



Treponema pallidum

Treponema pallidum is a Gram-negative spirochaete with four subspecies. *T. pallidum pallidum* causes syphilis worldwide; *T. pallidum endemicum* causes bejel or endemic syphilis (non-venereal) mainly in the Mediterranean and West Africa; *T. pallidum carateum* causes pinta in Mexico, Central America, and South America; and *T. pallidum pertenue* causes yaws in tropical climate countries.

Humans are the only known natural reservoir. Syphilis can be transmitted by kissing, close contact and from the mother to baby during pregnancy or birth, and blood transfusions, but the main route of transmission is through sexual activity. There are four stages to syphilis infection: primary, secondary, latent and tertiary. Earlier infections are more easily treatable compared to late-stage infections; morbidity increases at each successive stage.

In the UK, there has been an increase in syphilis cases, up to 33% between 2013-2014 particularly in men who engage in sexual activity with other men. Early diagnosis is crucial since if left untreated complications can arise such as gumma, meningitis, heart problems, and other potentially life-threatening manifestations. Pregnant women are advised to screen for *T. pallidum* antibodies during pregnancy so any cases can be treated antenatally, as infection can cause miscarriages, stillbirth, or congenital syphilis in newborns. There have been studies suggesting that syphilis is associated with higher risks of contracting HIV.

Diagnosis of syphilis can be difficult. The mainstay of diagnosis of established syphilis is serology which falls into two main categories: Non-treponemal tests (VDRL, RPR) which detect antibodies to cardiolipin, produced as a response to treponemal infection. These are sensitive and titres may decline over time with treatment, but not very specific and may give false negatives due to the prozone phenomenon (high titres give false negatives) or false negatives in pregnancy, TB infection and endocarditis amongst others. Treponemal specific tests (EIA, TPHA, FTA-ABS) detect treponemal specific antibodies and are more specific, but can only be used qualitatively and remain positive after treatment.

Primary syphilis was traditionally diagnosed using microscopy of slides made from a swab taken from the primary ulcer site. As *Treponema* spp. are extremely thin (0.15 µm) and long (10 µm) dark field microscopy is required to visualise the motile helical rods, requiring specialist equipment and high-level skills by the operator. Additionally, differentiating *T. pallidum* from other spirochetes found in the mouth can make a diagnosis from a mouth ulcer using microscopy particularly tricky. Therefore, diagnosis of primary syphilis from swabs taken from the primary ulcer, along with detection in other sterile sites such as eye samples and CSFs, now largely relies on NAATs.

At Micropathology Ltd, *T. pallidum* DNA is detected using a nested assay which detects the *polA* gene present in all four *T. pallidum* subspecies. Accredited specimen types are genital swabs and CSF, though other samples may be tested and reported along with an appropriate caveat stating the assay is not accredited for other sample types.