Syphilis in pregnancy

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Key points
There has been a worldwide resurgence of syphilis in recent years, and it is likely to remain a common disease worldwide.

More than 80% of women with syphilis are of reproductive age; therefore, there is a serious risk of vertical transmission to the fetus.

There are no specific contraindications to general anaesthesia or regional blockade. However, HIV and syphilis affect the similar group of patients and co-infection is common. Universal precautions are mandatory before anaesthetizing these patients.

For several decades, syphilis has been out of sight, mind, and memory, but the incidence in the Western world is now on the rise again and it could once more become a major health concern. This change has followed the rapidly rising number of human immunodeficiency virus (HIV) positive individuals worldwide, together with the advent of health tourists, economic migrants, asylum seekers, and the easy availability of low-cost travel.

Just as syphilis has all but disappeared as an entity in the working memory of most anaesthetists, it has suddenly re-emerged as a co-existing condition in women presenting for Caesarean section. Figure 1 shows the changing incidence of syphilis in the UK over the last 10 years. This review is intended to inform anaesthetists caring for women with syphilis.

Aetiology
Treponema pallidum is the causative organism for syphilis. It is a delicate, motile spirochete bacterium. Humans are its only natural source. Syphilis is usually transmitted by sexual contact through exposure to mucocutaneous syphilitic lesions that contain infectious spirochetes. The infecting organism in body fluid gains access through microscopic abrasions in skin or mucosal surfaces, and begins to replicate locally. After inoculation, the incubation period is around 3 weeks (10–90 days), at the end of which a primary sore develops at the site of infection, usually the genitalia.

Classification
Syphilis is classified2 as congenital or acquired as shown in Figure 2. There are four stages of syphilis: primary, secondary, latent, and late (tertiary).

Primary syphilis
The first development is a chancre at the site of inoculation, classically in the anogenital region which is a painless, solitary, round indurated ulcer with a bright red margin.1 Chancre appear on average about 3 weeks after sexual contact and heal in 3–6 weeks. However, with a small inoculum, this incubation period may be as long as 90 days. One of the common sites for lesions is the cervix; therefore, the clinical manifestations of primary syphilis may go unnoticed by the patient and her partner.3

Secondary syphilis
Untreated patients will progress to secondary syphilis after the signs for primary syphilis resolve (within 4–10 weeks3). The lesions are numerous, variable, and affect many systems. A symmetrically distributed, maculopapular, non-irritating rash is found on the palms and the soles with painless lymphadenopathy. The highly infectious condyloma lata are found on warm and moist areas such as genitalia, perianal region, perineum, and axillae. Both meningism and headache can occur, especially at night. Their cause can be confirmed by the presence of an elevated cell count and elevated proteins in cerebrospinal fluid. Less common accompaniments to secondary syphilis include alopecia, laryngitis, mild hepatitis, nephrotic syndrome, bone pain, and uveitis.

Latent syphilis
The natural history of untreated secondary syphilis is marked by spontaneous resolution after a period of 3–12 weeks, leaving the patient entirely free of symptoms. This naturally attained asymptomatic state is called latency.4 The latency is arbitrarily subdivided into early (<2 yr from the onset of the infection) and late (>2 yr) stages. During this time, the patient remains serologically positive for syphilis. Approximately 60% of patients remain latent for the rest of their lives. In the early latent stage, 25% will relapse with a secondary syphilitic manifestation, whereas the likelihood of such relapses in the late latent stage is small.1

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Late syphilis (tertiary syphilis)

Tertiary syphilis develops in 30–40% of untreated patients. The three main manifestations of late syphilis are cardiovascular, gummatous, and neurosyphilis. Cardiovascular syphilis usually occurs 15–30 yr after primary syphilis and may occur in any large vessel. It is characterized by an aortitis, aortic incompetence, coronary ostial stenosis (presenting as angina), and aortic medial necrosis causing aortic aneurysm. Gummatous syphilis is granulomatous locally destructive lesions that usually occur 3–12 yr after inoculation. They can occur in almost any tissue. Neurosyphilis presents with a variety of syndromes including general paresis, tabes dorsalis, syphilitic meningitis, and meningovascular syphilis. The incubation period is 5–12 yr.5

Syphilis in pregnancy

Antenatal syphilis poses a significant threat to the pregnancy and fetus. T. pallidum readily crosses the placenta, resulting in fetal infection. Vertical transmission can occur at any time during pregnancy and at any stage of syphilis.6 Risk of transmission correlates with the extent of spirochetal presence in the circulation. Vertical transmission of syphilis is more common in primary (50%) and secondary syphilis (50%), compared with early latent (40%), late latent (10%), and tertiary syphilis (10%). Seventy to one hundred per cent of infants born to untreated infected mothers are infected. Pregnancies complicated by syphilis may result in intrauterine growth restriction, non-immune hydrops fetalis, stillbirth, preterm delivery, and spontaneous abortion in up to 50% of pregnancies. Women who had documented treatment for syphilis in the past do not need treatment during current or subsequent pregnancies.

