# Maternal and congenital syphilis – a problem that hasn't gone away

**IAN JONES** ChM, MEdStudies, FRANZCOG, FRCOG

**ALISTER JONES** BSc, MB BS

**Syphilis remains an important health issue for women, fetuses and neonates. Education, safe sexual practices, early diagnosis and adequate treatment (penicillin remains the gold standard) are the keys to management. All pregnant women should be screened for syphilis at their first antenatal visit.**

Syphilis in pregnancy can be almost completely eliminated by universal early antepartum screening. The US Centers for Disease Control and Prevention (CDC), the Royal Australian and New Zealand College of Obstetricians and Gynaecologists and the American College of Obstetricians and Gynecologists recommend screening for syphilis early in every pregnancy.[1-3] The co-existence of more than one sexually acquired infection is well recognised.[4]

The existence of syphilis has been known for over 500 years. The incidence of the disease dropped after the discovery of penicillin in the 1940s but rose again in the early 1990s. In addition, there has been another steady rise in the incidence of syphilis in men and women in the USA and Europe between 2000 and 2007.[5-7] Also, after 14 years of decline in the USA, the rate of congenital syphilis increased by 13% between 2006 and 2007.[5]

Professor Ian Jones is Professor of Obstetrics and Gynaecology at the University of Queensland and Executive Director of the Women's and Newborn Services, Royal Brisbane and Women's Hospital, Brisbane. Dr Alister Jones is a Resident Medical Officer at the Gold Coast Hospital, Southport, Qld.

Reports from Australia show that syphilis remains a serious health issue.[8-12] One Australian report, from Victoria, showed a rise in the incidence of syphilis in men who have sex with men, from 0.5% of patients tested in 2000 to 2.5% in 2004.[12] However, the incidence of notified syphilis in Australia varies considerably from year to year, as shown in Table 1.[13]

It appears that syphilis among heterosexuals is an emerging problem in the USA, despite most cases of syphilis in that country occurring in men who have sex with men.[5] A similar trend may also be appearing in Australia, and all health service providers need to remember that syphilis is not an eradicated disease.

## Mother-to-fetus transmission of syphilis

Syphilis is a chronic infection caused by the spirochaete *Treponema pallidum* (Figure 1). Almost all new syphilitic infections are acquired sexually or *in utero*; syphilis acquired by injecting drug use or blood transfusion is exceedingly rare and has not been documented in Australia. The incubation period ranges from 10 to 90 days, with a larger inoculum resulting in an incubation period shorter than the average of 21 days. Transmission of the spirochete requires exposure to open lesions containing the organism, such as abraded skin, although it can pass across intact mucous membranes. HIV infection does not appear to have an effect on syphilis transmission but syphilis enhances HIV transmission.

The placenta is not a barrier to the transmission of *T. pallidum* and vertical transmission during any stage of pregnancy and at delivery can result in congenital syphilis. Perinatal transmission occurs in almost all mothers with primary or secondary syphilis, with fewer congenital infections among those infants born to mothers with early latent syphilis (40%), late latent syphilis (10%) or tertiary syphilis (10%).[14]

Pregnancies affected by early syphilis (primary or secondary syphilis of less than two years' duration) may result in miscarriage, intrauterine growth restriction,

**Table 1. Notifications of infectious syphilis and congenital syphilis in Australia, 2004 to 2007**

| Year | Syphilis* | | | Congenital syphilis | | | |
|---|---|---|---|---|---|---|---|
| | Male | Female | Total | Male | Female | Unknown | Total |
| 2007 | 1231 | 150 | 1381 | 5 | 2 | 1 | 8 |
| 2006 | 689 | 182 | 871 | 6 | 7 | – | 13 |
| 2005 | – | – | 653 | 8 | 6 | 1 | 15 |
| 2004 | – | – | 636 | 11 | 2 | – | 13 |

* Syphilis of less than two years' duration.
Source: Australian Commonwealth Department of Health and Aging, 2009.[13]

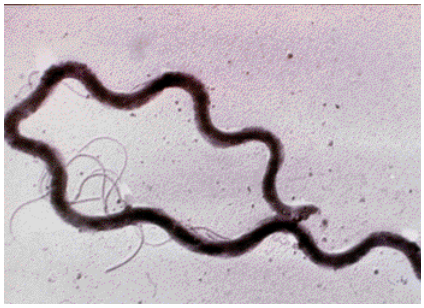

Figure 1. *Treponema pallidum*, the causative organism of syphilis.

hydrops fetalis, preterm birth (20%), stillbirth (20%), neonatal death, congenital infections and anomalies (40%).[14] The infection also, of course, can have serious consequences for the mother if it is not detected or adequately treated, with a 25 to 40% risk of her developing tertiary syphilis.

