Interventions for treating genital chlamydia trachomatis infection in pregnancy (Review)

Brocklehurst P, Rooney G

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

http://www.thecochranelibrary.com

TABLE OF CONTENTS

Interventions for treating genital chlamydia trachomatis infection in pregnancy (Review)

Brocklehurst P, Rooney G

This record should be cited as:
Brocklehurst P, Rooney G. Interventions for treating genital chlamydia trachomatis infection in pregnancy. *Cochrane Database of Systematic Reviews* 1998, Issue 4. Art. No.: CD000054. DOI: 10.1002/14651858.CD000054.

This version first published online: 26 October 1998 in Issue 4, 1998.
Date of most recent substantive amendment: 23 June 1998

ABSTRACT

Background
Chlamydia trachomatis is a sexually transmitted infection. Mother-to-child transmission can occur at the time of birth and may result in ophthalmia neonatorum or pneumonitis in the newborn.

Objectives
The objective of this review was to assess the effects of antibiotics in the treatment of genital infection with Chlamydia trachomatis during pregnancy with respect to neonatal and maternal morbidity.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (September 2006).

Selection criteria
Randomised trials of any antibiotic regimen compared with placebo or no treatment or alternative antibiotic regimens in pregnant women with genital Chlamydia trachomatis infection.

Data collection and analysis
Two review authors assessed trial quality and extracted data independently. Study authors were contacted for additional information.

Main results
Eleven trials were included. Trial quality was generally good. Amoxycillin appeared to be as effective as erythromycin in achieving microbiological cure (odds ratio 0.54, 95% confidence interval 0.28 to 1.02). Amoxycillin was better tolerated than erythromycin (odds ratio 0.16, 95% confidence interval 0.09 to 0.30). Clindamycin and azithromycin also appear to be effective, although the numbers of women included in trials are small.

Authors' conclusions
Amoxycillin appears to be an acceptable alternative therapy for the treatment of genital chlamydial infections in pregnancy when compared with erythromycin. Clindamycin and azithromycin may be considered if erythromycin and amoxycillin are contra-indicated or not tolerated.

PLAIN LANGUAGE SUMMARY

Antibiotics for chlamydia in pregnancy

Chlamydia is a sexually transmitted infection which, if a mother has it during pregnancy and labour, can cause eye or lung infections in the newborn baby. The risk of transmission during birth varies, but is about 20% to 50% for eye infections and about 10% to 20% for infection of the lungs. Mothers may also be at increased risk of infection of the uterus. The review looked at various antibiotics being used during pregnancy to reduce these problems and to assess any adverse effects. Tetracyclines taken in pregnancy are known to be

associated with teeth and bone abnormalities in babies, and some women find erythromycin unpleasant to take because of feeling sick and vomiting. The review found eleven trials, involving 1449 women, on erythromycin, amoxycillin, azithromycin and clindamycin, and the overall trial quality was good. However, all the trials assessed 'microbiological cure' (that is they looked for an eradication of the infection) and none assessed whether the eye or lung problems for the baby were reduced. Also, none of the trials were large enough to assess potential adverse outcomes adequately. The review found amoxycillin was an effective alternative to erythromycin but lack of long-term assessment of outcomes caused concern about its routine use in practice. If erythromycin is used, some women may stop taking it because of adverse effects. Azithromycin and clindamycin are potential alternatives. More research is needed.

BACKGROUND

Chlamydia trachomatis is a sexually transmitted infection. Mother-to-child transmission can occur at the time of delivery and may result in ophthalmia neonatorum or pneumonitis in the neonate. Estimates of the risk of transmission at the time of delivery vary. The risk of mother-to-child transmission resulting in moderate to severe conjunctivitis appears to be approximately 15% to 25% and for pneumonitis 5% to 15%. Postpartum endometritis has also been associated with chlamydial infection, although the risk of this occurring in women infected with chlamydia at the time of delivery is not known.

The drugs of choice for the treatment of Chlamydia trachomatis infection are the tetracyclines; however, as the use of tetracyclines in pregnancy are known to be associated with teeth and bone abnormalities, erythromycin has been recommended as the first-line treatment. Some women find erythromycin unpleasant to take because of nausea and vomiting and this may result in poor compliance which may lead to persisting infection.

As a consequence other antibiotic regimens have been investigated as alternatives to erythromycin.

OBJECTIVES

To determine whether antibiotic therapy in women infected with genital Chlamydia trachomatis is effective in the prevention of neonatal chlamydial infection and postpartum endometritis. In the absence of this information, eradication of maternal infection as determined by microbiological cure has been taken as a surrogate outcome. The occurrence of side-effects of treatment is also included.

If antibiotics are effective, the review will seek to determine which antibiotics are effective and review their side-effect profile.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trials comparing antibiotic therapy with placebo or no therapy and all randomised controlled trials comparing two different antibiotic regimens in pregnant women with genital Chlamydia trachomatis infection (any method of diagnosis).

Types of participants

Women identified at any stage during the antenatal period as having genital Chlamydia trachomatis infection (symptomatic or asymptomatic). Co-infection with other sexually transmitted infections will not be a reason to exclude women from the review.

Types of intervention

1. Any antibiotic (any dosage and any route of administration) versus placebo or no therapy.
2. Comparisons of any two different antibiotic regimens.

Types of outcome measures

(i) Neonatal death
(ii) Ophthalmia neonatorum
(iii) Neonatal pneumonitis
(iv) Maternal postpartum endometritis
(v) Delivery less than 37 weeks' gestation
(vi) Failure to achieve microbiological cure
(vii) Side-effects sufficient to stop treatment/change treatment
(viii) Side-effects not sufficient to stop treatment
(ix) Fetal anomalies

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (September 2006).

