

MATERNAL INFECTION SYNTHESIS

Research Gaps from Cochrane Reviews (Cochrane Library Issue 2, 2006)

(This document focuses on maternal outcomes – see ‘Infection in newborns’ for neonatal outcomes)

The faces indicate the direction of findings in each review:

- ☺ **Likely to be effective**
- ☹ **Both benefits and risks**
- ❓ **Uncertain or limited effect**
- ☹ **Likely to be ineffective or potentially harmful**

Important research implications are more likely to arise from reviews with uncertain findings or where the benefits and risks are mixed

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DURING PREGNANCY

Infections in general

- ☹ **Prophylactic antibiotics for women with unspecified risk for maternal infection (Thinkhamrop 2002)**
Need a trial of sufficient size to evaluate effects on reducing prelabour rupture of membranes
- ☺ **Prophylactic antibiotics reduce the risk of postpartum endometritis in high-risk pregnant women (Thinkhamrop 2002)**
Need to identify the most appropriate type and dosage of antibiotics in high-risk pregnant women

- ☺ **Prophylactic antibiotics for women in preterm labour with intact membranes (maternal infection reduced but reduction not shown for neonatal infection and some suggestion of neonatal harm with antibiotics) (King 2002)**
 - Need to research the type of antibiotic/s, especially addressing the possibility of improved outcomes with antibiotics active against anaerobes
 - Need to develop sensitive serological and/or bacteriological markers of subclinical infection for women in preterm labour with intact membranes
- ☺ **Antibiotic treatment of asymptomatic bacteriuria (Smaill 2001)**
 - Since antibiotics help prevent pyelonephritis and pre-term births, additional randomized trials of asymptomatic bacteriuria with a 'no treatment' arm are not advised
 - Sulphonamide, penicillin or nitrofurantoin are appropriate regimens for the management of asymptomatic bacteriuria, but the optimal time during pregnancy to perform the urine culture is unknown
- ☺ **Dose of antibiotics for asymptomatic bacteriuria (Villar 2000)**

Need to test whether single-dose drug is as effective as longer treatment regimens in prevention of preterm birth, pyelonephritis and recurrent infection (a WHO study of this is underway)
- ☺ **Antibiotics for symptomatic urinary tract infections during pregnancy (Vazquez 2003)**

Need to evaluate antibiotics such as nitrofurantoin, trimethoprim-sulfamethoxazole, cephalosporins and penicillins, in terms of duration (in single-dose or 3, 7, 10 or 15-day doses, or for the remainder of the pregnancy), acceptability (route and side effects), maternal outcomes, preterm birth and costs
- ☺ **Antibiotics for treating bacterial vaginosis (McDonald 2005)**
 - Future studies need to focus on earlier detection and treatment of bacterial vaginosis in the first trimester of pregnancy, or better still, pre-conception
 - Large trials are needed which can determine the effect of a screening programme for asymptomatic bacterial vaginosis on neonatal mortality and major measures of morbidity
 - Need to identify those subgroups of pregnant women who are at highest risk for adverse sequelae of bacterial vaginosis (including women with recurrent or persistent bacterial vaginosis)

Specific infections

- ☺ **Topical treatments for vaginal candidiasis (thrush) in pregnancy in pregnancy (Young 2001)**
 - Longer acting formulations could be tried to improve compliance
 - Research into the relative safety of any systemic treatment may be of limited value since topical treatment usually works
- ☺ **Antibiotics for treating chlamydia (Brocklehurst 1998)**

Further trials of clindamycin and azithromycin with amoxicillin as control are needed
- ☺ **Third trimester antiviral therapy for preventing recurrent genital herpes (Hollier 2004)**
 - Cochrane protocol
 - Not yet covered in a Cochrane review
- ☺ **Antibiotics for treating gonorrhoea (Brocklehurst 2002)**

Any further trials of antibiotic treatment for gonorrhoea in pregnancy should include more substantive outcome measures (than microbiological cure) as well as adverse effects
- ☺ **Prophylactic drugs for helminthic infections (Haider 2005)**
 - Cochrane protocol
 - Not yet covered in a Cochrane review
- ☺ **Antibiotics for treating sypilis (Walker 2001)**

No RCTs were located – while it is clear that penicillin is effective, the optimum regimens are uncertain
- ☺ **Antibiotics for treating symptomatic trichomoniasis (Gülmezoglu 2002)**