Between 70 and 100% of infants born to mothers untreated for their syphilis are infected, compared with 1 to 2% of infants born to adequately treated mothers.[15] The outcome for the fetus depends on its gestation at the time of infection, the duration of untreated infection, the spirochete load and the immune state of the mother. Fetal infection is firstly characterised by placental changes and liver dysfunction. Placental changes include hydropic change, chronic villitis, placental vascular thickening, necrotising funisitis and acute chorioamnionitis. Later, ascites and nonimmune hydropic changes appear in the fetus (Figure 2). In addition, thrombocytopenia, anaemia and a positive fetal anti-treponemal IgM may be detected by *in utero* fetal blood testing.

## Clinical manifestations

The various stages of syphilis – primary, secondary, latent and tertiary – have characteristic clinical features that are the same whether the patient is pregnant or not. These features are summarised in Table 2.

### Congenital syphilis

Two-thirds of babies with congenital syphilis are asymptomatic at birth.[16] The features of early and late congenital syphilis are listed in Table 3.

Early congenital syphilis, by arbitrary definition, is syphilis that becomes clinically evident in the first two years of life. Its features include a profuse haemorrhagic nasal discharge, generalised rash, hepatosplenomegaly, jaundice, failure to thrive and pseudoparalysis of a limb.[16]

The features of late congenital syphilis (onset greater than aged 2 years) include intellectual, hearing and visual impairment, nasal bone damage resulting in the characteristic saddle nose deformity and nasal breathing difficulties, bony joint disorders and changes to the shape of dentition.[16] The characteristic bony joint disorders are Clutton's joints (painless symmetrical hydrathrosis), sabre shins (periostitis of the tibia) and tabes dorsalis. The characteristic changes to the shape of dentition are Moon's molars and Hutchinson's notched incisors.

### Risk factors for congenital syphilis

Humphrey and Bradford have detailed risk factors for congenital syphilis.[8] These include lack of adequate antenatal care, failure to repeat tests for syphilis in the third trimester when earlier testing had been negative, past history of sexually transmitted infections, multiple sexual partners, substance abuse and being a member of a marginalised population group.

## Diagnosis

Although *T. pallidum* cannot be cultured in the laboratory or visualised by light microscopy, spirochaetes can be identified in body secretions by dark field microscopy. Direct fluorescent antibody stains have now replaced dark field microscopy in the diagnosis of syphilis but a fluorescent microscope and a skilled technician are required.

### Maternal syphilis

Serological testing of the maternal antibody response to the infecting organism is the main method used to diagnose the presence of maternal syphilis. These tests rely on the mother mounting a detectable humoral immune response to the organism. Two types of serological tests are available:

- treponemal antibody tests – for example, the fluorescent treponemal antibody absorption (FTA-ABS) test and the *Treponema pallidum* haemaglutination (TPHA) test; these tests are sensitive and specific but they are expensive and correlate poorly with disease activity because they remain positive despite adequate treatment
- nontreponemal serum antibody tests – for example, the Venereal Disease Research Laboratory (VDRL) test and the rapid plasma reagin (RPR) test; these tests are relatively inexpensive and are reported as a titre of antibody, the levels of which follow the patient's response to treatment.