Congenital syphilis

In spite of a downward trend in the incidence of syphilis, congenital syphilis, an infection passed from mother to child through the placenta during fetal development or birth, remains a great concern. An infected woman’s potential to infect her fetus remains for many years, although the risk of infecting a fetus declines gradually during the course of untreated illness. After 8 yr, there is little risk, even in the untreated mother. Nearly half of all children infected with syphilis during gestation die shortly before or after birth.

Infants who survive develop early-stage and late-stage symptoms of syphilis, if not treated. Early-stage symptoms include irritability, failure to thrive, non-specific fever, a rash and condyloma lata on the borders of the mouth, anus, and genitalia. Some of these lesions may resemble the wart-like lesions of adult syphilis. A small percentage of infants have a watery nasal discharge (snot) and a saddle nose deformity resulting from destruction of the cartilage of the nose. Bone lesions are common, especially in the upper arm (humerus). Later signs appear as tooth abnormalities (Hutchinson teeth), bone changes (sabre shins), neurological involvement, blindness, and deafness.

Incidence of syphilis

The 1999 WHO estimates suggest an annual rate for syphilis of ∼12 million active infections. The risk of contracting syphilis through a sexual contact with a person with primary or secondary syphilis is 30–50%. More than 80% of women with syphilis are in reproductive age; therefore, there is a serious risk of vertical transmission to the fetus.6 Worldwide, a million pregnancies are adversely affected each year by syphilis because of maternal infection. About 270 000 babies are born with congenital syphilis, 460 000 pregnancies end in abortion or perinatal death, and 270 000 babies are born prematurely or with low birth weight.7

Laboratory diagnosis of syphilis

Diagnosis of syphilis is based on microscopy and serology. At the first antenatal visit, all women in UK are screened for sexually transmitted diseases including syphilis and HIV. The serological tests are repeated at three monthly intervals in cases of anogenital ulceration if the initial tests are negative. All infants born to seropositive mothers should be examined at birth and at monthly
intervals for 3 months until it is confirmed that serological tests are and remain negative.

Microscopy

Microscopic demonstration of *T. pallidum* from the lesions or infected lymph nodes in early syphilis depends on the following three tests:

- **Dark-field microscopy**: if a lesion such as chancre is present, dark-field microscopy should be attempted to visualize the characteristic motile spirochetes in the exudates collected from the lesion. The sensitivity rate is up to 97%, so failure to find the organism does not exclude a diagnosis of syphilis. (For an explanation of sensitivity and specificity, please see Lalkhen and McCluskey.8)
- **Direct fluorescent antibody (DFA) test**: this uses the indirect fluorescent technique with killed *T. pallidum* as antigen. The organisms are fixed on a slide to which serum is added. The antibody in the serum unites with treponemes and is made visible with fluorescent stain.1
- **Polymerase chain reaction (PCR) test**: it may be useful for the detection of primary syphilis with sensitivity up to 98.6%.

Serological tests

**Non-treponemal tests**

These tests detect the cross-reaction of antibody to *T. pallidum* with cardiolipin. The result is reported as reactive or non-reactive; a reactive test is accompanied by a quantitative titre and should be confirmed with a treponemal test. False positive non-treponemal tests may occur in patients who are pregnant, i.v. drug users, those with systemic inflammatory diseases such as systemic lupus erythematosus, or after a recent viral infection.3

- **VDRL** (venereal disease research laboratory) test: this is simple and inexpensive and is the preferred test worldwide.
- **RPR** (rapid plasma reagin) test: this is used for screening purposes and is the least technically demanding test as no microscope is needed. It uses carbon-containing cardiolipin antigen and requires a minimal quantity of blood.

**Treponemal tests**

These tests specifically detect antibodies against *T. pallidum*. They are positive for life in the vast majority of infected patients regardless of stage or treatment history.3 They are very valuable and simple tests using an indirect haemagglutination method with red cells or by gelatine particles. Together with VDRL, it is probably the best combination for routine use. False positive reactions occur in up to 2%.1

- **EIA (enzyme immuno assay)**: treponemal enzyme immunoassay is the screening test of choice and can detect IgG and IgM antibodies as it is positive in earlier stages of syphilis. A positive test is then confirmed with the TPHA/TPPA or VDRL/RPR tests.
- **FTA-ABS (fluorescent treponemal antibody absorption) assay**: this uses the indirect fluorescent technique with killed *T. pallidum* as an antigen. The organisms are fixed on a slide to which serum is added. The antibody in the serum unites with treponemes. The test has been made more specific by absorbing the group antibodies. This is the most sensitive and specific test available. It becomes positive earlier during the initial stage of primary syphilis. However, it is not suitable for assessing the activity, as the positive test persists long after successful treatment.1

Neurological involvement9 is confirmed by a positive VDRL, raised cell count (>5/mm³), and raised protein (40 mg dl⁻¹) in the CSF obtained by lumbar puncture. Chest X-ray, electrocardiography, echocardiography, cardiac catheterization, and biopsy of gumma can reveal involvement of other systems.