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) monthly searches of MEDLINE;
(3) handsearches of 30 journals and the proceedings of major conferences;

(4) weekly current awareness search of a further 37 journals.

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 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

We did not apply any language restrictions.

METHODS OF THE REVIEW

All potential trials were selected for eligibility according to the criteria specified in the protocol. The information necessary for the review was abstracted from the report by each of the review authors independently and, where necessary, we requested additional information from the authors.

All trials were assessed for methodological quality using standard Cochrane criteria. Summary odds ratios have been calculated if appropriate (ie if there is no evidence of significant heterogeneity) using the Cochrane statistical software, RevMan.

DESCRIPTION OF STUDIES

For details of included studies, *see* table of 'Characteristics of included studies'. For details of excluded studies, *see* the table of 'Characteristics of excluded studies'.

METHODOLOGICAL QUALITY

We assessed the methodological quality for each included trial using a simple checklist, which included whether the allocated treatment was adequately concealed and the proportion of women lost to follow up.

Overall, the quality of the trials was good. Four of the eleven included trials were double blind and all trials reported losses to follow up. The description of the interventions was good (with the exception of Martin 1997) and the main outcome of all the trials was well described in most.

The process by which the interventions were randomly assigned was not well specified in two of the trials, although both papers stated that the allocation was random and both of these trials were double blind (Alger 1991; Bell 1982).

RESULTS

Antibiotic therapy for genital chlamydial infection in pregnancy reduces the number of women with positive cultures following treatment by approximately 90% when compared with placebo.

All the tested antibiotic regimens demonstrate a high level of 'microbiological cure' (with the exception of Martin 1997, which did not report this outcome). The data suggest that amoxycillin may even be superior to erythromycin in achieving microbiological cure, although this difference is not statistically significant.

When compared with erythromycin the use of amoxycillin was associated with a lower incidence of side-effects in general, and in particular with a lower incidence of side-effects sufficient to stop treatment. With the relatively small amount of data presented, azithromycin appears to be very well tolerated. Side-effects of clindamycin appear to be no different, in frequency, from those of erythromycin.

There is little evidence from any of the included trials that 'microbiological cure' is the same as prevention of neonatal infection or postnatal infection in the mother. One trial (Alary 1994), assessed neonatal infection by taking chlamydial cultures from the neonate at one week of age. No positive cultures were found from 152 neonates tested.

DISCUSSION

The suggestion that amoxycillin is a useful treatment for genital chlamydial infection is surprising. In vitro studies suggest that Chlamydia trachomatis is relatively insensitive to amoxycillin (Kuo 1977). This review, however, suggests very strongly that amoxycillin does eradicate chlamydial infection in pregnancy.

The number of women included in these trials is too small to assess whether the newer antibiotics included in this review such as azithromycin and clindamycin are safe for use in pregnancy, as rare adverse outcomes are unlikely to be detected and clinical experience with their use is limited.

'Microbiological cure' is used in these trials as an alternative to eradication of infection. This assumption may not hold true, however, and the extent to which it is true may vary between the different antibiotics being tested. Thus, if two antibiotics appear to be equally effective in terms of 'microbiological cure' there may still be differences in their effect on more substantive outcomes such as neonatal chlamydial infection. Unfortunately, no trial reported this information in terms of clinical disease.

AUTHORS' CONCLUSIONS

Implications for practice

This review suggests that, in terms of microbiological 'cure', amoxycillin is an effective alternative to erythromycin for women with genital Chlamydia trachomatis infection in pregnancy. The lack of suitable data on the longer-term effectiveness of amoxycillin in terms of the risk of neonatal infection does, however, cause concern about its routine use in clinical practice.

The decision to implement using amoxycillin as the first line treatment for genital Chlamydia trachomatis infection in pregnancy will depend on the extent to which clinicians are satisfied that a negative 'test of cure' in the woman is equivalent to prevention of neonatal infection.

If erythromycin continues to be used as the treatment of choice in pregnancy then there seems little doubt that if women are intolerant of erythromycin then amoxycillin seems a suitable alternative. Clindamycin and azithromycin may be considered further alternatives if erythromycin and amoxycillin are contra-indicated or not tolerated.

Implications for research

Further studies are necessary to determine whether amoxicillin is associated with true eradication of Chlamydia trachomatis from the genital tract during pregnancy. Long-term follow up of a cohort of mothers and neonates treated with amoxycillin for genital chlamydial infection in pregnancy to precisely determine the risk of neonatal infection may be enough to reassure clinicians that the treatment is suitable for more widespread use. However, a large randomised comparison of amoxycillin and erythromycin which addressed their relative effectiveness in preventing neonatal infection would be ideal.

The results obtained with clindamycin and azithromycin could usefully be repeated in larger trials which rely more on substantive outcome measures. If amoxycillin is adopted widely as first-line treatment for chlamydia in pregnancy then amoxycillin would be the appropriate control treatment for such trials.

POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

We are grateful to Dr Alary, Dr Alger and Dr Silverman who provided us with extra information from their trials.

SOURCES OF SUPPORT

External sources of support

- Department of Health UK

Internal sources of support

- No sources of support supplied

REFERENCES

References to studies included in this review

Adair 1998 *{published data only}*

Adair CD, Gunter M, Stovall TG, Mcelroy G, Veille J-C, Ernest JM. Chlamydia in pregnancy: a randomized trial of azithromycin and erythromycin. *Obstet Gynecol* 1998;**91**:165–168.

Alary 1994 *{published data only}*

Alary M, Joly JR, Moutquin J-M, Mondor M, Boucher M, Fortier A, Pinault J-J, Paris G, Carrier S, Chamberland H, Bernatchez H, Paradis J-F. Randomised comparison of amoxycillin and erythromycin in treatment of genital chlamydial infection in pregnancy. *Lancet* 1994; **344**:1461–1465.

