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[Intervention Review]

Anti-D administration after childbirth for preventing Rhesus alloimmunisation

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ABSTRACT

Background

The development of Rhesus immunisation and its prophylactic use since the 1970s has meant that severe Rhesus D (RhD) alloimmunisation is now rarely seen.

Objectives

The objective of this systematic review was to assess the effects of giving anti-D to Rhesus negative women, with no anti-D antibodies, who had given birth to a Rhesus positive infant.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (March 2010) and reference lists of relevant articles.

Selection criteria

Randomised trials in Rhesus negative women without antibodies who were given anti-D immunoglobulin postpartum compared with no treatment or placebo.

Data collection and analysis

Assessments of inclusion criteria, trial quality and data extraction were done by each author independently. Initial analyses included all trials. Other analyses assessed the effect of trial quality, ABO compatibility and dose.

Main results

Six eligible trials compared postpartum anti-D prophylaxis with no treatment or placebo. The trials involved over 10,000 women, but trial quality varied. Anti-D lowered the incidence of RhD alloimmunisation six months after birth (risk ratio (RR) 0.04, 95% confidence interval (CI) 0.02 to 0.06), and in a subsequent pregnancy (RR 0.12, 95% CI 0.07 to 0.23). These benefits were seen regardless of the ABO status of the mother and baby, when anti-D was given within 72 hours of birth. Higher doses (up to 200 micrograms) were more effective than lower doses (up to 50 micrograms) in preventing RhD alloimmunisation in a subsequent pregnancy.

Authors' conclusions

Anti-D, given within 72 hours after childbirth, reduces the risk of RhD alloimmunisation in Rhesus negative women who have given birth to a Rhesus positive infant. However the evidence on the optimal dose is limited.

Anti-D administration after childbirth for preventing Rhesus alloimmunisation (Review)

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PLAIN LANGUAGE SUMMARY

Anti-D administration after childbirth for preventing Rhesus alloimmunisation

Immunisation of Rhesus negative women with anti-D after the birth of a Rhesus positive infant reduces the chances of developing Rhesus antibodies.

Mothers and babies may have incompatible blood characteristics (such as Rhesus positive babies and Rhesus negative mothers). After the birth of a Rhesus positive infant, Rhesus negative women are given an injection of anti-D, which aims to prevent the women forming antibodies that would attack the red cells of a Rhesus positive baby in a future pregnancy. Such antibodies may make the baby anaemic and if severe enough can cause the baby to die. This review of six trials, involving over 10,000 women, found that anti-D given to Rhesus negative women within 72 hours of giving birth to a Rhesus positive infant decreased the likelihood of the women developing Rhesus antibodies within six months of the birth and in their next pregnancy.

BACKGROUND

Rhesus D (RhD) alloimmunisation leading to haemolytic disease of the fetus and newborn remained a major cause of perinatal mortality, morbidity, and long-term disability until the 1970s. With the development of Rhesus immunoglobulin and its evaluation and then utilisation in clinical practice, severe RhD alloimmunisation is rarely seen today. The dramatic reduction in deaths from Rhesus haemolytic disease by the use of postpartum anti-D immunoglobulin has been a major obstetrical achievement. Nevertheless Rhesus haemolytic disease is unlikely to disappear and is still a problem for women and their babies who are affected.

Over 100 years ago, Von Dungern ([Von Dungern 1900](#)) showed that active immunisation can be prevented in the presence of a passive antibody to a particular antigen. However, it was another 60 years before it was shown that sensitisation to Rhesus positive blood could be prevented by administering anti-D antibody ([Stern 1961](#)). After this pioneering work, studies continued, mainly in the UK and North America ([Clarke 1963](#); [Freda 1964](#)) culminating in the clinical trials of Rhesus prophylaxis after childbirth - an international collaborative effort. With anti-D being in short supply in some countries, it is important to be able to determine minimum effective doses ([NHMRC 1999](#)).

For trials of Rhesus prophylaxis during pregnancy, see the Cochrane review 'Anti-D administration in pregnancy for preventing Rhesus alloimmunisation' ([Crowther 1999](#)).