Treatment of syphilis during pregnancy

Penicillin is the drug of choice for treating all stages of syphilis. Parenteral rather than oral treatment has been the route of choice as the therapy is supervised and bioavailability is guaranteed. Most women treated during pregnancy will deliver before their serological response to treatment can be assessed definitively. Neonates born to such women should be evaluated for congenital syphilis. The UK national guidelines9 for the treatment of early syphilis during pregnancy are described as follows:

**First-line therapy**: intramuscular (i.m.) procaine penicillin 750 mg daily for 10 days. If it is not possible to give daily procaine penicillin on the weekend, then either long-acting procaine penicillin in aluminium stearate, 2 million units (MU) or long-acting benzathine penicillin 1.2 MU should be given IM on the Friday.

**Patients with penicillin allergy**: erythromycin 500 mg four times a day should be given for 14 days. Alternatively, azithromycin 500 mg should be given daily for 10 days. In addition to this, examination, tests, and treatment of all babies at birth should be carried out. Desensitization to penicillin may be considered, followed by the first-line treatment. Mothers treated with erythromycin or azithromycin may be considered for retreatment with doxycycline after delivery and when breast-feeding is stopped.

**Patients suspected of non-compliance**: benzathine penicillin 2.4 MU i.m. on Days 1 and 8.

Penicillin reactions

Approximately 5–10% of pregnant women with syphilis report a history of penicillin allergy. The Jarisch–Herxheimer reaction is an acute response that may occur after treatment for acquired early syphilis. It occurs in up to 45% of pregnant women and consists of fever, chills, myalgia, headache, hypotension, tachycardia, and
transient accentuation of the cutaneous lesions. It typically begins within several hours of treatment and resolves within 24–36 h. The release of *T. pallidum* lipoprotein, which possesses inflammatory activity from dead or dying organisms, is implicated as a likely inducer of this phenomenon. In pregnant women, the Jarisch–Herxheimer reaction can cause uterine contractions and precipitate labour. This is possibly mediated secondarily by prostaglandins as the concentrations are increased during reactions.

**Syphilis and HIV**

Syphilis commonly co-exists in patients with HIV (prevalence is 14–36%). All HIV-infected patients under regular follow-up should have syphilis serology documented at baseline and subsequently 12 monthly thereafter. HIV-infected patients with early syphilis have an increased risk of neurological involvement. Features of syphilis in HIV include: generalized lymphadenopathy; splenomegaly; hepatitis; skin rashes, alopecia or both; oral manifestations; cognitive impairment; meningitis; cranial nerve palsies; myopathies; and uveitis.

**Anaesthetic considerations**

There is little specific advice available on the anaesthetic management of patients with syphilis. Universal precautions should be considered at all times when anaesthetizing patients with syphilis. Accidental transmission of syphilis involves direct contact through a small skin abrasion. It has been reported under the following circumstances: doctors and nurses who have examined a syphilitic lesion without wearing gloves; laboratory workers by needle stick injury when inoculating treponemes into rabbits, or during isolation or purification procedures; and patients being transfused with blood from a donor suffering from early syphilis.

Infection by blood transfusion is rare in the UK because screening tests are routinely performed for evidence of donor infection with syphilis. After storage in blood for more than 4 days at 4°C, spirochetes are non-viable. The risk of accidental infection by infected blood is highest when fresh heparinized blood is used. Such blood is used for exchange transfusion in neonates. Cutaneous lesions of the breast and nipples carry a risk of transmission through breast feeding. After needle-stick injury, the risk of transmission is very low. Antibiotics are not routinely recommended for needle-stick injuries; however, each wound should be assessed individually by the relevant healthcare professionals.

There is no additional risk with general anaesthesia. There is a single report of a 73-year-old woman with late congenital pharyngolaryngeal syphilis, who presented with a potentially difficult intubation during the induction of general anaesthesia. Syphilis poses no specific problems for regional blockade. The three main manifestations of late syphilis (neuro-, cardiovascular, and gummatous syphilis) can have a wide range of presentation. It is prudent to assess and document all existing signs and symptoms (including neurological examination) in the anaesthetic record. There is no evidence to suggest that regional blockade can affect the extent or likelihood of neurosyphilis. The lesion in tabes dorsalis is concentrated on the dorsal spinal roots and dorsal columns of the spinal cord, most often at the lumbar or sacral region. There have been reports that spinal anaesthesia induces severe lightning pain in the lower limbs of patients with phantom limb pain, tabes dorsalis, or causalgia. The exact mechanism of this phenomenon is controversial. Some hypothesize that complete loss of sensory input after spinal anaesthesia may decrease the level of inhibition and increase the self-sustained neural activity.

Options for delivery include elective Caesarean section because it is associated with less vertical transmission. When considering postoperative analgesia, those techniques that do not expose staff to needle-stick injury should be favoured.

**References**


Please see multiple choice questions 23–25