

Antenatal anti-D prophylaxis Evidence and Guidelines

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Some history

- **1930's Diamond & Blackfan recognised neonatal hydrops, jaundice and anaemia as a single disease**
- **Early 1940's Levine identified the cause as Rhesus antibodies**

The potential size of the task

- **105,000 births per year in E & W to RhD negative women (17% of all births)**
- **59% (62,000) of their babies are RhD positive (10% of all births)**

Some more history

- **1969 post-delivery anti-D prophylaxis began in the UK**
- **Deaths from RhD alloimmunisation pre-1969 46 per 100,000 births (i.e. 1 in 2,200 births) with HDN in 1% of births**
- **Deaths from RhD alloimmunisation 1990 1.6 per 100,000 births (i.e. 1 in 62,500)**

But Rhesus D alloimmunisation continued to occur

- **500 fetuses per year with HDN in E & W**
- **25 – 30 deaths per year from HDN**
- **15 babies per year with major handicaps**
- **30 babies per year with minor handicaps**
- **About 20 miscarriages per year**

Why was HDN still occurring?

- **1991 (Prescribers' Journal) guidelines not being fully applied (previous guidelines from SMAC 1976, 1981)**
- **18-27% of cases due to sensitisation during 3rd trimester of 1st pregnancy without a recognised sensitising event**
- **Similar proportion in 2nd or subsequent pregnancies (impossible to distinguish from failure of prophylaxis after previous delivery)**

Current national guidelines

- **Royal College of Obstetricians & Gynaecologists – May 2002**
- **National Institute for Clinical Excellence – May 2002**
- **British Committee for Standards in Haematology – June 2006**

Key points

- Give anti-D to unsensitised RhD negative women after any potential sensitising event
- 250 i.u. IM before 20 weeks, at least 500 i.u. IM after 20 weeks
- Kleihauer (+/- flow cytometry) to quantitate FMH after 20 weeks
- Give more anti-D if >4 ml (0.8% of deliveries)
- As soon as possible, at least within 72 hours (up to 10 days may be useful)

Routine antenatal prophylaxis

- **At 28 weeks and at 34 weeks**
- **At least 500 i.u. IM each time**
- **Does not affect policy with sensitising events, including delivery**
- **Must screen for anti-D antibodies before the 28 weeks injection (as well as at “booking”)**

Cannot distinguish active and passive anti-D in the mother

- If there is a record of anti-D administration within the past 8 weeks and level is below 1 i.u./ml likely to be passive
- Repeat antibody quantitation every 4 weeks to 28 weeks, then every 2 weeks
- Continue to give prophylaxis regardless

Recurrent sensitising events

- **Before 20 weeks, give 250 i.u. anti-D at minimum of 6 week intervals**
- **After 20 weeks, undertake FMH quantitation at least every 2 weeks, and give at least 500 i.u. anti-D at minimum of 6 week intervals**

Does “routine” antenatal anti-D prophylaxis work?

- 6,400 primigravidae given 500 i.u. at 28 and 34 weeks – postnatal anti-D sensitisation
0.89% (95% C.I. 0.21 – 1.56%) in controls
0.30% (95% C.I. 0.22 – 0.38%) in treated group
- 4,700 primigravidae in UK community based study (same regimen) postnatal sensitisation
0.95% (95% C.I. 0.18 – 1.71%) in controls
0.35% (95% C.I. 0.29- 0.40%) in treated group

The risks of giving anti-D immunoglobulin

- Infection – prion, virus (“less than 1 in a million”)
- Rare allergic responses
- Speculation on effect on fetal immune system (no evidence of adverse events so far)

Documentation and Audit

- **Status of anti-D as a medication or a blood product is confused**
- **Practice on prescription documentation varies**
- **EU recommends that batch number etc should be documented in blood bank records**
- **Audits of practice should be undertaken on a continuing basis**

Different products available in UK

- **D-GAM (BPL) in 250, 500, 2500 i.u. vials**
- **Partobulin (Baxter) in 1250 i.u. pre-filled syringe**
- **Rhophylac (Behring) in 1500 i.u. pre-filled syringe**
- **WinRho (Baxter) in 1500, 5000 i.u. vials**

Different prophylaxis regimens

- **UK recommendations “at least” 500 i.u. at 28 weeks, 34 weeks and after delivery (of RhD positive infant, with Kleihauer/flow cytometry for quantitation)**
- **Some European countries give a single 1500 i.u. dose at 28 weeks, and 1000 or 1500 i.u. after delivery with no quantitation of FMH**

The problems

- **The guidelines are not actually completely clear nor completely consistent!**
- **Current generation of maternity staff unfamiliar with relevant issues**
- **Pregnancy care increasingly devolved to midwives and the community**
- **Since 1983 ~50% rbc antibodies are not anti-D**

The future

- **More effective and continuing education of midwives and maternity staff**
- **Clear information for Rhesus negative women**
- **Clarification of status and documentation of anti-D administration**
- **Antenatal testing of fetal blood group from circulating fetal DNA in maternal plasma**
- **Ongoing audit of the conduct of anti-D prophylaxis**