OBJECTIVES

To assess the effects of giving anti-D after birth to Rhesus negative women, with no anti-D antibodies, who had given birth to a Rhesus positive infant.

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished, ongoing randomised and quasi-randomised trials with reported data which assess outcomes in Rhesus negative women without antibodies, and their babies, who were given anti-D immunoglobulin prophylaxis after birth, compared with Rhesus negative women without antibodies not given anti-D, and their babies.

Types of participants

Rhesus negative women without anti-D antibodies who gave birth to a Rhesus positive baby.

Types of interventions

Anti-D immunoglobulin given after birth irrespective of parity, ABO compatibility, size of feto-maternal haemorrhage, dose or timing.

Types of outcome measures

Primary outcomes

Main outcomes considered were subsequent development of Rhesus D alloimmunisation, maternal concerns and adverse effects of treatment, and neonatal morbidity in a subsequent pregnancy.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (March 2010).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the [Cochrane Pregnancy and Childbirth Group](#).

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We screened the reference lists of relevant papers.

We did not apply any language restrictions.

Data collection and analysis

Trials under consideration were evaluated for appropriateness for inclusion and methodological quality without consideration of their results. This was assessed separately by each author. There was no blinding of authorship. Included trial data were processed as described in the *Cochrane Reviewers' Handbook* ([Clarke 2000](#)).

Quality scores for concealment of allocation were assigned to each trial, using the criteria described in [Clarke 2000](#):

- (A) adequate concealment of the allocation;
- (B) unclear whether adequate concealment of the allocation;
- (C) inadequate concealment of allocation (includes quasi-randomised studies);
- (D) indicates the score was not assigned.

In addition, quality scores were assigned to each trial for completeness of follow up and blinding of outcome assessment as follows.

Completeness of follow up:

- (A) less than 3% of participants excluded;
- (B) 3% to 9.9% of participants excluded;
- (C) 10% to 19.9% of participants excluded;
- (D) 20% or more excluded.

For blinding of assessment of outcome:

- (A) double blind, neither investigator nor participant knew or were likely to guess the allocated treatment;

(B) single blind, either the investigator or the participant knew the allocation. Or, the trial is described as double blind, but side effects of one or other treatment mean that it is likely that for a significant proportion (20% or more) of participants the allocation could be correctly identified;

(C) no blinding, both investigator and participant knew (or were likely to guess) the allocated treatment.

Data were extracted independently by the two review authors and double entered. Discrepancies were resolved by discussion.

Descriptive data included authors, year of publication, setting, country, time span of the trial, use of placebo and type if used, dosage and timing of anti-D, pre-trial calculation of sample size and number randomised and analysed.

Categorical data were compared using risk ratios and 95% confidence intervals. Statistical heterogeneity between trials was tested for using the chi-squared test with n (the number of trials contributing data) minus one degrees of freedom. With no significant heterogeneity ($P > 0.10$), data were pooled using a fixed-effect model. If significant heterogeneity was found, the random-effects model was used.

All eligible trials were included in the initial analysis and pre-specified analyses have been carried out to evaluate the effects of ABO compatibility and dose. Sensitivity analysis assessed the effect of trial quality by excluding trials given a C or D rating for quality of treatment allocation.

RESULTS

Description of studies

Six studies that involved over 10,000 women met the inclusion criteria ([International 1966](#); [Liverpool 1971](#); [MRC 1974](#); [Netherlands 1968](#); [UK Baltimore 1965](#); [Western Canada 1968](#)). See [Characteristics of included studies](#) for further detail. Four other studies were considered, but excluded from this review as detailed in the [Characteristics of excluded studies](#) table.

Both the dose of anti-D used and the timing varied: ([International 1966](#), 300 ug within 72 hours of birth with a higher dose of 4000 to 6000 ug for a small group of women in the early phase of the trial; [Liverpool 1971](#), 200 ug within 36 hours of birth; [MRC 1974](#), 20 ug, 50 ug, 100 ug, or 200 ug within 36 hours of birth; [Netherlands 1968](#), 250 ug within 24 hours of birth; [UK Baltimore 1965](#), 1000 ug or up to 5000 ug in Baltimore within 36 hours of birth; [Western Canada 1968](#), 145 ug or 435 ug within 48 hours of birth).