The nontreponemal tests are subject to false-positive results when the patient has one of a number of acute diseases including viral hepatitis, HIV infection, tuberculosis, malaria and pneumococcal

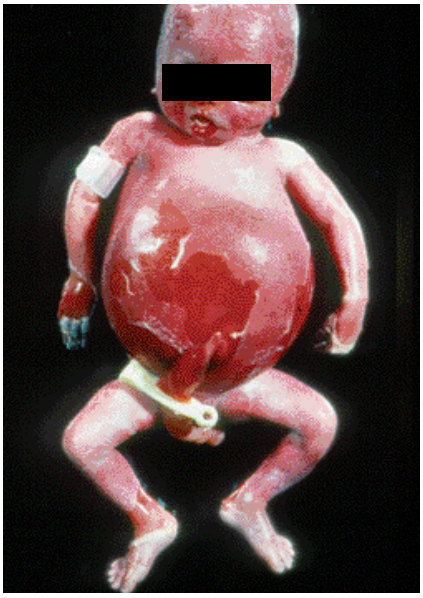

Figure 2. Stillborn fetus showing nonimmune hydrops.

## Table 2. Stages of syphilis

| Stage | Characteristics | Time period |
|---|---|---|
| **Primary**<br>– infectious stage | Solitary papule develops at inoculation site that ulcerates to a painless, firm chancre<br>Painless regional lymphadenopathy<br>Afebrile | Lesion visible at 10 to 90 days<br>Spontaneous healing in two to three weeks without treatment |
| **Secondary**<br>– infectious stage | General: constitutional symptoms, anorexia, generalised lymphadenopathy<br>Skin rash: red-brown maculopapular non-itchy, follicular, pustular, annular or scaly rash (classically palms and feet without facial involvement); condylomata lata<br>Mucosa: oropharynx and genitalia 'snail track' ulcers<br>Less commonly: hepatitis, nephropathy, proctitis, arthritis, optic neuritis or other neuropathy | Occurs three to 10 weeks after primary lesion has healed<br>Resolves over three to 12 weeks without treatment |
| **Early latent**<br>– asymptomatic but serologically reactive | Considered infectious and primarily disseminates through the body during this time<br>Defined by previous negative serology or a four-fold rise in titre levels in past 12 months | Up to two years' postinoculation |
| **Late latent**<br>– asymptomatic but serologically reactive | Not considered infectious but can be transmitted *in utero*<br>Diagnosis based on reactive syphilis serology with no clinical manifestations for at least two years | More than two years' postinoculation |
| **Latency of unknown duration**<br>– asymptomatic but serologically reactive | Serological results not available and symptom duration unreliable | More than two years' postinoculation |
| **Tertiary/late syphilis**<br>– not considered infectious | Gummas (granulomatous lesions) of bone, skin and viscera<br>Cardiovascular: aortitis, aneurysms and aortic regurgitation<br>Neurosyphilis: asymptomatic neurosyphilis, meningovascular syphilis, general paralysis of the insane (GPI), tabes dorsalis | One to 30 years after primary infection |

pneumonia. Chronic diseases that can cause false positives with nontreponemal tests include malignancy, chronic liver disease, myeloma, connective tissue diseases and multiple blood transfusions. Treponemal tests can give false positives in patients who have leprosy, malaria, infectious mononucleosis, leptospirosis or systemic lupus erythematosus.

Examination of the cerebrospinal fluid is essential if there is any suggestion of neurosyphilis.

### Congenital syphilis

The diagnosis of congenital syphilis is complicated because of the transplacental transfer of maternal treponemal and nontreponemal IgG antibodies to the fetus. This makes the interpretation of positive tests in the infant difficult.

Identification of syphilis in the mother and adequacy of maternal treatment as well as clinical, laboratory and radiological evidence of syphilis and comparisons between the serological results of mother and infant all guide the clinician when making treatment decisions. In practice, a combination of clinical history, examination findings and specific treponemal and nontreponemal antibody tests are used to diagnose congenital syphilis and monitor treatment.

## Treatment

Pregnant women with syphilis should be treated with the penicillin regimen appropriate to the stage of their disease.