Alger 1991 *{published and unpublished data}*

Alger LS, Lovchik JC. Comparative efficacy of clindamycin versus erythromycin in eradication of antenatal Chlamydia trachomatis. *Am J Obstet Gynecol* 1991;**165**:375–381.

Bell 1982 *{published data only}*

Bell TA, Sandstrom IK, Eschenbach DA, Hummel D, Kuo C-C, Wang S-P, Grayston JT, Foy HM, Stamm WE, Holmes KK. Treatment of Chlamydia trachomatis in pregnancy with amoxicillin. In: MardhPA, et al. editor(s). *Chlamydial Infections*. Elsevier Biomedical Press, 1982:221–224.

Bush 1994 *{published data only}*

Bush MR, Rosa C. Azithromycin and erythromycin in the treatment of cervical chlamydial infection during pregnancy. *Obstet Gynecol* 1994;**84**:61–63.

Edwards 1996 *{published data only}*

Edwards MS, Newman RB, Carter SG, LeBoeuf FW, Menard MK, Rainwater KP. Randomized clinical trial of azithromycin for the treatment of Chlamydia cervicitis in pregnancy. *Infect Dis Obstet Gynecol* 1996;**4**:333–337.

Magat 1993 *{published data only}*

Magat AH, Alger LS, Nagey DA, Hatch V, Lovchik JC. Double-blind randomized study comparing amoxicillin and erythromycin for the treatment of Chlamydia trachomatis in pregnancy. *Obstet Gynecol* 1993;**81**:745–749.

Martin 1997 *{published data only}*

Martin DH, Eschenbach DA, Cotch MF, Nugent RP, Roa AV, Klebanoff MA, Lou Y, Rettig PJ, Gibbs RS, Pastorek JG, Regan

JA, Kaslow RA. Double-blind placebo-controlled treatment trial of Chlamydia trachomatis endocervical infections in pregnant women. *Inf Dis Obstet Gynecol* 1997;**5**:10–17.

Rosenn 1995 *{published data only}*

Rosenn M, Macones GA, Silverman N. A randomized trial of erythromycin and azithromycin for the treatment of chlamydia infection in pregnancy (abstract). *Am J Obstet Gynecol* 1996;**174**:410.

Rosenn MF, Macones GA, Silverman NS. Randomized trial of erythromcyin and azithromycin for treatment of chlamydial infection in pregnancy. *Inf Dis Obstet Gynecol* 1995;**3**:241–244.

Silverman 1994 *{published data only}*

Silverman N, Hochman M, Sullivan M, Womack M. A randomized prospective trial of amoxicillin versus erythromycin for the treatment of chlamydia in pregnancy (abstract). *Am J Obstet Gynecol* 1993;**168**: 420.

Silverman NS, Sullivan M, Hochman M, Womack M, Jungkind DL. A randomized, prospective trial comparing amoxicillin and erythromycin for the treatment of Chlamydia trachomatis in pregnancy. *Am J Obstet Gynecol* 1994;**170**:829–832.

Turrentine 1995 *{published data only}*

Turrentine MA, Troyer L, Gonik B. Randomized prospective study comparing erythromycin, amoxicillin and clindamycin for the treatment of Chlamydia trachomatis in pregnancy. *Inf Dis Obstet Gynecol* 1995;**2**:205–209.

References to studies excluded from this review

Crombleholme 1990

Crombleholme WR, Schachter J, Grossman M, Landers DV, Sweet RL. Amoxicillin therapy for Chlamyida trachomatis in pregnancy. *Obstet Gynecol* 1990;**75**:752–756.

McGregor 1990

McGregor JA, French JI, Richter R, Vuchetich M, Bachus V, Seo K, Hillier S, Judson FN, McFee J, Schoonmaker J, Todd JK. Cervicovaginal microflora and pregnancy outcome: results of a double-blind, placebo-controlled trial of erythromycin treatment. *Am J Obstet Gynecol* 1990;**163**:1580–1591.

Thomason 1990

Thomason JL, Kellett AV, Gelbart SM, James JA, Broekhuizen FF. Short-course erythromycin therapy for endocervical chlamydia during pregnancy. *J Family Practice* 1990;**30**:711–712.

References to studies awaiting assessment

Jacobson 2001

Jacobson GF, Autry AM, Kirby RS, Liverman EM, Motley RU. A randomized controlled trial comparing amoxicillin and azithromycin for the treatment of chlamydia trachomatis in pregnancy. *American Journal of Obstetrics and Gynecology* 2001;**184**(7):1352–4.

Kacmar 2001

Kacmar J, Cheh E, Montagno A, Peipert JF. A randomized trial of azithromycin versus amoxicillin for the treatment of Chlamydia trachomatis in pregnancy. *Infectious Diseases in Obstetrics & Gynecology* 2001;**9**:197–202.

Nadafi 2005

Nadafi M, Abdali KH, Parsanejad ME, Rajaee-Fard AR, Kaviani M. A comparison of amoxicillin and erythromycin for asymptomatic chlamydia trachomatis infection in pregnancy. *International Journal of Gynecology & Obstetrics* 2005;**90**(2):142–3.

Wehbeh 1996

Wehbeh H, Ruggiero R, Ali Y, Lopez G, Shahem S, Zarou D. A randomized clinical trial of a single dose of zithromycin in treatment of chlamydia amongst pregnant women. *American Journal of Obstetrics and Gynecology* 1996;**174**(1 Pt 2):361.

