SYPHILIS is a predominantly sexually transmitted infection caused by the spirochaete bacterium *Treponema pallidum*. In the early stages the disease is usually easily treatable but not all of those infected experience symptoms and, if untreated, serious complications, including blindness, stroke, aortic aneurysm and paralysis, can arise.

**Numbers**

The World Health Organization estimates that around 12 million new cases of syphilis occur worldwide every year. The bulk (eight million) of these are in south-east Asia and sub-Saharan Africa but high rates are also observed in central Asia and eastern Europe.1

In western Europe the WHO estimates there are 140,000 new cases of syphilis each year and diagnosis has risen substantially in the past decade in the UK. In 2007, 3,762 diagnoses of infectious syphilis were made — more than in any other year since 1950.2 There was a slight decrease in 2010 but by last year cases of infectious syphilis had increased by 10 per cent.3

The prevalence of new infections is significantly greater in men than in women, with men accounting for 90 per cent of new diagnoses.3

In the UK syphilis is largely concentrated among men who have sex with men (MSM) — where sexual orientation was recorded in male cases, 75 per cent of diagnoses was among this group. MSM syphilis diagnoses in England increased by 28 per cent from 2010 to 2011. A number of factors are likely to have contributed to this sharp rise.

**Transmission and risks**

*T pallidum* is a human pathogen that does not naturally appear in other species. Transmission is by penetration of through mucous membranes by the spirochaete or through abrasions on epithelial surfaces. This usually occurs by direct contact with an infectious lesion or skin rash, (eg, during sexual contact) but visible sores or rash are not necessary for transmission. The person remains sexually infectious until about two years after secondary syphilis (see later) has cleared. The infection can also be transmitted in pregnancy (vertical transmission) or via infected blood products.

*T pallidum* cannot survive drying or exposure to disinfectants, so fomite transmission (eg, from toilet seats) is almost impossible.

Patients should be advised to refrain from sexual contact of any kind until the results of the first follow-up blood tests confirm they are clear of infection.“Those with lesions
should also wait until these are fully healed. Unprotected sex, promiscuous sex and intravenous drug use are the major risk factors for transmission of syphilis.

Ongoing high levels of high-risk sexual behaviour have probably contributed to the rise of the disease in MSM and this group remains a priority for targeted STI prevention and health promotion work.

Because it causes genital ulcers, syphilis is associated with an increased risk of HIV transmission and acquisition. Co-infection is common in those with syphilis (27 per cent). As the number of syphilis cases in women of reproductive age has grown this has resulted in an increase in cases of congenital infection.

Healthcare workers are at potential risk of transmission through needlestick injuries or contact with lesions.

**Stages and symptoms**

Syphilis is classified as acquired or congenital. Acquired syphilis is divided into early and late disease. Early acquired syphilis can be further subdivided into primary, secondary and early latent (less than two years of infection) disease and late acquired syphilis can be subdivided into latent (over two years of infection) and tertiary (including gummatous, cardiovascular and neurological) disease. Figure 1 provides a summary.

Congenital syphilis is also divided into early and late disease, diagnosed in the first two years of life and presenting after two years of disease, respectively.

Syphilis was famously referred to as “the great imitator” by Sir William Osler because of its varied presentations, which are similar to many other conditions.

**Acquired syphilis**

Primary syphilis is usually characterised by the appearance of a single skin lesion (called a chancre) which is typically firm, small, round and painless, occurring at the point of contact with the infectious lesion(s) of another person. However, chancres may also be multiple, painful and purulent. They do not have to be genital. For example, they may appear on the lips or in the mouth (see image on p263). Multiple lesions are more common when a patient is co-infected with HIV.

The time from initial exposure to start of initial symptoms can range from 10 to 90 days (average 21 days). Swelling (lymphoedema) frequently occurs (80 per cent) around the area of infection, usually seven to 10 days after chancre formation. The chancre lasts three to six weeks without treatment. Untreated, primary syphilis will always progress to secondary syphilis. This occurs four to 10 weeks after first exposure. Secondary syphilis typically involves the skin, mucous membranes and lymph nodes. There is often a symmetrical, reddish brown rash on the trunk and extremities, including the palms and soles of the feet (see image on p263). The rash is classically non-itchy but can be itchy, particularly in dark-skinned patients. It may become maculopapular or pustular and form wart-like lesions (known as condylomata lata) on mucous membranes.

Other symptoms can include fever, lymphoedema, sore throat, malaise, weight loss, hair loss and headaches. The acute symptoms usually resolve after six weeks, but about 25 per cent of people experience a recurrence of secondary symptoms. Latent syphilis (both early latent and late latent) has no signs and symptoms and can last for years. The distinction between early latent and late latent is for treatment purposes (see later). It is difficult to tell exactly how long someone has had the infection, but serological tests and medical and sexual histories can help clinicians make a good estimate.

In around a third of cases tertiary (or late symptomatic) syphilis can occur three to 15 years after infection. It can
Syphilis can occur during Infection with congenital syphilis, which are described in Panel 1.

Neurosyphilis (6.5 per cent), cardiovascular disease (40 per cent), neurosyphilis of life and common symptoms develop over the first two years of life and common symptoms are born without signs of the disease. Early congenital syphilis is untreated, there is a high risk of stillbirth, prematurity or neonatal death. If infected during delivery, the baby will develop a number of symptoms over time.

