

STIs in Pregnancy and Lactation



Seen at Watchersweb.com

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[Overview]

- Therapeutic STI drug use in pregnancy
- Therapeutic STI drug use in lactation
- Screening for STIs in pregnancy
- Clinical Scenario

United States – FDA 1979

United States FDA Pharmaceutical Pregnancy Categories

Pregnancy Category A

Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).

Pregnancy Category B

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies which have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.

Pregnancy Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Pregnancy Category D

There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Pregnancy Category X

Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Australia – ADEC

ADEC Pregnancy Categories (Australia)

Pregnancy Category A

Drugs which have been taken by a large number of pregnant women and women of childbearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Pregnancy Category B1

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Pregnancy Category B2

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Pregnancy Category B3

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Pregnancy Category C

Drugs which, owing to their pharmaceutical effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible.

Pregnancy Category D

Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.

Pregnancy Category X

Drugs that have such a high risk of causing permanent damage to the fetus that they should NOT be used in pregnancy or when there is a possibility of pregnancy.

NZ – Drugs in Pregnancy

- Risk:benefit approach – incomplete data
- Consider effect of the drug on the pregnancy, foetus or neonate
 - Teratogenicity
 - Pharmacological risks
- Pregnancy pharmacokinetics
 - Absorption, distribution, metabolism, elimination
- Timing of drug exposure
- Maternal infection carries the greater risk so Rx will be indicated – PTD, abortion, LBW, PPI



MENSTRUAL PERIOD

CONCEPTION
(Ovulation)

MISSED MENSTRUAL PERIOD

All drugs cross the placenta*

Principles of passive diffusion:
MWt<500, lipid solubility,
unionised, unbound to
proteins

Foetal [] \approx maternal []

THREE STAGES OF PREGNANCY

PRE-EMBRYONIC PERIOD

(days 0 - 17 post-conception)

EMBRYONIC PERIOD

(days 18 - 56 post-conception)

Greatest period of organogenesis

FOETAL PERIOD

(days 56 post-conception - term)

Therapeutic Drugs in Lactation (WHO/Unicef 2002) – Categories

1. Compatible with breastfeeding
2. Compatible with breastfeeding – monitor infant for side effects
3. Avoid if possible – monitor infant
4. Avoid if possible – may inhibit lactation
5. Avoid

Therapeutic Drugs in Lactation (WHO/Unicef 2002) Dept CAHD

- Mechanism of entry into breast milk: lipid solubility, mol Wt, maternal blood level, binding, oral bioavailability (mother and infant) and $T_{1/2}$
- Drugs should rarely preclude breastfeeding

Additional considerations:

- Premature babies and infants < 1/12 have ↓ capacity to absorb and excrete drugs
- Alcohol is the most common drug in pregnancy

Examples of Common STI Drugs

- Doxycycline: Pregnancy D (US) D (Aus)
Avoid in breastfeeding
 - Dose 100mg twice daily for 7 days (14 days in complicated)
 - FDA approved 1967. POM US/UK/Australasia
 - Legal indications in NZ for STIs and other infections
 - Warning against 2nd ½ pregnancy, infancy and children < 12yrs
 - Bioavailability 100%
 - T_{1/2} 18-22 hours and may have prolonged post Ab effect
 - Can cause permanent teeth discolouration in children and may inhibit bone growth in premature infants while treated
 - Not found to be teratogenic* or carcinogenic
 - *Risk of implantation failure in early pregnancy very small
 - NO significant loss of effectiveness of COC

Examples of Common STI Drugs

- Azithromycin: Pregnancy B (US) B1 (Aus)
Compatible with breastfeeding
 - Dose 1g single stat dose
 - FDA approved 1991. POM US/UK/Australasia
 - Legally indicated for use at any gestation
 - Bioavailability 38 – 50%
 - T_{1/2} 68 hours
 - Mostly bacteriostatic
 - Not known to be teratogenic or have foetal effects
 - Stat dose unlikely to ↓ effectiveness of COC but caution

Examples of Common STI Drugs

- Metronidazole: Pregnancy B (US) B2 (Aus)
 - Avoid if possible in breastfeeding – if using 1g stat dose express 1st + discontinue for 12 hrs
 - Dose 400mg bd for 7 days (or 14) or 1g oral stat dose
 - FDA approved but warning in **early** pregnancy + lactation remains
 - MNZ use in early pregnancy has been controversial because it is mutagenic in vitro in bacteria and carcinogenic in rodents
 - No similar effects found in humans – legally indicated in NZ for use at any gestation with warning for pregnancy and lactation
 - Bioavailability 100% (oral), 59-94% (rectal)
 - Hepatic metabolism, 80% renal excretion, 6-15% biliary
 - T_{1/2} 6 to 7 hours
 - Avoid peak serum levels in pregnancy (use 7 day course)
 - Does alter the taste of breast milk
 - Unlikely to ↓ effectiveness of COC but caution