Wehbeh 1998

Wehbeh HA, Ruggeirio RM, Shahem S, Lopez G, Ali Y. Single-dose azithromycin for chlamydia in pregnant women. *Journal of Reproductive Medicine* 1998;**43**(6):509–14.

Zul'karneev 1998

Zul'karneev RSh, Kalinin IuT, Afanas'ev SS, Rubal'skii OV, Denisov LA, Vorob'ev AA, Sorokin SV. Use of recombinant alpha2-interferon and a complex immunoglobulin preparation for the treatment of chlamydiosis in pregnancy women. *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* 1998, (2):115–8.

Additional references

Kuo 1977

Kuo CC, Wang SP, Grayston TJ. Antimicrobial activity of several antibiotics and a sulfonamide against Chlamydia trachomatis organisms in cell culture. *Antimicrob Agents Chemother* 1977;**12**:80–80.

TABLES

Characteristics of included studies

Study	Adair 1998
Methods	Random numbers generated in blocks of 20. Allocation cards in sealed opaque envelopes.
Participants	106 pregnant women with positive cervical swabs of Chlamydia trachomatis using a direct DNA probe. Exclusions - hypersensitivity to study drugs.

Characteristics of included studies (*Continued*)

Interventions	Azithromycin 1 g stat Erythromycin 500 mg four times a day for 7 days All partners referred for treatment.
Outcomes	Test of cure using DNA probe 3 weeks after start of treatment Side effects.
Notes	Not blinded 9/54 of azithromycin and 7/52 of erythromycin lost to follow-up (no outcome data).
Allocation concealment	A – Adequate

Study	**Alary 1994**
Methods	Random allocation.
Participants	210 pregnant women with positive cervical or urethral cultures of Chlamydia trachomatis. Exclusions - >38 weeks at diagnosis, treatment with antibiotics between the cervical culture being taken and randomisation, known allergy to the study drugs.
Interventions	Erythromycin 500 mg four times a day for 7 days Amoxicillin 500 mg three times a day for 7 days All partners treated with doxycycline.
Outcomes	Test of cure by culture 21 days after the completion of study drug Swabs taken from babies' eyes, nose, pharynx, rectum and genitals for culture of Chlamydia trachomatis at age 1 week.
Notes	Double blind. Amoxicillin recipients received a dummy dose to make both drug regimens four times a day. 5/105 in amoxicillin group and 6/105 in erythromycin group lost to follow-up (no outcome data).
Allocation concealment	D – Not used

Study	**Alger 1991**
Methods	'Random allocation' - method not specified.
Participants	135 pregnant women with positive cervical cultures of Chlamydia trachomatis. Exclusions - >24 weeks at diagnosis, recent antibiotic use, known allergy to study drugs, impaired hepatic function, colitis, current use of insulin, warfarin, steroids and carbamazepine.
Interventions	Erythromycin 333 mg plus clindamycin placebo four times a day for 14 days Clindamycin 450 mg plus erythromycin placebo four times a day for 14 days Clindamycin placebo and erythromycin placebo four times a day for 14 days All partners treated with doxycycline.
Outcomes	Test of cure by culture 14 days after first dose of study drug Second test of cure 4 weeks later Final test of cure in labour.
Notes	Double blind 9/135 women lost to follow-up (no outcome data).
Allocation concealment	D – Not used

Study	**Bell 1982**
Methods	'Random allocation' - method not specified.
Participants	27 pregnant women with positive cervical cultures of Chlamydia trachomatis. Exclusions - >24 weeks at diagnosis, known allergy to study drugs.
Interventions	Amoxicillin 500 mg three times a day for 10 days Matching placebo

Characteristics of included studies (*Continued*)

	All partners treated with tetracycline or doxycycline.
Outcomes	Infant infection determined by multiple culture and serology of blood and tears Maternal post partum endometritis.
Notes	Double blind 2/13 in amoxicillin group and 4/14 in placebo group lost to follow-up (no outcome data).
Allocation concealment	B – Unclear

Study	**Bush 1994**
Methods	Random allocation by sealed opaque envelopes.
Participants	30 pregnant women with positive cervical swabs of Chlamydia trachomatis using DNA assay.
Interventions	Erythromycin 500 mg four times a day for 7 days Azithromycin 1 g single dose All partners treated with doxycycline.
Outcomes	Test of cure using DNA assay 14 days after completion of study drug.
Notes	Not double blind No loss to follow-up.
Allocation concealment	D – Not used

Study	**Edwards 1996**
Methods	Random number table.
Participants	140 pregnant women with positive cervical swab for Chlamydia trachomatis using DNA hybridisation. Exclusions - <15 years, known allergy to study drugs.
Interventions	Erythromycin 500 mg four times a day for 7 days Azithromycin 1 g stat All partners referred for treatment.
Outcomes	Test of cure 2 weeks after starting study drugs using DNA hybridisation.
Notes	Not blinded 7/72 in erythromycin group and 3/68 in azithromycin group lost to follow-up (no outcome data).
Allocation concealment	A – Adequate

Study	**Magat 1993**
Methods	Random allocation.
Participants	143 pregnant women with positive cervical cultures of Chlamydia trachomatis. Exclusions - >36 weeks at diagnosis, current antibiotic use, known allergy to study drugs, gastrointestinal upset, colitis.
Interventions	Erythromycin 500 mg four times a day for 7 days Amoxicillin 500 mg three times a day for 7 days All partners treated with doxycycline.
Outcomes	Test of cure by culture 4 weeks after first dose of study drug.
Notes	Not double blind 6/71 erythromycin group and 7/72 in amoxycillin group lost to follow-up (no outcome data).
Allocation concealment	D – Not used

Study	**Martin 1997**
Methods	Random number generator with random block sizes of 2, 4 and 6