No maternal research implications were listed

- ☹ **Antibiotics for treating asymptomatic trichomoniasis (Gülmezoglu 2002)**
No maternal research implications were listed
 - ☹ **Treating toxoplasmosis in pregnancy (Peyron 1999)**
 - A large study could randomise health care clinics to no screening (existing practice in some countries) or screening, with follow up of seronegative women and treatment if they seroconvert
 - In countries where screening is already routine, all women would be offered routine screening, but treatment after seroconversion would be randomised e.g. to the following groups: spiramycin, with sulphonamides and pyrimethamine if fetal infection was identified at amniocentesis; spiramycin alone; sulfadoxine-pyrimethamine alone; and sulfadiazine with pyrimethamine
 - ☹ **Timing and type of prenatal treatment for congenital toxoplasmosis (Thiébaud 2003)**
 - Cochrane protocol
 - Not yet covered in a Cochrane review
 - ☹ **Antibiotics for treating ureaplasma (Raynes-Greenow 2004)**
No maternal research implications were listed
- Miscarriage** (see Miscarriage umbrella for full list of research gaps)
- ☹ **Significantly less infection seen for expectant compared with surgical management (Nanda 2006)**
Expectant management needs to be compared with medical management of miscarriage – see below
 - ☹ **Vaginal misoprostol for the treatment of non-viable pregnancies before 24 weeks (Neilson 2006)**
No research implications given related to infection
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PERI-PARTUM

Admission Procedures

- ☹ **Routine perineal shaving on admission in labour (Basevi 2000)**
Midwives and doctors who continue to perform routine perineal shaving on admission in labour may consider entering women into methodologically sound randomised controlled trials to evaluate the effectiveness and safety of their practice

Caesarean Section

- ☹ **Prophylactic antibiotics for women undergoing elective or non-elective cesarean section (Smail 2002)**
 - Further placebo controlled trials of the effectiveness of antibiotics with caesarean section are not ethically justified
 - Need to research methods to implement effective policies of routine prophylaxis for women undergoing caesarean section
 - Need to evaluate interventions to reduce further the incidence of infection e.g. topical antibiotics, and determine the role of surgical technique, pre- and intra-operative preparation and infection control policies on infection rates
 - Need to determine what role antimicrobial prophylactic regimens have in the development of antimicrobial resistance
 - Need to know more about the role of bacterial vaginosis and infectious complications following caesarean section and whether this has implications for current prophylactic recommendations
- ☹ **Few differences seen between ampicillin and first generation cephalosporins, broader spectrum agents or single versus multiple dose regimens (Hopkins 1999)**
Need a RCT comparing pre-operative administration versus administration immediately after the cord is clamped
- ☹ **Elective caesarean delivery versus vaginal delivery to reduce the incidence of perinatal transmission of the hepatitis C virus (McIntyre 2005)**
 - Cochrane protocol

- Not yet covered in a Cochrane review

☺ **Maternal infection after closure or non-closure of the peritoneum (Bamigboye 2003)**

Need to research long-term benefits and possible complications of non-closure of the peritoneum at caesarean section (a multicentre trial of techniques of caesarean section is in progress)

☺ **Effect of different techniques and materials for closure of the abdominal wall in caesarean section (Anderson 2004)**

- Need to research blunt needles which may protect operators and patients from blood-borne infections
- There are currently no published trials looking at different suture techniques or materials for closure of the rectus sheath or subcutaneous fat at caesarean section

Enemas

☺ **Two trials of enemas versus no enemas showed no differences for any maternal infections, but women not having enemas needed significantly more antibiotics (Cuervo 1999)**

Blinded trials are needed

Group B Streptococcus

☺ **Intrapartum antibiotics for Group B streptococcal colonisation (Smail 1996)**

- Need a sensitive rapid screening test to detect accurately women in labour who are colonized with GBS to make prevention strategies more efficient
- Uncertain whether prophylaxis should only be given to women with identified risk factors or to all women colonized with GBS. Need better data on maternal risk factors for neonatal GBS in different populations if the impact of different prevention strategies is to be more accurately evaluated

☺ **Vaginal chlorhexidine during labour to prevent early-onset neonatal group B streptococcal infection (Stade 2004)**

A large multi-centred double-blinded randomized trial measuring relevant outcomes including colonization of infants with GBS, early-onset GBS infection, early-onset GBS pneumonia and meningitis, and mortality rates must be conducted. The trial must overcome the methodological limitations of past trials

Immersion in water

☺ **Effect of immersion during pregnancy, labour and birth (Cluett 2002)**

Maternal infection during pregnancy, labour or birth has not been reported in any of the studies included in this Cochrane review

Induction of labour

☺ **Not clear if amniotomy increases maternal infection (Bricker 2000)**

Need to research different time intervals between the primary (amniotomy alone) and secondary intervention (addition of a pharmacological agent)

☺ **Intravenous oxytocin and amniotomy versus amniotomy for maternal infection (Howarth 2001)**

Need to research different time intervals between the primary (amniotomy alone) and secondary intervention (addition of a pharmacological agent)

☺ **Mechanical methods for induction of labour for maternal infection (Boulvain 2001)**

- Future studies on mechanical methods for induction of labour should be of large sample size and report on substantive outcomes
- Hyperstimulation, including the effect on fetal well-being, and maternal discomfort should be carefully assessed
- An economic analysis comparing mechanical methods with prostaglandins for cervical ripening would be useful

☺ **Membrane sweeping for induction of labour for maternal infection (Boulvain 2005)**

Is sweeping of the membranes is more effective in specific subgroups (parity, state of cervix)?