STIs in Pregnancy

- STI incidence is related to young age, gender, ethnicity, partner change, non use of barrier contraception, and prior STI
- There is no evidence that STI incidence is lower in pregnant than for non pregnant women
- There are inconsistencies in antenatal screening guidelines and in clinical practice within NZ
- Screening programs are cost effective for both planned and unplanned pregnancies +/- TOPs

Cochrane Collaboration 2008

Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery (Intervention Review)

S U M M A R Y

A genital tract infection during pregnancy can cross into the amniotic fluid and result in prelabour rupture of the membranes and preterm labour. Such infections include bacterial vaginosis; chlamydial, trichomonas and gonorrhoeal infections; syphilis and HIV, but not candida. Preterm birth (before 37 weeks of gestation) is associated with poor infant health and early deaths, admission of the newborn to neonatal intensive care in the first few weeks of life, prolonged hospital stay and long-term neurologic disability including cerebral palsy.

The present systematic review found that a simple infection screening and treatment program during routine antenatal care may reduce preterm births and preterm low (below 2500 g) and very low (below 1500 g) birthweights, from only one identified controlled study.

[STIs in Pregnancy]

- STIs for which there is evidence that universal screening and treatment reduces maternal and/or neonatal morbidity/mortality
- Hepatitis B
- Chlamydia
- Gonorrhoea
- HIV
- Syphilis

[STIs in Pregnancy]

- STIs for which there is evidence that screening and treatment in *selected circumstances* improves pregnancy outcomes
- Bacterial vaginosis in women at risk of preterm delivery (wt < 50kg or previous PTD)
- Mothers with symptomatic genital herpes

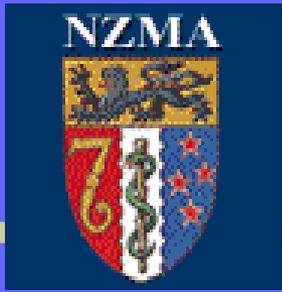
[STIs in Pregnancy]

- STIs for which there is insufficient evidence for routine screening*
- Asymptomatic *Trichomonas vaginalis*
- HCV

* Ongoing research required

[STIs in Pregnancy]

- STIs for which there is no evidence that screening affects pregnancy outcomes
- Genital HPV
- Molluscum contagiosum
- Pubic lice



Rates of *Chlamydia trachomatis* testing and chlamydial infection in pregnant women

Aims To determine the rate of *Chlamydia trachomatis* testing and chlamydial infection in pregnancy (by auditing a community medical laboratory database).

Results The overall rate of *C. trachomatis* testing for 6614 matched deliveries was 37.5%, with 4.8% of those tests positive for chlamydial infection. The rate of testing differed significantly between age-bands ($p < 0.0001$), and by ethnicity ($p < 0.0001$). The rate of infection showed a significant effect of age ($p < 0.0001$) and ethnicity ($p < 0.0001$). Maori and Pacific women, and those under the age of 25 years, had the highest rates—both of testing and of *C. trachomatis* infection.

Conclusions There is a high rate of maternal *C. trachomatis* in under 25-year-olds, and in Maori and Pacific women, together with incomplete testing for the infection in pregnancy. This highlights the need to instigate routine testing for *C. trachomatis* in pregnancy—to reduce the significant, yet preventable, morbidity associated with chlamydia in both the mother and the neonate.