Characteristics of included studies (*Continued*)

	Stratified by centre.
Participants	423 pregnant women at 23-29 weeks gestation with positive cervical Chlamydia trachomatis cultures. Exclusions - <16 years, medical complications related to preterm delivery, antibiotics after initial culture and prior to trial entry, allergy to erythromycin, receiving theophylline, co-infection with gonorrhoea.
Interventions	Erythromycin base 333 mg three times a day until completion of 35th week gestation (minimum of 6 weeks) Matching placebo All partners referred for treatment All women treated with doxycycline, tetracycline or erythromycin after delivery - infants either treated empirically or followed-up.
Outcomes	Test of cure with culture 2-4 weeks after enrolment (results not reported) Low birth weight Premature rupture of membranes Preterm delivery.
Notes	Double blind 1 week run-in period to assess compliance - 180/594 (30%) excluded following run-in 3/208 in erythromycin group and 6/215 in placebo group lost to follow-up (no outcome data).
Allocation concealment	A – Adequate

Study	**Rosenn 1995**
Methods	Random numbers in block size 6. Sequentially numbered sealed opaque envelopes.
Participants	48 pregnant women positive for Chlamydia trachomatis screened at their first prenatal visit by DNA PCR. Exclusions - 36 weeks or greater, antibiotics in 14 days prior to enrolment, co-infection with gonorrhoea, sensitivity to study drugs.
Interventions	Erythromycin 500 mg four times a day for 7 days Azithromycin 1 g stat All partners treated.
Outcomes	Test of cure by DNA PCR 3 weeks after study drug finished.
Notes	Not double blind 1/24 in azithromycin group and 2/24 in erythromycin group lost to follow-up (no outcome data).
Allocation concealment	A – Adequate

Study	**Silverman 1994**
Methods	Sequentially numbered opaque envelopes.
Participants	74 pregnant women with positive cervical cultures of Chlamydia trachomatis. Exclusions - >36 weeks at diagnosis, recent antibiotic use (within 14 days), known allergy to study drugs.
Interventions	Erythromycin 500 mg four times a day for 7 days Amoxicillin 500 mg three times a day for 7 days All partners treated with doxycycline.
Outcomes	Test of cure by culture 3-4 weeks after starting study drugs.
Notes	Not double blind 4/36 in erythromycin group and 4/38 in amoxicillin group lost to follow-up (no outcome data).
Allocation concealment	D – Not used

Study	**Turrentine 1995**
Methods	Random allocation.

Participants	113 pregnant women with positive cervical cultures of Chlamydia trachomatis. Exclusions - >36 weeks at diagnosis, current antibiotic use, known allergy to study drugs, gastrointestinal upset.
Interventions	Erythromycin 500 mg four times a day for 7 days Amoxicillin 500 mg three times a day for 7 days Clindamycin 600 mg three times a day for 10 days All partners treated with doxycyline.
Outcomes	Test of cure by culture 4 weeks after study drug finished.
Notes	Not double blind 3/56 in erythromycin group, 2/57 in amoxicillin group and 3/55 in clindamycin group lost to follow-up (no outcome data).
Allocation concealment	D – Not used

DNA = deoxyribonucleic acid
PCR = polymerase chain reaction
stat = given once

Characteristics of excluded studies

Study	Reason for exclusion
Crombleholme 1990	Pregnant women with cervical Chlamydia trachomatis infection were 'offered' amoxycillin treatment. If they declined they were given erythromycin. No element of random allocation was included in this study.
McGregor 1990	Women were selected for trial entry on the basis of a high population risk of preterm delivery and treated with erythromycin or placebo. Of the 229 women enrolled, 26 had a positive culture for endocervical Chlamydia trachomatis. No outcome data is presented by infection status at recruitment.
Thomason 1990	Historical cohort study comparing standard duration of erythromycin therapy with a short course. Not random allocation.

ANALYSES

Comparison 01. Antibiotic therapy versus placebo or no therapy

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal death	1	405	Peto Odds Ratio 95% CI	7.43 [0.15, 374.24]
02 Ophthalmia neonatorum	0	0	Peto Odds Ratio 95% CI	Not estimable
03 Neonatal pneumonitis	0	0	Peto Odds Ratio 95% CI	Not estimable
04 Maternal postpartum endometritis	1	15	Peto Odds Ratio 95% CI	0.64 [0.03, 12.03]
05 Delivery < 37 weeks	1	405	Peto Odds Ratio 95% CI	0.89 [0.51, 1.56]
06 Failure to achieve microbiological cure	1	122	Peto Odds Ratio 95% CI	0.06 [0.03, 0.12]
07 Side-effects sufficient to stop treatment	2	141	Peto Odds Ratio 95% CI	4.83 [0.60, 38.67]
08 Side-effects not sufficient to stop treatment	3	546	Peto Odds Ratio 95% CI	1.36 [0.96, 1.94]
09 Fetal anomalies	0	0	Peto Odds Ratio 95% CI	Not estimable

Comparison 02. Amoxicillin versus erythromycin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal death	0	0	Peto Odds Ratio 95% CI	Not estimable
02 Ophthalmia neonatorum	0	0	Peto Odds Ratio 95% CI	Not estimable
03 Neonatal pneumonitis	0	0	Peto Odds Ratio 95% CI	Not estimable
04 Maternal postpartum endometritis	0	0	Peto Odds Ratio 95% CI	Not estimable
05 Delivery < 37 weeks	0	0	Peto Odds Ratio 95% CI	Not estimable
06 Failure to achieve microbiological cure	3	390	Peto Odds Ratio 95% CI	0.54 [0.28, 1.02]
07 Side-effects sufficient to stop treatment	4	503	Peto Odds Ratio 95% CI	0.16 [0.09, 0.30]
08 Side-effects not sufficient to stop treatment	3	304	Peto Odds Ratio 95% CI	0.25 [0.13, 0.48]
09 Fetal anomalies	0	0	Peto Odds Ratio 95% CI	Not estimable