☺ **Intravenous oxytocin alone versus other methods of induction for maternal infection (Kelly 2001)**

Need to look at different intervals of commencing oxytocin or different doses of oxytocin

☹ **Prostaglandins versus oxytocin for induction of labour for maternal infection (Luckas 2000)**

The large trials necessary to address this question are not justified

☹ **Oral prostaglandin E2 for induction of labour for maternal infection (French 2001)**

Oral misoprostol (synthetic prostaglandin) is likely to supersede the oral preparations of PGE2 that are in current use

Operative vaginal birth

☹ **Prophylactic antibiotics for operative vaginal birth (Liabsuetrakul 2004)**

Only one trial which stopped early was located - future trials should be based on the principle of antibiotic prophylaxis for caesarean section with a single dose of intravenous ampicillin or first-generation cephalosporins after cord clamping

Preterm PROM

☹ **Routine use of antibiotics (erythromycin) for preterm prelabour PROM (Kenyon 2003)**

Future trials of antibiotic prophylaxis for preterm prelabour rupture of membranes need to measure long term outcomes (Kenyon 2003)

☹ **Planned management for prelabour rupture of membranes at 34 to 37 weeks' gestation (Buchanan 2004)**

- Cochrane protocol
- Not yet covered in a Cochrane review (Buchanan 2004)

Preventing infections

☹ **Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV) (Lumbiganon 2004)**

Since chlorhexidine solution is quite safe, not expensive and vaginal irrigation is not difficult to perform, there is a need for a well-designed randomized controlled trial with adequate sample size to evaluate this simple intervention, as well as determining the optimal volume of the solution used for irrigation

Term PROM

☹ **Prelabour prophylactic antibiotics for term PROM (Flenady 2002)**

Future trials of prelabour prophylactic antibiotics for term PROM should be blinded, adequately sized to address clinically important maternal and neonatal outcomes and include a cost analysis

☹ **Planned management for prelabour rupture of membranes at term (37 weeks or more) (Dare 2006)**

- Future trial design should attempt to blind outcomes such as maternal and neonatal infection and to report these outcomes in a standardised way.
- Outcomes such as maternal satisfaction, maternal and neonatal infectious morbidity, other neonatal morbidities, and longer term child development/disability need to be included in future trials.

INTRAPARTUM

☹ **Antibiotics for treating intra-amniotic infections (Hopkins 2002)**

Need to look at comparisons of different regimens and to measure long term outcomes such as consequences of neonatal cerebral damage

THIRD STAGE OF LABOUR

☹ **Prophylactic antibiotics for manual removal of retained placenta in vaginal birth (Chongsomchai 2006)**

- Multicentre randomised controlled trials comparing antibiotic prophylaxis and placebo or no antibiotic use to prevent endometritis after manual removal of placenta in vaginal birth are urgently needed
 - The sample size for detecting the decreased incidence of endometritis from 6% to 3% with 80% power and two tailed significant level of 0.05 is approximately 780 for a two group comparison
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POSTPARTUM

Breast infections

☺ Use of creams, friction, massage and the expression of colostrum for breast infections (Blyth 2004)

- Cochrane protocol
- Not yet covered in a Cochrane review

☺ Antibiotics for mastitis (Ng 2005)

- Cochrane protocol
- Not yet covered in a Cochrane review

Endometritis (postpartum treatment)

☺ Antibiotics for endometritis after birth (French 2004)

- Any further studies that compare clindamycin and an aminoglycoside with an alternative regimen, should consider alternatives suitable for use in low-income countries
- Any new regimen compared with clindamycin and an aminoglycoside include ototoxicity and nephrotoxicity as outcomes
- Need to evaluate early switching to the oral route, as newer antibiotics have improved oral bioavailability
- Role of endometrial cultures, collected under conditions where contamination is avoided, for targeting antibiotic therapy more specifically to individual women
- Poor activity against penicillin resistant anaerobes was associated with failure of the regimen
- No RCT looked at the effect of treatment on the infant of a breastfeeding mother

Perineal trauma

☺ Prophylactic antibiotics for severe perineal tears (Buppasiri 2005)

No trials of prophylactic antibiotics in fourth-degree perineal tear during vaginal birth located - well-designed, multicentre, randomised controlled trials are needed

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