

Syphilis and their Sign & Symptoms, Causes with their Treatment: An Overview

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1. INTRODUCTION

Since its recognition in 15th-century Europe as a new disease, syphilis has been the subject of great mystery and legend. Speculation abounds, often with scant evidence, about famous persons who may have had syphilis—the implicated include political figures (1, 2,), musicians (87, 114, 254), and literary greats (113, 187, 258, 262). Many believe that syphilis was brought to Europe by Columbus and his sailors, although there is no objective proof of this theory (176). John Hunter, the eminent mid-18th-century Scottish physician and venereologist, in order to test whether syphilis and gonorrhoea were the same or different diseases, is said to have inoculated himself with pus from an individual infected with a sexually transmitted disease (46, 84, 159). Unfortunately for Hunter, the patient was infected with the etiologic agents of both diseases. This was also unfortunate for the medical community, as it caused decades of medical and scientific confusion. Finally Philippe Ricord's studies, published in 1838, clarified that syphilis and gonorrhoea are indeed distinct infections (253). The greatest mystery of syphilis, however, is how the spirochete *Treponema pallidum* subsp. *pallidum* causes the many clinical features of disease. Despite the inherent difficulties in investigating this organism, researchers have been successful in uncovering some of the secrets of *T. pallidum*'s biology and the pathogenesis of syphilis, but much remains to be discovered. In previous issues of this journal, a

ABSTRACT

Syphilis may be a persistent sexually transmitted malady caused by *Treponema pallidum* subsp. *pallidum*. Clinical appearances partitioned the malady into stages; late stages of malady are presently unprecedented compared to the preantibiotic period. *T. pallidum* has an curiously little genome and needs qualities that encode numerous metabolic capacities and classical harmfulness variables. The life form is amazingly touchy to natural conditions and has not been ceaselessly developed in vitro. In any case, *T. pallidum* is highly irresistible and survives for decades within the untreated have. Early syphilis injuries result from the host's safe reaction to the treponemes. Bacterial clearance and determination of early injuries comes about from a deferred extreme touchiness reaction, in spite of the fact that a few living beings elude to cause diligent contamination. One figure contributing to *T. pallidum*'s chronicity is the lack of indispensably external film proteins, rendering intaglio living beings for all intents and purposes imperceptible to the resistant framework. Antigenic variety of TprK, a putative surface-exposed protein, is likely to contribute to safe avoidance. *T. pallidum* remains stunningly touchy to penicillin, but macrolide resistance has as of late been distinguished in a number of geographic districts. The advancement of a syphilis immunization, in this way distant tricky, would have a critical positive affect on worldwide wellbeing

1999 review focused on the epidemiological and clinical aspects of syphilis (290) and a 2005 review provided a detailed description of secondary syphilis (20). Here, we address research on the biology of *T. pallidum* and syphilis pathogenesis, highlighting investigative efforts over the last five years.

Syphilis is a chronic disease, and *T. pallidum*'s only known natural host is the human. Syphilis is acquired by direct contact, usually sexual, with active primary or secondary lesions. Studies have shown that 16 to 30% of individuals who have had sexual contact with a syphilis-infected person in the preceding 30 days become infected (205, 274); actual transmission rates may be much higher (6, 106, 271). Infection also occurs when organisms cross the placenta to infect the fetus in a pregnant woman. In the United States, the incidence of syphilis during the Second World War was over 500,000 infections per year. Between the years 1945 and 2000, syphilis declined to 31,575 reported infections, with alternating peaks and troughs of infectious cases. Since 2000, there has been an increase in the number of syphilis cases in the United States, mainly among men who have sex with men (MSM) (47-50, 52); these outbreaks have been reported along the west coast of the United States and in New York. Similar increases in syphilis in MSM have been reported in western Europe and the United Kingdom (111, 145, 166, 288, 321). Outbreaks among MSM are

associated with a rise in unsafe sexual behavior, perhaps a consequence of improved antiretroviral treatment for human immunodeficiency virus (HIV); in recent surveys, 37% to 52% of MSM reported multiple risk behaviors (69, 145, 146).