Comparison 03. Azithromycin versus erythromycin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal death	1	130	Peto Odds Ratio 95% CI	Not estimable
02 Ophthalmia neonatorum	0	0	Peto Odds Ratio 95% CI	Not estimable
03 Neonatal pneumonitis	0	0	Peto Odds Ratio 95% CI	Not estimable
04 Maternal postpartum endometritis	0	0	Peto Odds Ratio 95% CI	Not estimable
05 Delivery < 37 weeks	1	130	Peto Odds Ratio 95% CI	0.73 [0.24, 2.20]
06 Failure to achieve microbiological cure	4	290	Peto Odds Ratio 95% CI	0.38 [0.19, 0.74]
07 Side-effects sufficient to stop treatment	3	160	Peto Odds Ratio 95% CI	0.15 [0.05, 0.45]
08 Side-effects not sufficient to stop treatment	4	289	Peto Odds Ratio 95% CI	0.13 [0.08, 0.20]
09 Fetal anomalies	1	130	Peto Odds Ratio 95% CI	1.00 [0.06, 16.16]

Comparison 04. Clindamycin versus erythromycin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal death	0	0	Peto Odds Ratio 95% CI	Not estimable
02 Ophthalmia neonatorum	0	0	Peto Odds Ratio 95% CI	Not estimable
03 Neonatal pneumonitis	0	0	Peto Odds Ratio 95% CI	Not estimable
04 Maternal postpartum endometritis	0	0	Peto Odds Ratio 95% CI	Not estimable
05 Delivery < 37 weeks	0	0	Peto Odds Ratio 95% CI	Not estimable
06 Failure to achieve microbiological cure	1	78	Peto Odds Ratio 95% CI	0.42 [0.11, 1.68]
07 Side effects sufficient to stop treatment	2	187	Peto Odds Ratio 95% CI	0.40 [0.13, 1.18]
08 Side effects not sufficient to stop treatment	2	187	Peto Odds Ratio 95% CI	0.49 [0.22, 1.11]

09 Fetal anomalies	0	0	Peto Odds Ratio 95% CI	Not estimable

Comparison 05. Clindamycin versus amoxicillin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal death	0	0	Peto Odds Ratio 95% CI	Not estimable
02 Ophthalmia neonatorum	0	0	Peto Odds Ratio 95% CI	Not estimable
03 Neonatal pneumonitis	0	0	Peto Odds Ratio 95% CI	Not estimable
04 Maternal postpartum endometritis	0	0	Peto Odds Ratio 95% CI	Not estimable
05 Delivery < 37 weeks	0	0	Peto Odds Ratio 95% CI	Not estimable
06 Failure to achieve microbiological cure	0	0	Peto Odds Ratio 95% CI	Not estimable
07 Side-effects sufficient to stop treatment	1	107	Peto Odds Ratio 95% CI	2.14 [0.41, 11.01]
08 Side-effects not sufficient to stop treatment	1	107	Peto Odds Ratio 95% CI	2.97 [0.41, 21.69]
09 Fetal anomalies	0	0	Peto Odds Ratio 95% CI	Not estimable

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [*therapeutic use]; Chlamydia Infections [*drug therapy; *transmission]; *Chlamydia trachomatis; Disease Transmission, Vertical [*prevention & control]; Genital Diseases, Female [*drug therapy]; Pregnancy Complications, Infectious [*drug therapy]

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Interventions for treating genital chlamydia trachomatis infection in pregnancy
Authors	Brocklehurst P, Rooney G
Contribution of author(s)	Information not supplied by author
Issue protocol first published	1996/2
Review first published	1997/2
Date of most recent amendment	20 February 2007
Date of most recent SUBSTANTIVE amendment	23 June 1998
What's New	February 2007 Plain language summary added. We updated the search in September 2006. The six new reports of trials identified through the updated search (Jacobson 2001; Kacmar 2001; Nadafi 2005; Wehbeh 1996; Wehbeh 1998; Zul'karneev 1998) have been added to the 'Studies awaiting assessment' and will be assessed for the 2007 update later this year.
Date new studies sought but none found	Information not supplied by author

Date new studies found but not yet included/excluded	05 September 2006
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Prof Peter Brocklehurst Director National Perinatal Epidemiology Unit University of Oxford Old Road Campus Old Road Headington Oxford OX3 7LF UK E-mail: peter.brocklehurst@npeu.ox.ac.uk Tel: +44 1865 289700 Fax: +44 1865 289701
DOI	10.1002/14651858.CD000054
Cochrane Library number	CD000054
Editorial group	Cochrane Pregnancy and Childbirth Group
Editorial group code	HM-PREG

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 01 Neonatal death

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy
Comparison: 01 Antibiotic therapy versus placebo or no therapy
Outcome: 01 Neonatal death

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Martin 1997	1/202	0/203		100.0	7.43 [0.15, 374.24]
Total (95% CI)	202	203		100.0	7.43 [0.15, 374.24]
Total events: 1 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.00 p=0.3					

Analysis 01.04. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 04 Maternal postpartum endometritis

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 01 Antibiotic therapy versus placebo or no therapy

Outcome: 04 Maternal postpartum endometritis

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Bell 1982	1/9	1/6		100.0	0.64 [0.03, 12.03]
Total (95% CI)	9	6		100.0	0.64 [0.03, 12.03]
Total events: 1 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.30 p=0.8					