Risk of bias in included studies

In three trials, the method of treatment allocation was unclear ([International 1966](#); [MRC 1974](#); [Western Canada 1968](#)), and quasi-randomised in three trials ([Liverpool 1971](#); [Netherlands 1968](#); [UK Baltimore 1965](#)). A placebo was used in a subset of the [International 1966](#) trial ([Stenchever 1970](#); [White 1970](#)), although the other reports of this trial state that no placebo was used. Three trials report losses to follow up (about 10% for [MRC 1974](#) and [Netherlands 1968](#)) and at least 11% ([International 1966](#)). Losses to follow up in the other trials are unknown. It is unclear whether blinding of assessment of outcome was achieved from any of the trial reports.

Effects of interventions

In all five trials of postpartum anti-D prophylaxis versus no prophylaxis, Rhesus D (RhD) alloimmunisation was less common six months after birth in women who received anti-D (risk ratio (RR) 0.04, 95% confidence interval (CI) 0.02 to 0.12, random-effects model). In the four trials for which data were available, the administration of anti-D immunoglobulin reduced the incidence of RhD alloimmunisation in a subsequent pregnancy, (RR 0.14, 95% CI 0.06 to 0.35, random-effects model). These beneficial effects were seen regardless of the ABO status of mother and baby, when anti-D is given within 72 hours of birth. Significant heterogeneity was detected between trials for these outcomes, but no reasons were found to explain this. Use of the random-effects model made little change to the RR or 95% CIs.

In doses available for comparison, 200 ug (1000 international units (IU)) anti-D and above, the risk of sensitisation at six months after delivery (RR 0.04, 95% CI 0.00 to 0.64) and in a subsequent pregnancy were reduced (RR 0.23, 95% CI 0.07 to 0.78), compared with no prophylaxis.

Sensitivity analyses, excluding the three trials given a C rating for quality of treatment allocation, did not alter the beneficial results seen.

The data on comparative doses show that up to 50 ug (250 IU) anti-D compared with higher doses up to 200 ug (1000 IU) increased the risk of sensitisation in a subsequent pregnancy. No evidence was seen that a lower dose of 100 ug (500 IU) anti-D was substantially less effective than a higher dose of 150 ug (750 IU) anti-D, although the number of immunisations were few.

See summary of analyses tables.

DISCUSSION

Prophylaxis with postpartum anti-D immunoglobulin is effective in reducing the risk of sensitisation after pregnancy and in a subsequent pregnancy irrespective of the ABO status of mother and baby. From these trials, effective prophylaxis is shown when anti-D is given within 72 hours of birth.

The evidence on the optimal amount of anti-D to recommend for prophylaxis is limited. Recommendations in different countries will depend on the relative availability and costs of anti-D, and the costs of laboratory assessments of the volume of foeto-maternal haemorrhage. In the UK, postnatal administration of at least 100 ug (500 IU) is recommended ([RCOG](#)), in Australia 125 ug (625 IU) ([NHMRC 1999](#)) and in the USA and parts of Europe 200 ug to 300 ug (1000 IU to 1500 IU). It is generally accepted that 25 ug (125 IU) anti-D protects against 1 ml of fetal anti-D cells or 2 ml of whole blood. Therefore, 100 ug (500 IU) should protect against a foeto-maternal haemorrhage of up to 8 ml and 300 ug anti-D against a foeto-maternal haemorrhage of up to 30 ml of fetal blood. A foeto-maternal haemorrhage of 30 ml or more is uncommon but does occur in up to 0.6% of births ([Zipursky 1977](#)).

There is a paucity of information about the attitudes of women towards anti-D prophylaxis and the health of infants in subsequent pregnancies. No adverse effects of the treatment are reported, though risks of rare adverse effects of sensitivity reactions and transmission of infectious diseases remain possible.