Compared to syphilis rates in developed countries, the worldwide burden of syphilis is formidable. The World Health Organization estimates that 12 million new cases of syphilis occur each year (107). The vast majority of these are seen in developing nations, but an increase in new cases has also been noted in eastern Europe since the dissolution of the Soviet Union (264, 336). Congenital syphilis is of particular concern in developing nations, where the lack of prenatal testing and antibiotic treatment of infected pregnant women results in congenital infection of the fetus. Congenital syphilis causes spontaneous abortion, stillbirth, death of the neonate, or disease in the infant; a recent report from Tanzania estimates that up to 50% of stillbirths are caused by syphilis (330). Of particular importance to worldwide health is the recognition that syphilis infection greatly increases the transmission and acquisition of HIV (115, 300). These factors, along with the highly destructive nature of late disease, make syphilis an important public health concern.

2. Signs and symptoms

Syphilis can display in one of four distinct stages: essential, optional, inert, and tertiary,[2] and may likewise happen congenitally.[15] It was alluded to as "the incredible imitator" by Sir William Osler because of its changed presentations.[2][16]

Primary

Essential syphilis is commonly gained by direct sexual contact with the irresistible sores of another person.[17] Approximately 3 to 90 days after the underlying introduction (normal 21 days) a skin injury, called a chancre, shows up at the purpose of contact. This is traditionally (40% of the time) a solitary, firm, effortless, non-bothersome skin ulceration with a perfect base and sharp fringes roughly 0.3– 3.0 cm in size.[2] The sore may take on practically any structure. In the exemplary structure, it develops from a macule to a papule lastly to a disintegration or ulcer.[18] Occasionally, various injuries might be available (~40%),[2] with different sores being increasingly basic when coinfecting with HIV. Sores might be difficult or delicate (30%), and they may happen in spots other than the private parts (2– 7%). The most widely recognized area in ladies is the cervix (44%), the penis in hetero men (99%), and anally and rectally in men who engage in sexual relations with men (34%).[18] Lymph hub growth much of the time (80%) happens around the zone of infection,[2] happening seven to 10 days after chancre formation.[18]The injury may endure for three to about a month and a half whenever left untreated.[2]

Secondary

Optional syphilis happens roughly four to ten weeks after the essential infection.[2] While auxiliary sickness is known for the various ways it can show, manifestations most regularly include the skin, mucous films, and lymph nodes.[19] There might be a symmetrical, ruddy pink, non-bothersome rash on the storage compartment and furthest points, including the palms and soles.[2][20] The rash may progress toward becoming maculopapular or pustular. It might shape level, expansive, whitish, mole like sores on

mucous films, known as condyloma latum. These sores harbor microscopic organisms and are irresistible. Different side effects may incorporate fever, sore throat, disquietude, weight reduction, male pattern baldness, and headache.[2] Rare appearances incorporate liver irritation, kidney ailment, joint aggravation, periostitis, irritation of the optic nerve, uveitis, and interstitial keratitis.[2][21] The intense side effects more often than not resolve after three to six weeks;[21] about 25% of individuals may give a repeat of optional manifestations. Numerous individuals who present with optional syphilis (40– 85% of ladies, 20– 65% of men) don't report beforehand having had the established chancre of essential syphilis.[19]

Latent

Latent syphilis is defined as having serologic proof of infection without symptoms of disease.[17] It is further described as either early (less than 1 year after secondary syphilis) or late (more than 1 year after secondary syphilis) in the United States.[21] The United Kingdom uses a cut-off of two years for early and late latent syphilis.[18] Early latent syphilis may have a relapse of symptoms. Late latent syphilis is asymptomatic, and not as contagious as early latent syphilis.[21]