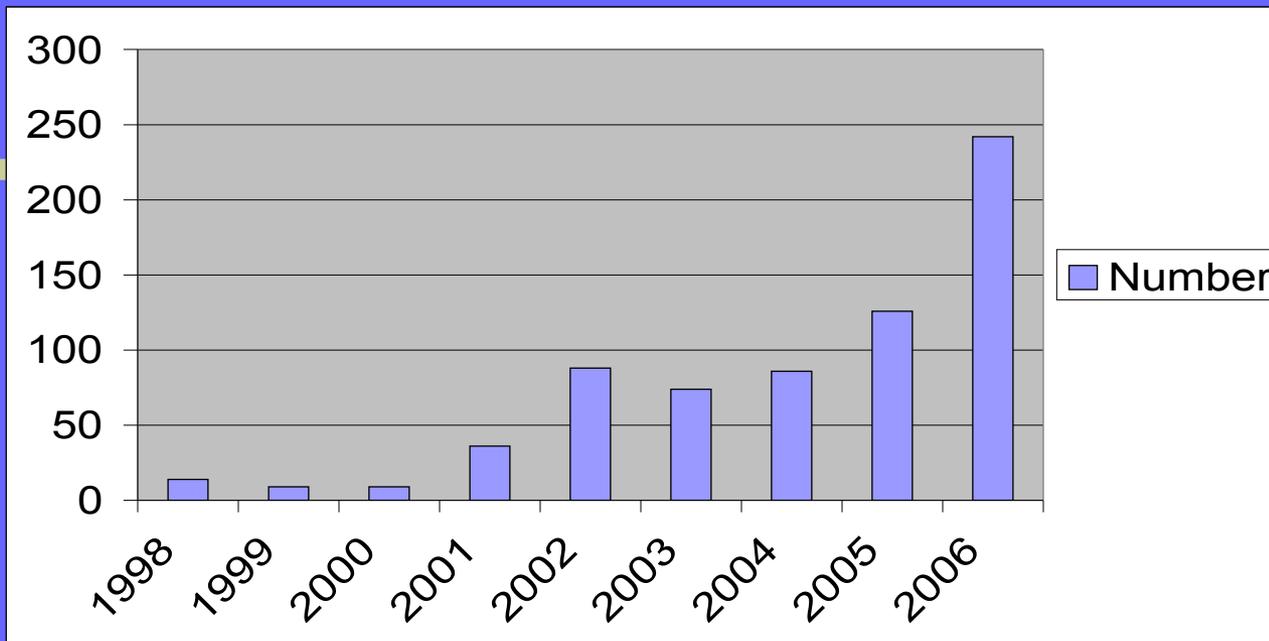


High rates of chlamydia in patients referred for termination of pregnancy: treatment, contact tracing, and implications for screening

Aims To determine the rate of chlamydia and other STIs and to describe treatment and factors associated with chlamydia in patients presenting for a TOP

Results Ten percent of patients tested positive for an STI. Chlamydia was most commonly detected, in 7.7% of all patients. Higher rates of chlamydia were observed at clinic B (10.2% vs 5.2%, $p=0.005$) and in under 25 year olds (11.2% vs 3.6%, $p<0.001$). Rates of chlamydia in Pacific women were 18.6%, in Maori 12.9%, in Asian 7.3% and 4.4% in New Zealand European women. All patients testing positive for chlamydia were treated prior to TOP but only 41% of partners were treated. Other infections detected included 18 cases of human papillomavirus (HPV), three cases of trichomoniasis, one case of gonorrhoea, and one case of syphilis.

Conclusions There is a high rate of chlamydia in women presenting for TOP, particularly in under 25 year olds, Pacific, and Maori women. There is an immediate need for policymakers to respond to this increasing burden of chlamydia by instigating targeted education, guidelines, and mandatory chlamydia screening and contact tracing for pregnant women.



Canterbury Health Laboratories positive gonorrhoea swabs. Data includes samples from Medlab South

| Year | 2003 | 2004 | 2005 | 2006 | 2007 |
|-------------------|------|------|------|------|------|
| % cipro sensitive | 93 | 78 | 87 | 90 | 52 |
| % pen sensitive | 50 | 22 | 13 | 19.8 | 22 |

Antenatal STI Screening Guidelines

- National Screening Unit – HIV
- MOH – none
(Sexual Health Advisory Group proposed Chlamydia Management Programme)
- RANZCOG – universal STS, HBV, HIV, HCV and risk-based Chlamydia testing
- RNZCGP – none
- NZCOM – none

More babies have chlamydia

The Press | Thursday, 08 May 2008



More than 100 babies were born infected with a sexually transmitted disease last year, a report into deteriorating sexual health shows.

“Chlamydia was spread at birth in 116 cases last year, while seven children aged under one were infected with gonorrhoea, according to incomplete laboratory data. These figures were higher than 2006 levels and are thought to underestimate actual levels.

The rates of infant infection called for effective screening during pregnancy, the report suggested. Both chlamydia and gonorrhoea can be treated with antibiotics.

Chlamydia posed a “considerable burden of disease” on both genders and could also lead to other reproduction difficulties including infertility, pelvic inflammatory disease and ectopic pregnancy, where the egg grows outside the uterus”

News Headline ?? 2008



THE PRESS

Integrated antenatal STI screening guideline
for NZ maternity services providers

Clinical Scenario

- 20 year old woman 8/40 G1P0
- No drug allergies, clinically well
- LAP 2/52, positive Chlamydia at antenatal booking
- BV on examination, cervical motion and uterine tenderness
- Antibiotic treatment regimen?

[Acknowledgements]

- Canterbury Drug Information Service
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