AUTHORS' CONCLUSIONS

Implications for practice

Anti-D, given within 72 hours after childbirth, reduces the risk of Rhesus D alloimmunisation in Rhesus negative women who have given birth to a Rhesus positive infant.

The clear results of this review support the policy of giving anti-D immunoglobulin prophylaxis within 72 hours (irrespective of ABO status) to all Rhesus negative women, without anti-D antibodies, who give birth to a Rhesus positive baby or a baby whose Rhesus status cannot be determined.

Implications for research

No further placebo controlled trials are warranted to establish the effectiveness of anti-D given within 72 hours after birth.

As the evidence on the optimal amount of anti-D to recommend for postpartum prophylaxis is limited, further good quality comparative trials would be appropriate. In particular, the cost-effectiveness of smaller doses of anti-D immunoglobulin, combined with screening for the degree of feto-maternal haemorrhage and administering additional anti-D as necessary, should be compared with the use of larger doses of anti-D.

In further trials, the attitudes of women towards anti-D prophylaxis and the health of infants born in subsequent pregnancies should be evaluated. Any adverse effects of the treatment, including sensitivity reactions and transmission of infectious diseases, should be documented.

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Professor Jack Gravenhorst compiled the first version of this review, and Professor Marc Keirse was a reviewer of the 'pre-Cochrane' reviews. We also thank Lynn Hampson and Denise Atherton for their help with this update.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

International 1966

Methods	'Randomly allocated, although some degree of variation between centres, eg. 'admitted to either study or control group' which suggests that randomisation may not have been standard across all 43 centres.
Participants	Over 3000 mothers; Rh negative, not immunised, any parity with infants who were Rh positive and ABO compatible with negative Coombs test.
Interventions	At least 300 ug of anti-D within 72 hours of delivery and a higher dose of 4000-6000 ug for a small group of women recruited in the early phase of the trial. Most trial reports state no placebo was given, however in 2 reports (Stenchever 1970 and White 1970), the control group received 1 ml of gamma globulin without anti-Rh antibody.
Outcomes	Immunisation after 6 months. Immunisation at a subsequent pregnancy.
Notes	This 43 centre trial was an exemplary international collaborative effort. However, there does seem to have been some variation in study quality between the centres. The final figures for immunisation after 6 months have been taken from White 1970 and the final figures for immunisation at a subsequent pregnancy have been taken from Schumacher 1971. Losses to follow up are not given for the overall trial, but an early study report showed losses to follow up of nearly 11%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Liverpool 1971

Methods	Alternate treatment and control.
Participants	715 mothers; Rh negative, primiparous. Babies: Rh positive, ABO compatible, with less than 2 ml fetal/maternal bleed, 'low risk'.
Interventions	200 ug of anti-D, mostly within 36 hours of delivery. Control: no treatment given.
Outcomes	Immunisation after 6 months. Immunisation at a subsequent pregnancy.
Notes	Losses to follow up not given.

Risk of bias

Liverpool 1971 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

MRC 1974

Methods	All women received anti-D. Method of dose allocation was 'by coded serial number, assigned randomly'.	
Participants	1800 mothers; Rh negative, no anti-D, primiparous, married, white, no history of abortion or blood transfusion. Babies: Rh positive, ABO compatible.	
Interventions	20, 50, 100 or 200 ug anti-D within 36 hours of delivery.	
Outcomes	Immunisation after 6 months. Immunisation at a subsequent pregnancy. Infant health at the subsequent pregnancy (limited information).	
Notes	A total of 2000 doses were given, meaning a loss to follow up of 10%.	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Netherlands 1968

Methods	'Randomised by treating with anti-D those with odd-numbered birthdays.'	
Participants	740 mothers; Rh negative, no anti-D. Babies: Rh positive, irrespective of parity or ABO compatibility.	
Interventions	250 ug of anti-D within 24 hours of delivery. Controls were given no treatment.	
Outcomes	Immunisation after 4-6 months.	
Notes	Figures for losses to follow up not given. Immunisation at a subsequent pregnancy was followed, but figures were only given for the treated group.	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