Tertiary

Tertiary syphilis may happen around 3 to 15 years after the underlying contamination, and might be isolated into three distinct structures: gummatous syphilis (15%), late neurosyphilis (6.5%), and cardiovascular syphilis (10%).[2][21] Without treatment, 33% of tainted individuals create tertiary disease.[21] People with tertiary syphilis are not infectious.[2]

Gummatous syphilis or late favorable syphilis more often than not happens 1 to 46 years after the underlying disease, with a normal of 15 years. This stage is portrayed by the arrangement of interminable gummas, which are delicate, tumor-like wads of aggravation which may fluctuate extensively in size. They regularly influence the skin, bone, and liver, yet can happen anywhere.[2]

Neurosyphilis alludes to a disease including the focal sensory system. It might happen early, being either asymptomatic or as syphilitic meningitis, or late as meningovascular syphilis, general paresis, or sexually transmitted disease, which is related with poor parity and lightning torments in the lower limits. Late neurosyphilis commonly happens 4 to 25 years after the underlying disease. Meningovascular syphilis ordinarily gives lack of care and seizures, and general paresis with dementia and emaciation dorsalis.[2] Also, there might be Argyll Robertson understudies, which are respective little students that tighten when the individual spotlights on close articles (convenience reflex) yet don't contract when presented to splendid light (pupillary reflex).Cardiovascular syphilis for the most part happens 10– 30 years after the underlying contamination. The most well-known entanglement is syphilitic aortitis, which may result in aortic aneurysm formation.[2]

Congenital

Intrinsic syphilis is what is transmitted amid pregnancy or amid birth. 66% of syphilitic babies are conceived without indications. Regular indications that create over the primary couple of long stretches of life incorporate extension of the liver and spleen (70%), rash (70%), fever (40%), neurosyphilis (20%), and lung irritation (20%). In the event

that untreated, late inborn syphilis may happen in 40%, including saddle nose misshapening, Higoumenakis sign, saber shin, or Clutton's joints among others.[6] Infection amid pregnancy is likewise connected with miscarriage.[22]

3. Cause

Bacteriology

Treponema pallidum subspecies pallidum is a winding molded, Gram-negative, exceedingly portable bacterium.[10][18] Three other human illnesses are brought about by related Treponema pallidum subspecies, including yaws (subspecies pertenuae), pinta (subspecies carateum) and bejel (subspecies endemicum).[2] Unlike subspecies pallidum, they don't cause neurological disease.[6] Humans are the main known regular store for subspecies pallidum.[15] It is unfit to endure in excess of a couple of days without a host.[18] This is because of its little genome (1.14Mbp) neglecting to encode the metabolic pathways important to make the majority of its macronutrients.[18] It has a moderate multiplying time of more noteworthy than 30 hours.[18]

Transmission

Syphilis is transmitted essentially by sexual contact or amid pregnancy from a mother to her baby; the spirochete can go through unblemished mucous layers or bargained skin.[2][15] It is hence transmissible by kissing close to an injury, just as oral, vaginal, and butt-centric sex.[2][23] Approximately 30% to 60% of those presented to essential or optional syphilis will get the disease.[21] Its infectivity is exemplified by the way that an individual immunized with just 57 creatures has a half possibility of being infected.[18] Most (60%) of new cases in the United States happen in men who engage in sexual relations with men; and in this populace 20% of syphilis were because of oral sex alone.[23][2] Syphilis can be transmitted by blood items, however the hazard is low because of screening of gave blood in numerous countries.[2] The danger of transmission from sharing needles shows up limited.[2]

It isn't commonly conceivable to contract syphilis through latrine seats, every day exercises, hot tubs, or sharing eating utensils or clothing.[24] This is predominantly in light of the fact that the microscopic organisms kick the bucket in all respects rapidly outside of the body, making transmission by articles amazingly difficult.[25]

