At a conference convened by the Royal College of Physicians of Edinburgh and the Royal College of Obstetricians and Gynaecologists, a consensus panel considered specific issues relating to anti-D prophylaxis in the UK. This statement is based on presentations given at the meeting, published research and expert opinion.

The panel reached the following conclusions:

**Overview**

(1) Perinatal deaths due to RhD alloimmunisation have fallen 100-fold since the introduction in 1969 of a policy to administer anti-D IgG to RhD-negative women after sensitising events in pregnancy and the birth of RhD-positive infants. In the 1990s pregnancy loss and death in the 1st week after delivery due to RhD alloimmunisation is in the order of 50 per year in the UK.

(2) RhD alloimmunisation still occurs. One to two of every 100 RhD-negative women at risk still become sensitised. This appears to be for two main reasons: (1) some women do not receive the benefit of the current policy, and (2) women are sensitised by small bleeds from the fetus, mainly in the last 12 weeks of pregnancy, which go undetected.

**Current Guidelines on Anti-D Prophylaxis – Are they Effective, can they be Improved?**

(3) The panel is concerned that there is abundant evidence that the guidelines are not being fully applied.

(4) The generally accepted UK guidelines are Recommendations For The Use Of Anti-D Immunoglobulin (National Blood Transfusion Service Immunoglobulin Working Party, 1991). The panel recommends that these should at present remain the reference standard for good clinical practice and that there should be no change to the dosage principle of 500 IU for 4 ml of fetal red blood cells. We are reassured to learn that there is an expert group currently undertaking review and revision of the current guidelines, with particular attention being given to the use of anti-D IgG in the first trimester of pregnancy. Failures of compliance are particularly common following potentially sensitising events during pregnancy, both in respect of the administration of anti-D IgG and the estimation of size of feto-maternal haemorrhage (FMH) by Kleihauer, or alternative, tests.

(5) Awareness of the need for anti-D IgG and a Kleihauer (or alternative) test is essential among staff involved in the care of pregnant women in obstetric and midwifery units, and also in A&E departments and in primary care.

(6) It is recommended that information leaflets about the guidelines should be given to RhD-negative women and their partners, and relevant health professionals.

**Antenatal Anti-D Prophylaxis – is it Worthwhile, and can we Afford it?**

(7) A current recommendation is that anti-D IgG should be given after events signalling the possibility of FMH. The panel believes that routine antenatal anti-D prophylaxis is of proven benefit and that this would significantly reduce levels of RhD alloimmunisation. The currently available studies however make it difficult to estimate the scale of the reduction.

(8) The panel proposes that because all RhD-negative pregnant women are at risk from hidden bleeds, they should be given anti-D IgG prophylactically.
(9) A paucity of recent cost-effectiveness studies makes it difficult to make definite and accurate statements regarding the efficiency of extending the current policy to include routine antenatal prophylaxis. The cost of offering routine antenatal prophylaxis will depend on dose and frequency. Estimates of cost per dose vary.

(10) Evidence to date suggests that antenatal prophylaxis has the potential over time to save more resources than it costs if restricted to primigravidae, although this will involve a modest degree of preliminary investment in order to increase the supply of anti-D IgG. Increasing the programme to include all RhD-negative pregnant women will have a positive net cost which might be considerable, but the cost per life year saved is still likely to compare favourably with other NHS interventions.

(11) The panel considers there to be no effective argument against protecting all RhD-negative women, as opposed to just primigravidae. While the greatest cost benefits of routine anti-D IgG prophylaxis have been demonstrated in primigravidae, it cannot be ethically or economically justified to limit the policy to this group of women.

(12) It is expected that UK blood transfusion centres will be able to meet requirements for supply of polyclonal anti-D at least for a programme in primigravidae. In the long term however, it is reasonable to expect supply will be sufficient to protect all RhD-negative pregnant women. Until a safe monoclonal product is available the principal source of donors will have to be sensitised men and women. No serious adverse reactions have been reported in women receiving intramuscular anti-D IgG, but it is important that the viral and other safety issues raised by changes in product manufacture are kept under rigorous review.

(13) It remains to be decided which dosage and schedule of prophylaxis is the most effective. There are two main options—a dose of 500 IU at 28 and 34 weeks, or alternatively a single larger dose early in the third trimester. Both seem to work.

(14) In introducing antenatal prophylaxis we suggest that health authorities should first check on compliance with current guidelines. If initially there is insufficient anti-D IgG for all women at risk, primigravidae should be given priority. Early consultation with professionals in primary care will be essential.

Monoclonal Anti-D – is it Safe, will it Work and can it Replace Polyclonal Anti-D?

(15) In 1991 the guidelines authors hoped that an effective monoclonal anti-D would soon be available to supplement polyclonal anti-D and that there would be sufficient quantities to allow antenatal prophylaxis to be started. In 1997 it appears that: (a) Monoclonal preparations, of which supply would be theoretically limitless, could in principle replace polyclonal anti-D. (b) Only Phase I trials are at present complete on monoclonal preparations. It is not yet certain if these preparations will be safe and efficacious, reliable or affordable. There may be advantages from an intravenous preparation that can also be given intramuscularly. (c) It is also uncertain how long it will be before monoclonal products are available in sufficient quantity, and whether they will be acceptable to regulators. (d) The process of introducing monoclonal products and possibly phasing out polyclonal anti-D will need to be agreed nationally, and will require a comparative trial. Polyclonal products should not be phased out until the monoclonal supply has been shown to be secure.

Should Anti-D be used for the Treatment of Immune-Mediated Thrombocytopenia?

(16) The panel accepts that anti-D IgG may have a place in the treatment of RhD-positive non-splenectomised patients, especially children, with chronic immune thrombocytopenia, and that in these patients it may have a similar role to high-dose intravenous immunoglobulin. However with current UK practice it is only likely to be used in a small number of patients. In the UK there is an imported anti-D IgG preparation available for use in immune-mediated thrombocytopenia on a named-patient basis.

Ethical Considerations of Anti-D Provision from Immunised Volunteers.

(17) The donor should be empowered to make a full and free informed choice before consenting to the immunisation procedure. Voluntary consent to this procedure must be genuine and explanation geared to capacity to understand and act on what is required. A comprehensive information leaflet should be made available for prospective donors.

(18) It is likely there will continue to be a need for immunised donors well into the 21st century, and until the safety, efficacy and quality of monoclonal anti-D is established to the standard of European regulatory requirements.

(19) The question of compensation for non-negligent harm is vexed but clearly some effective and transparent arrangement to compensate volunteers is desirable.

For this purpose we include multigravid women without a living child.