UK Baltimore 1965

Methods	Aimed for alternation, but reverted to days of the week and consecutive dosages. The researchers reported 'considerable upset' to their original methodology.
Participants	349 mothers; Rh negative, free of Rh antibodies, primiparous, ABO compatible with baby. Babies: Rh positive, fetomaternal bleeds of greater than 0.2 ml, 'high risk'.
Interventions	Treatment groups: 1000 ug (5 ml) of anti-D within 36 hours of delivery or up to 5000 ug in Baltimore. Control group: untreated.
Outcomes	Immunisation of mother after 6 months. Immunisation of mother after a subsequent pregnancy.
Notes	No information given about losses to follow up.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Western Canada 1968

Methods	While the trial was 'intended to be random', this may not have been adhered to throughout the whole trial, eg. some mothers who refused treatment were used as controls.
Participants	444 mothers; Rh negative, no anti-D, any parity. Babies: Rh positive, ABO compatible, negative Coombs test.
Interventions	145 ug or 435 ug of anti-D vs untreated control. 145 ug vs 435 ug of anti-D, within 48 hours of delivery.
Outcomes	Immunisation after 6 months.
Notes	Results from Saskatoon have not been included as this site did not use concurrent controls. Figures for losses to follow up were not given.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Rh: Rhesus
vs: versus

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Beer 1969	Separate results not given for numbers of mothers immunised. Alternate allocation of treatment.
Hamilton 1967	Historical controls; allocation of treatment not randomised.

Study	Reason for exclusion
Schneider 1966	Cannot establish whether controls were used and there is no information on allocation of treatment.
Zipursky 1967	No mention of how treatment groups were chosen; no mention of randomisation.

DATA AND ANALYSES

Comparison 1. Anti-D prophylaxis postpartum (overall, irrespective of ABO status)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	5	7580	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.08 [0.06, 0.11]
2 Immunisation in subsequent pregnancy	4	1071	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.07, 0.19]
3 Health of infant in subsequent pregnancy	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Adverse effects of treatment	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Anti-D prophylaxis postpartum (overall, irrespective of ABO status), Outcome 1 Immunisation after 6 months.

Analysis 1.2. Comparison 1 Anti-D prophylaxis postpartum (overall, irrespective of ABO status), Outcome 2 Immunisation in subsequent pregnancy.

Comparison 2. Anti-D prophylaxis postpartum (ABO compatible, irrespective of dose)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	4	6918	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.07 [0.05, 0.10]
2 Immunisation in subsequent pregnancy	4	1071	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.07, 0.19]

Analysis 2.1. Comparison 2 Anti-D prophylaxis postpartum (ABO compatible, irrespective of dose), Outcome 1 Immunisation after 6 months.

Analysis 2.2. Comparison 2 Anti-D prophylaxis postpartum (ABO compatible, irrespective of dose), Outcome 2 Immunisation in subsequent pregnancy.

Comparison 3. Anti-D prophylaxis postpartum, up to 200 ug versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	1	715	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.13 [0.04, 0.40]
2 Immunisation at subsequent pregnancy	1	255	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.10, 0.72]

Analysis 3.1. Comparison 3 Anti-D prophylaxis postpartum, up to 200 ug versus no treatment, Outcome 1 Immunisation after 6 months.

Analysis 3.2. Comparison 3 Anti-D prophylaxis postpartum, up to 200 ug versus no treatment, Outcome 2 Immunisation at subsequent pregnancy.

Comparison 4. Anti-D prophylaxis postpartum, up to 250 ug versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after six months	2	1377	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.19 [0.09, 0.37]
2 Immunisation at subsequent pregnancy	1	255	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.10, 0.72]

Analysis 4.1. Comparison 4 Anti-D prophylaxis postpartum, up to 250 ug versus no treatment, Outcome 1 Immunisation after six months.

Analysis 4.2. Comparison 4 Anti-D prophylaxis postpartum, up to 250 ug versus no treatment, Outcome 2 Immunisation at subsequent pregnancy.