Diagnosis

Syphilis is hard to analyze clinically amid early infection.[18] Confirmation is either through blood tests or direct visual review utilizing dim field microscopy. Blood tests are all the more regularly utilized, as they are simpler to perform.[2] Diagnostic tests are unfit to recognize the phases of the disease.[26]

Blood test

Blood tests are partitioned into nontreponemal and treponemal tests [18]. Nontreponemal tests are utilized at first, and incorporate venereal sickness look into research center (VDRL) and fast plasma reagin (RPR) tests. False positives on the nontreponemal tests can happen with some popular contaminations, for example, varicella (chickenpox) and measles. False positives can likewise happen with lymphoma, tuberculosis, intestinal sickness, endocarditis, connective tissue ailment, and pregnancy.[17]

On account of the likelihood of false positives with nontreponemal tests, affirmation is required with a treponemal test, for example, treponemal pallidum molecule agglutination (TPHA) or fluorescent treponemal counter acting agent assimilation test (FTA-Abs).[2] Treponemal immunizer tests typically turned out to be sure two to five weeks after the underlying infection.[18] Neurosyphilis is analyzed by discovering high quantities of leukocytes (predominately lymphocytes) and high protein levels in the cerebrospinal liquid in the setting of a known syphilis infection.[2][17]

Direct testing

Dull field microscopy of serous liquid from a chancre might be utilized to make a quick analysis. Emergency clinics don't generally have gear or experienced staff individuals, and testing must be done inside 10 minutes of procuring the example. Affectability has been accounted for to be almost 80%; in this manner the test must be utilized to affirm a conclusion, not to preclude one. Two different tests can be done on an example from the chancre: direct fluorescent immune response (DFA) and polymerase chain response (PCR) tests. DFA utilizes antibodies labeled with fluorescein, which connect to explicit syphilis proteins, while PCR utilizes procedures to identify the nearness of explicit syphilis qualities. These tests are not as time-delicate, as they don't require living microorganisms to make the diagnosis.[18]

4. Prevention

Vaccine

As of 2018, there is no vaccine high-quality for prevention.[15] Several vaccines primarily based on treponemal proteins limit lesion development in an animal model but research continues.[27]

Sex

Condom use reduces the possibility of transmission at some point of sex, however does now not definitely take away the risk.[28] The Centers for Disease Control and Prevention (CDC) states, "Correct and constant use of latex condoms can minimize the hazard of syphilis only when the contaminated region or website of possible publicity is protected. However, a syphilis sore backyard of the area included with the aid of a latex condom can nevertheless enable transmission, so warning need to be exercised even when the use of a condom." [29]

Abstinence from intimate physical contact with an infected man or woman is wonderful at reducing the transmission of syphilis. The CDC states, "The surest way to avoid transmission of sexually transmitted diseases, including syphilis, is to abstain from sexual contact or to be in a long-term together monogamous relationship with a companion who has been examined and is recognized to be uninfected." [29]

Congenital disease

Congenital syphilis in the newborn can be prevented by using screening mothers at some stage in early pregnancy and treating these who are infected.[31] The United States Preventive Services Task Force (USPSTF) strongly recommends universal screening of all pregnant women,[32] whilst the World Health Organization (WHO) recommends all girls be tested at their first antenatal visit and again in the 0.33 trimester. If they are positive, it is endorse their companions additionally be treated.[33] Congenital syphilis is nonetheless common in the creating world, as many ladies

do not acquire antenatal care at all, and the antenatal care others get hold of does now not consist of screening. It nonetheless every now and then takes place in the developed world, as these most possibly to accumulate syphilis are least in all likelihood to obtain care for the duration of pregnancy.[31] Several measures to expand get entry to to trying out show up fantastic at decreasing quotes of congenital syphilis in low- to middle-income countries.[33] Point-of-care testing to become aware of syphilis seemed to be reliable even though extra lookup is wished to investigate its effectiveness and into enhancing outcomes in moms and babies.[34]