Analysis 01.05. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 05 Delivery < 37 weeks

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 01 Antibiotic therapy versus placebo or no therapy

Outcome: 05 Delivery < 37 weeks

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Martin 1997	27/202	30/203		100.0	0.89 [0.51, 1.56]
Total (95% CI)	202	203		100.0	0.89 [0.51, 1.56]
Total events: 27 (Treatment), 30 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.41 p=0.7					

Analysis 01.06. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 06 Failure to achieve microbiological cure

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 01 Antibiotic therapy versus placebo or no therapy

Outcome: 06 Failure to achieve microbiological cure

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Alger 1991	9/78	34/44		100.0	0.06 [0.03, 0.12]
Total (95% CI)	78	44		100.0	0.06 [0.03, 0.12]
Total events: 9 (Treatment), 34 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=7.27 p<0.00001					

Analysis 01.07. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 07 Side-effects sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 01 Antibiotic therapy versus placebo or no therapy

Outcome: 07 Side-effects sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
× Bell 1982	0/9	0/6		0.0	Not estimable
Alger 1991	4/82	0/44		100.0	4.83 [0.60, 38.67]
Total (95% CI)	91	50		100.0	4.83 [0.60, 38.67]
Total events: 4 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.48 p=0.1					

Analysis 01.08. Comparison 01 Antibiotic therapy versus placebo or no therapy, Outcome 08 Side-effects not sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 01 Antibiotic therapy versus placebo or no therapy

Outcome: 08 Side-effects not sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Bell 1982	1/9	0/6		0.8	5.29 [0.10, 289.29]
Alger 1991	17/82	13/44		17.0	0.62 [0.26, 1.45]
Martin 1997	109/199	89/206		82.2	1.59 [1.08, 2.34]
Total (95% CI)	290	256		100.0	1.36 [0.96, 1.94]
Total events: 127 (Treatment), 102 (Control)					
Test for heterogeneity chi-square=4.31 df=2 p=0.12 I^2 =53.6%					
Test for overall effect z=1.73 p=0.08					

Analysis 02.06. Comparison 02 Amoxicillin versus erythromycin, Outcome 06 Failure to achieve microbiological cure

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 02 Amoxicillin versus erythromycin

Outcome: 06 Failure to achieve microbiological cure

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Silverman 1994	6/34	5/32		24.9	1.15 [0.32, 4.17]
Magat 1993	10/65	18/65		59.4	0.49 [0.21, 1.12]
Alary 1994	1/100	5/94		15.7	0.24 [0.05, 1.21]
Total (95% CI)	199	191		100.0	0.54 [0.28, 1.02]
Total events: 17 (Treatment), 28 (Control)					
Test for heterogeneity chi-square=2.38 df=2 p=0.30 I^2 =15.9%					
Test for overall effect z=1.89 p=0.06					

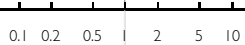
Analysis 02.07. Comparison 02 Amoxicillin versus erythromycin, Outcome 07 Side-effects sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 02 Amoxicillin versus erythromycin

Outcome: 07 Side-effects sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Alary 1994	1/100	12/99		30.4	0.16 [0.05, 0.50]
Turrentine 1995	2/55	6/53		18.6	0.33 [0.08, 1.38]
Magat 1993	1/65	15/65		35.2	0.14 [0.05, 0.39]
Silverman 1994	0/34	7/32		15.8	0.10 [0.02, 0.49]
Total (95% CI)	254	249		100.0	0.16 [0.09, 0.30]
Total events: 4 (Treatment), 40 (Control)					
Test for heterogeneity chi-square=1.36 df=3 p=0.72 I^2 =0.0%					
Test for overall effect z=5.75 p<0.00001					



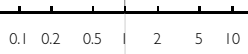
Analysis 02.08. Comparison 02 Amoxicillin versus erythromycin, Outcome 08 Side-effects not sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 02 Amoxicillin versus erythromycin

Outcome: 08 Side-effects not sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Turrentine 1995	1/55	8/53		22.2	0.18 [0.05, 0.70]
Magat 1993	4/65	15/65		43.6	0.26 [0.10, 0.69]
Silverman 1994	5/34	12/32		34.2	0.31 [0.10, 0.92]
Total (95% CI)	154	150		100.0	0.25 [0.13, 0.48]
Total events: 10 (Treatment), 35 (Control)					
Test for heterogeneity chi-square=0.38 df=2 p=0.83 I^2 =0.0%					
Test for overall effect z=4.20 p=0.00003					



Analysis 03.01. Comparison 03 Azithromycin versus erythromycin, Outcome 01 Neonatal death

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 01 Neonatal death

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
× Edwards 1996	0/65	0/65		0.0	Not estimable
Total (95% CI)	65	65		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

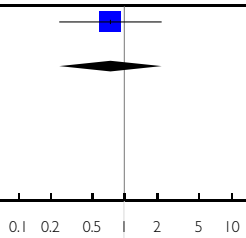
Analysis 03.05. Comparison 03 Azithromycin versus erythromycin, Outcome 05 Delivery < 37 weeks

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 05 Delivery < 37 weeks

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Edwards 1996	6/65	8/65		100.0	0.73 [0.24, 2.20]
Total (95% CI)	65	65		100.0	0.73 [0.24, 2.20]
Total events: 6 (Treatment), 8 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.56 p=0.6					



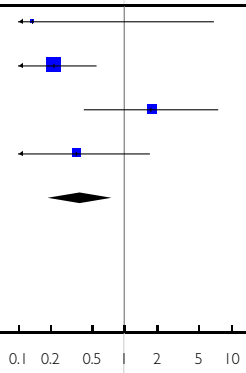
Analysis 03.06. Comparison 03 Azithromycin versus erythromycin, Outcome 06 Failure to achieve microbiological cure