### Table 3. Features of early and late congenital syphilis

**Early congenital syphilis**

- Early rash (small blisters on palms and soles)
- Failure to thrive
- Fever
- Generalised lymphadenopathy
- Glomerulonephritis
- Hepatosplenomegaly
- Hydrops
- Irritability
- Jaundice
- Pseudoparalysis
- Rash in mouth, on genitalia and anus
- Severe congenital pneumonia
- Snuffles, with bloody watery nasal discharge
- Thrombocytopenia

**Late congenital syphilis**

- Blindness
- Bone pain
- Bossing of frontal bones and abnormal maxilla development
- Clutton's joints (painless joint swelling, usually the knees)
- Grey mucous-like patches on anus and introitus
- Hearing impairment and deafness
- Hutchinson's incisors
- Impaired intellectual development
- Keratitis
- Moon's molars
- Paroxysmal cold haemoglobinuria
- Periostitis of tibia (sabre shins)
- Pseudoparalysis of limbs
- Rhagades (scarring of skin around the mouth, genitalia and anus)
- Saddle nose deformity

Pregnant women who have a history of contact with a person with documented syphilis should also be treated, as should those who have been treated previously but have a persistently elevated or rising nontreponemal serum antibody titre.

The antibiotic treatment for syphilis must be prolonged because the organism divides slowly, averaging one doubling per day. Therefore, long-acting penicillin preparations are used to treat the disease. A single dose of benzathine penicillin 2.4 million units (1.8 g) intramuscularly is the standard treatment for primary, secondary and early latent-phase syphilis. Late latent-phase syphilis, latent syphilis of unknown duration and tertiary syphilis require three doses of benzathine penicillin 2.4 million units intramuscularly given at weekly intervals. Infants are treated with intravenous benzylpenicillin at a dose of 50 mg/kg 12-hourly for 10 days. Procaine penicillin 1 g/day intramuscularly for 10 days is an alternative treatment for early latent-phase syphilis.

A reaction to treatment in most patients is fever, headache and myalgias (the Jarisch–Herxheimer reaction).[17] This reaction occurs four to 12 hours after the beginning of treatment and resolves within several hours. The symptoms are treated with antipyretics and are not grounds for ceasing treatment, although a severe reaction may cause a threatened miscarriage.

Confirmed syphilis is a notifiable disease in Australia and all cases must be reported to the health department in each state and territory. Follow up of all cases is vital. Adults should be re-examined both clinically and serologically every six months after treatment until there is a fourfold reduction in nontreponemal antibody titre. This level of reduction in titre is considered evidence of an appropriate response to treatment. Patients with tertiary syphilis should be followed for three years. Adults who fail to respond require another course of benzathine penicillin (three doses of 2.4 million units at weekly intervals), plus further follow up. Neonates should be followed up every two months for 12 months and the treatment dose of penicillin should be determined by body weight.

For patients who are sensitive to penicillin, alternative therapies include doxycycline (but not for pregnant women) and erythromycin. Ceftriaxone has also been used (off-label) for those sensitive to penicillin but there is a 5% cross-sensitivity rate and so caution is recommended if this alternative to penicillin is used. Azithromycin has also been used (off-label) to treat syphilis in the nonpregnant patient, but azithromycin resistance has emerged and is increasing in the USA, Canada and Ireland.[18] We are not aware of penicillin-resistant syphilis at the present time.[17,19]

Further advice on the management and diagnosis of maternal and congenital syphilis can be obtained from infectious diseases physicians, sexual health physicians, neonatologists and microbiologists.

## Conclusion

Syphilis remains an important health issue for women, fetuses and neonates. About 80% of women with syphilis are in the reproductive age group, and failure to detect or adequately treat maternal syphilis has serious consequences for the mother, fetus and neonate. Education, safe sexual practices, diagnosis and treatment are the keys to management. Penicillin remains the gold standard of treatment of syphilis for all patients, including pregnant women and their offspring.

