors, has two viral inactivation steps and has a good history of safety. Although the product is licensed for this indication, consent should be obtained for administration of any blood product. There should be maintenance of adequate cold chain (storage at 2 – 6 degrees Celsius in a monitored refrigerator), and there must be traceability with regard to the patient receipt and the batch details. The product can be ordered directly from the ARCBS (9694 0200).




CSL support antenatal care with a series of education products for both patients and professionals. Melbourne Pathology support routine antenatal care through their administration clinics which assist scheduling of prophylaxis, collection of antibody screen and Kleihauer assessments, provision of immunisation cards to patients and reports to doctors and maternity units as required.


### Dr Ellen Maxwell

MBBS, FRACP, FRCPA

Medical Director &
Director of Haematology


Dr Maxwell is a University of Melbourne graduate who completed combined fellowships with the College of Physicians and the College of Pathologists in 1997.

She trained initially at the Austin and Repatriation Medical Centres and later the Alfred Hospital where she developed a keen interest in coagulation and transfusion medicine.

Dr Maxwell is a current member of the Victorian Blood User Group, the National Blood Transfusion Committee, The Australian Red Cross Blood Service Advisory Committee and the Serious Transfusion Incident Reporting Working Group (DHS Victoria). She has been an active member of many committees for the RCPA and ANZSBT. Dr Maxwell was appointed Medical Director at Melbourne Pathology in September 2009.