Comparison 5. Anti-D prophylaxis postpartum, up to 300 ug versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	3	5936	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.08 [0.05, 0.11]
2 Immunisation at subsequent pregnancy	2	872	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.11 [0.06, 0.21]

Analysis 5.1. Comparison 5 Anti-D prophylaxis postpartum, up to 300 ug versus no treatment, Outcome 1 Immunisation after 6 months.

Analysis 5.2. Comparison 5 Anti-D prophylaxis postpartum, up to 300 ug versus no treatment, Outcome 2 Immunisation at subsequent pregnancy.

Comparison 6. Anti-D prophylaxis postpartum, 4000-7000 ug versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	2	584	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.10 [0.04, 0.22]
2 Immunisation at subsequent pregnancy	1	16	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.02 [0.00, 1.69]

Analysis 6.1. Comparison 6 Anti-D prophylaxis postpartum, 4000-7000 ug versus no treatment, Outcome 1 Immunisation after 6 months.

Analysis 6.2. Comparison 6 Anti-D prophylaxis postpartum, 4000-7000 ug versus no treatment, Outcome 2 Immunisation at subsequent pregnancy.

Comparison 7. Dosage comparison, up to 50 ug versus more than 50 ug anti-D

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	1	1800	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.36 [0.97, 11.63]
2 Immunisation in subsequent pregnancy	1	807	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.53 [1.02, 6.27]

Analysis 7.1. Comparison 7 Dosage comparison, up to 50 ug versus more than 50 ug anti-D, Outcome 1 Immunisation after 6 months.

Analysis 7.2. Comparison 7 Dosage comparison, up to 50 ug versus more than 50 ug anti-D, Outcome 2 Immunisation in subsequent pregnancy.

Comparison 8. Dosage comparison, up to 100 ug versus more than 100 ug anti-D

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	1	1800	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.27 [0.55, 9.45]
2 Immunisation in subsequent pregnancy	1	807	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.69 [0.60, 4.79]

Analysis 8.1. Comparison 8 Dosage comparison, up to 100 ug versus more than 100 ug anti-D, Outcome 1 Immunisation after 6 months.

Analysis 8.2. Comparison 8 Dosage comparison, up to 100 ug versus more than 100 ug anti-D, Outcome 2 Immunisation in subsequent pregnancy.

Comparison 9. Dosage comparison, up to 150 ug versus more than 150 ug anti-D

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Immunisation after 6 months	2	3010	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.27 [0.55, 9.45]
2 Immunisation in subsequent pregnancy	1	807	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.69 [0.60, 4.79]

Analysis 9.1. Comparison 9 Dosage comparison, up to 150 ug versus more than 150 ug anti-D, Outcome 1 Immunisation after 6 months.

Analysis 9.2. Comparison 9 Dosage comparison, up to 150 ug versus more than 150 ug anti-D, Outcome 2 Immunisation in subsequent pregnancy.

WHAT'S NEW

Date	Event	Description
31 March 2010	New search has been performed	Search updated. No new trials identified.

HISTORY

Protocol first published: Issue 2, 1997

Review first published: Issue 2, 1997

Date	Event	Description
10 November 2008	Amended	Corrected error in Plain Language Summary. Contact details updated.
6 March 2008	Amended	Converted to new review format.
25 June 2007	New search has been performed	Search updated. No new trials identified.
10 November 2004	New search has been performed	Search updated. No new trials identified.
22 November 2000	New search has been performed	Search updated. Minor editing to background, discussion and references.

CONTRIBUTIONS OF AUTHORS

Both review authors contributed to the development of the protocol, identification and selection of studies for inclusion, data extraction and preparation of the text of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Discipline of Obstetrics and Gynaecology, The University of Adelaide, Australia.
- Australasian Cochrane Centre, Australia.

External sources

- No sources of support supplied

INDEX TERMS**Medical Subject Headings (MeSH)**

Postpartum Period; Rh Isoimmunization [*prevention & control]; Rho(D) Immune Globulin [*therapeutic use]

MeSH check words

Female; Humans