Two-thirds of syphilitic infants are born without signs of the disease. Early congenital syphilis develops over the first two years of life and common symptoms include hepatosplenomegaly (70 per cent), rash (70 per cent), fever (40 per cent), neurosyphilis (20 per cent) and pneumonitis (20 per cent).

Left untreated, late congenital syphilis occurs in 40 per cent of babies. Symptoms include saddle nose deformation (loss of height of nose due to collapse of the bridge), Higoumenakis sign (unilateral enlargement of the sternoclavicular portion of the clavicle), saber shin (malformation of tibia) and Clutton’s joints (symmetrical joint swelling).

Congenital syphilis kills more than a million babies a year worldwide but is preventable if infected mothers are identified early and treated appropriately. The World Development Report cites antenatal screening and treatment for syphilis as one of the most cost-effective health interventions available. In England in 2005, 95 per cent of pregnant women were screened for syphilis, although uptake varied from 77 to 100 per cent between regions.

**Diagnosis and investigation**

Syphilis can be difficult to diagnose in the early stages. Confirmation is required with blood tests or direct visual microscopy.

For all suspected cases a full sexual health screen, including HIV testing, should be performed.

A thorough investigation should be undertaken for the clinical manifestations of syphilis, including full examinations of skin and mucosal surfaces, lymph nodes, cardiovascular and neurological systems.

In addition, history of travel to or living in countries where syphilis or other treponemal infections are endemic should be established. In women an obstetric history, including potential complications such as still births and miscarriages, should be taken.

**Sero logical tests**

Blood tests are routine. They can be divided into treponemal and non-treponemal.

Non-treponemal tests are used initially and include the venereal disease research laboratory (VDRL) test and rapid plasma reagin test. These are widely used for syphilis screening but false-positive reactions can occur with viral infections (such as varicella and measles), autoimmune disorders, infections (such as malaria, tuberculosis, and endocarditis) and pregnancy.

Treponemal specific tests detect antibodies to antigenic components of *T pallidum*. These tests are primarily used to confirm the diagnosis of syphilis in patients with a reactive non-treponemal test. They have sensitivities and specificities equal to or higher than non-treponemal tests but are more difficult and expensive, which limits their usefulness as screening tests.

**Direct testing**

Dark-field microscopy is the most specific technique for diagnosing syphilis when a chancre or condylomata are present. Serous exudate from the lesion is examined under a microscope equipped with a microscope equipped with a
of breath, itchy wheals on their skin, facial swelling or tightness in their chest or throat. Penicillin desensitisation may be considered for patients reporting penicillin allergy.

Jarisch-Herxheimer reaction
The Jarisch-Herxheimer reaction is an acute febrile illness with headache, myalgia, chills and rigors that resolves within 24 hours. It is common in the treatment of patients with early syphilis (a figure of 50 per cent has been reported) but is usually not important unless there is neurological or opthalmic involvement, or in pregnancy when it may cause fetal distress and premature labour. The reaction is thought to occur as a result of destruction of spirochetes and activation of a pro-inflammatory cytokine cascade.

It is uncommon in late syphilis but can potentially be life threatening if there is involvement of coronary ostia, the larynx or the nervous system. Steroids are recommended when there is neurological or cardiovascular involvement and may also be used in pregnancy (additional fetal monitoring is required).

Procaine psychosis
Inadvertent intravenous injection of procaine penicillin can result in a reaction characterised by fear of impending death and may cause hallucinations or fits immediately after injection, lasting less than 20 minutes. Calm and verbal reassurance is required, and diazepam can be used if fits occur.

Role for pharmacists
Pharmacists, especially those working in community settings, are in a prime position to provide advice and signpost people to sexual health services. For example, women coming into the pharmacy requesting emergency contraception should always be advised that this does not protect against the risks of STIs and be referred for screening where appropriate. Emergency contraception consultations are also ideal opportunities to engage patients in discussions about future, more appropriate methods of contraception.

People might also visit a pharmacy requesting products for lesions that could be syphilitic. If syphilis cannot be excluded, these people should be referred to a GUM clinic or their GP.

In hospitals patients may be seen on wards or, more likely, in an outpatient clinic where prescriptions will need screening. This will involve checking the appropriateness and duration of therapy and potential interactions, and titrating doses for renal or hepatic impairment. There is also an important role for pharmacists in counselling patients on their therapy, and discussing any compliance issues and the importance of completing the course and attending follow-up appointments for monitoring.

Some patients may be prescribed long-term intravenous antibiotic courses. In such cases it is important to establish how the medicine will be prepared, how it will be administered and who will be administering it. This will require detailed discussions with the outpatient intravenous antibiotic therapy (OPAT) team, community nurses or homecare services. GUM clinics often have patient group directives for treatment of STIs and pharmacists are involved in the development of such services.

Despite intensive efforts, the unusual nature of _T pallidum_ has hindered progress towards the development of a vaccine to prevent infection. Good sexual health is a key component of the prevention of syphilis and pharmacists have a part to play in reinforcing this. In particular, people at risk should be encouraged to:

- Use barrier contraceptives
- Be aware of the symptoms of infection and seek early medical advice
- Get tested regularly (Consulting clinical services regularly increases the chances that infection can be identified, even if there are no symptoms. HIV testing should be considered every three months to annually for patients in high-risk groups.)

To avoid reinfection, partners of infected individuals should be advised to be screened and, if necessary, treated.

References available online