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 06 Failure to achieve microbiological cure

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Bush 1994	0/15	1/15		3.0	0.14 [0.00, 6.82]
Edwards 1996	4/65	18/65		56.2	0.22 [0.09, 0.55]
Adair 1998	5/42	3/43		22.4	1.77 [0.42, 7.53]
Rosenn 1995	2/23	5/22		18.4	0.35 [0.07, 1.73]
Total (95% CI)	145	145		100.0	0.38 [0.19, 0.74]
Total events: 11 (Treatment), 27 (Control)					
Test for heterogeneity chi-square=6.02 df=3 p=0.11 I^2 =50.2%					
Test for overall effect z=2.80 p=0.005					



Analysis 03.07. Comparison 03 Azithromycin versus erythromycin, Outcome 07 Side-effects sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 07 Side-effects sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
× Bush 1994	0/15	0/15		0.0	Not estimable
Adair 1998	1/42	8/43		64.2	0.18 [0.05, 0.73]
Rosenn 1995	0/23	5/22		35.8	0.11 [0.02, 0.66]
Total (95% CI)	80	80		100.0	0.15 [0.05, 0.45]

Total events: 1 (Treatment), 13 (Control)

Test for heterogeneity chi-square=0.23 df=1 p=0.63 I^2 =0.0%

Test for overall effect z=3.37 p=0.0007

Analysis 03.08. Comparison 03 Azithromycin versus erythromycin, Outcome 08 Side-effects not sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 08 Side-effects not sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Bush 1994	0/15	15/15		11.3	0.02 [0.01, 0.09]
Edwards 1996	12/65	42/64		45.9	0.15 [0.07, 0.29]
Adair 1998	5/42	25/43		28.5	0.14 [0.06, 0.33]
Rosenn 1995	4/23	10/22		14.3	0.28 [0.08, 0.97]
Total (95% CI)	145	144		100.0	0.13 [0.08, 0.20]

Total events: 21 (Treatment), 92 (Control)

Test for heterogeneity chi-square=7.99 df=3 p=0.05 I^2 =62.5%

Test for overall effect z=8.60 p<0.00001

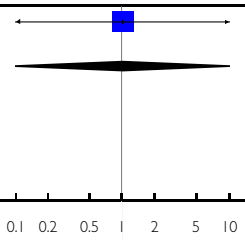
Analysis 03.09. Comparison 03 Azithromycin versus erythromycin, Outcome 09 Fetal anomalies

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 03 Azithromycin versus erythromycin

Outcome: 09 Fetal anomalies

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Edwards 1996	1/65	1/65		100.0	1.00 [0.06, 16.16]
Total (95% CI)	65	65		100.0	1.00 [0.06, 16.16]
Total events: 1 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					



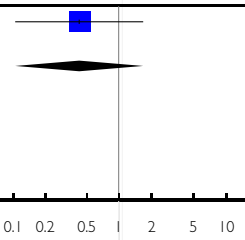
Analysis 04.06. Comparison 04 Clindamycin versus erythromycin, Outcome 06 Failure to achieve microbiological cure

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 04 Clindamycin versus erythromycin

Outcome: 06 Failure to achieve microbiological cure

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Alger 1991	3/41	6/37		100.0	0.42 [0.11, 1.68]
Total (95% CI)	41	37		100.0	0.42 [0.11, 1.68]
Total events: 3 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.22 p=0.2					



Analysis 04.07. Comparison 04 Clindamycin versus erythromycin, Outcome 07 Side effects sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 04 Clindamycin versus erythromycin

Outcome: 07 Side effects sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Alger 1991	0/42	4/40		29.6	0.12 [0.02, 0.88]
Turrentine 1995	4/52	6/53		70.4	0.66 [0.18, 2.41]
Total (95% CI)	94	93		100.0	0.40 [0.13, 1.18]

Total events: 4 (Treatment), 10 (Control)

Test for heterogeneity chi-square=1.98 df=1 p=0.16 I^2 =49.6%

Test for overall effect z=1.67 p=0.1

Analysis 04.08. Comparison 04 Clindamycin versus erythromycin, Outcome 08 Side effects not sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 04 Clindamycin versus erythromycin

Outcome: 08 Side effects not sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Alger 1991	7/42	10/40		57.8	0.61 [0.21, 1.75]
Turrentine 1995	3/52	8/53		42.2	0.37 [0.11, 1.29]
Total (95% CI)	94	93		100.0	0.49 [0.22, 1.11]

Total events: 10 (Treatment), 18 (Control)

Test for heterogeneity chi-square=0.34 df=1 p=0.56 I^2 =0.0%

Test for overall effect z=1.71 p=0.09

Analysis 05.07. Comparison 05 Clindamycin versus amoxicillin, Outcome 07 Side-effects sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 05 Clindamycin versus amoxicillin

Outcome: 07 Side-effects sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Turrentine 1995	4/52	2/55		100.0	2.14 [0.41, 11.01]
Total (95% CI)	52	55		100.0	2.14 [0.41, 11.01]
Total events: 4 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.91 p=0.4					

Analysis 05.08. Comparison 05 Clindamycin versus amoxicillin, Outcome 08 Side-effects not sufficient to stop treatment

Review: Interventions for treating genital chlamydia trachomatis infection in pregnancy

Comparison: 05 Clindamycin versus amoxicillin

Outcome: 08 Side-effects not sufficient to stop treatment

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Turrentine 1995	3/52	1/55		100.0	2.97 [0.41, 21.69]
Total (95% CI)	52	55		100.0	2.97 [0.41, 21.69]
Total events: 3 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.07 p=0.3					