The current recommendations of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists on antenatal screening with regard to syphilis testing are that all pregnant women should be tested for syphilis at their first antenatal visit and these tests should be repeated at 28 weeks in high-risk patients.[2] MT

## References

*A list of references is available on request to the editorial office.*

**COMPETING INTERESTS: None.**

Medicine Today 2010; 11(4): 69-72

# Maternal and congenital syphilis – a problem that hasn't gone away

**IAN JONES** ChM, MEdStudies, FRANZCOG, FRCOG **ALISTER JONES** BSc, MB BS

## References

1. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2006: pregnant women. Recommended screening tests. Available online at: www.cdc.gov/std/treatment/2006/specialpops.htm#specialpops1 (accessed March 2010).
2. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement C-Obs 3: Pre-pregnancy counselling and routine antenatal assessment in the absence of pregnancy complications, November 2009. Available online at: www.ranzcog.edu.au/publications/statements/C-obs3.pdf (accessed March 2010).
3. US Preventive Services Task Force. Screening for syphilis infection in pregnancy. Reaffirmation recommendation statement. Agency for Healthcare Research and Quality; May 2009. Available online at: www.ahrq.gov/clinic/uspstf09/syphilis/syphpgrs.htm (accessed March 2010).
4. Mackay EV, Beischer NA, Pepperell RJ, Wood C, eds. Illustrated textbook of gynaecology. 2nd ed. Sydney: W.B. Saunders; 1992. p. 319.
5. Centers for Disease Control and Prevention. Sexually transmitted diseases surveillance, 2007. Syphilis. Available online at: http://www.cdc.gov/std/stats07/syphilis.htm (accessed March 2010).
6. Weinstock H. Syphilis in the United States, epidemiology and emerging issues. Presented at: 2008 National STD Prevention Conference, Chicago, 10-13 March 2008. Abstract A6b.
7. Simms I, Broutet I. Congenital syphilis re-emerging. J Dtsch Dermatol Ges 2008; 6: 269-272.
8. Humphrey MD, Bradford DL. Congenital syphilis: still a reality in 1996. Med J Aust 1996; 165: 382-385.
9. Mak DB, Johnson GH, Plant AJ. A syphilis outbreak in remote Australia: epidemiology and strategies for control. Epidemiol Infect 2004; 132: 805-812.
10. Northern Territory Government. Guidelines for the investigation and treatment of infants at risk of congenital syphilis in the Northern Territory. Darwin: Centre for Disease Control, NT Government; 2005. Available online at: www.health.nt.gov.au/Centre_for_Disease_Control/Publications/CDC_Protocols/index.asp (accessed March 2010).
11. Hargrove A, Curtis N. Syphilis returns to the suburbs. Eur J Pediatr 2006; 165: 290-292.
12. Allen K, Guy R, Leslie D, et al. The rise of infectious syphilis in Victoria and the impact of enhanced clinical testing. Aust N Z J Public Health 2008; 32: 38-42.
13. Liu C, Stirzaker S, Knuckey D, et al; NNDSS Annual Report Writing Group. Australia's notifiable diseases status, 2007: annual report of the National Notifiable Disease Surveillance System – sexually transmissable diseases. Commun Dis Intell 2009; 33: 89-154. Available online at: www.health.gov.au/internet/main/publishing.nsf/Content/cda–cdi3302atoc.htm (accessed March 2010).
14. Johnson KE. Congenital syphilis. In: Overview of TORCH infections. UptoDate 2009. Available from: http://www.utdol.com/patients/content/topic.do?topicKey=~GMIrIBDVqVDd_S (accessed March 2010).
15. Alexander JM, Sheffield JS, Sanchez PJ, Mayfield J, Wendel GD. Efficacy of treatment for syphilis in pregnancy. Obstet Gynecol 1999; 93: 5-8.
16. Sanchez P, Gutman L. Syphilis. In: Feigin RD, Cherry JD, Demmler GJ, Caplan SL, eds. Textbook of pediatric infectious diseases. 5th ed. Philadelphia: Saunders; 2003. p. 1724.
17. Brunton LL, Goodman LS, et al. Treatment of syphilis. In: Brunton LL, Blementhal D, Buxton I, Parker K, eds. Goodman and Gilman's manual of pharmacology and therapeutics. 11th ed. New York: McGraw-Hill Professional Publishers; 2007. p. 736.
18. Katz KA, Klausner JD. Azithromycin resistance in *Treponema pallidum*. Curr Opin Infect Dis 2008; 21: 83-91.
19. McCalmont T. Syphilis: treatment and medication. eMedicine Dermatology, 2005, updated 2 Sept 2009. Available online at: http://emedicine.medscape.com/article/1053426-treatment (accessed March 2010).