5. Screening

The CDC recommends that sexually energetic men who have intercourse with guys be examined at least yearly.[35] The USPSTF additionally recommends screening among those at excessive risk.[36]

Syphilis is a notifiable disorder in many countries, including Canada[37] the European Union,[38] and the United States.[39] This skill fitness care carriers are required to notify public fitness authorities, which will then ideally supply associate notification to the person's partners.[40] Physicians might also also inspire sufferers to ship their partners to searching for care.[41] Several strategies have been observed to improve follow-up for STI testing, inclusive of e mail and textual content messaging of reminders for appointments.[42]

6. Treatment

Early infections

The first-line cure for effortless syphilis stays a single dose of intramuscular benzathine benzylpenicillin.[43] Doxycycline and tetracycline are alternative choices for these allergic to penicillin; due to the risk of delivery defects, these are now not encouraged for pregnant women.[43] Resistance to macrolides, rifampicin, and clindamycin is regularly present.[15] Ceftriaxone, a third-generation cephalosporin antibiotic, may also be as positive as penicillin-based treatment.[2] It is advocated that a treated man or woman keep away from intercourse until the sores are healed.[24]

Late infections

For neurosyphilis, due to the terrible penetration of benzathine penicillin into the central worried system, those affected are given massive doses of intravenous penicillin for a minimal of 10 days.[2][15] If a individual is allergic to

penicillin, ceftriaxone may additionally be used or penicillin desensitization attempted. Other late presentations may be dealt with once-weekly intramuscular benzathine penicillin for three weeks. Treatment at this stage fully limits in addition development of the ailment and has a restrained effect on injury which has already occurred.[2]

7. Jarisch-Herxheimer reaction

One of the manageable aspect consequences of treatment is the Jarisch-Herxheimer reaction. It regularly starts within one hour and lasts for 24 hours, with signs of fever, muscle pains, headache, and a fast heart rate.[2] It is brought about through cytokines launched by using the immune system in response to lipoproteins released from rupturing syphilis bacteria.[44]

Pregnanc Penicillin is an superb treatment for syphilis in pregnancy[45] but there is no agreement on which dose or route of delivery is most effective.[46]

The choice of cure is dependent upon the stage and web site of infection (see Table 1). Penicillins are the recommended first-line treatment. Primary syphilis can also be dealt with with a single intramuscular injection of benzathine penicillin[14],[20]. A longer duration is required for these who have had syphilis for more than two years (i.e. late syphilis) due to the fact there is an related threat of relapse after short courses of treatment[21]. In cases of neurosyphilis, precise treatment is selected primarily based upon cerebral spinal fluid (CSF) penetration ensuing in anti-treponemal levels[22].

Although penicillins are regarded the gold standard, medical scenarios may also happen the place this may be inappropriate. For example, cases of allergy; non-adherence; refusal of parenteral therapy; and resource-poor settings. There are numerous choices for sufferers who are allergic to penicillin. These include, if deemed appropriate, penicillin desensitisation therapy[23] or alternative treatments (see Table 1). Doxycycline is the preferred alternative in resource-poor settings owing to its low value and oral administration. Resistance and stated clinical failure limits the use of macrolides (e.g. erythromycin[14]); these have to only be used in settings with resistance trying out or in penicillin-allergic sufferers who are pregnant; however, follow-up should be carried out[24],[25]. In patients who can also now not adhere to complicated drug regimens, stat doses of azithromycin have confirmed efficacy in early syphilis[26] y

When treating pregnant patients, the trimester and staging of disease are important in determining an appropriate treatment regimen, as outlined in Table 1

Clinical stage	Recommended regimen	Alternative regimens
		Procaine penicillin G 600,000 units IM daily for 10 days Amoxicillin 500mg orally (PO), four times a day (QDS) plus probenecid 500mg for 14 days
Early syphilis (primary, secondary or latent <2 years) in adults	Benzathine penicillin 2.4 MU intramuscularly (IM) as a single dose	Penicillin allergic: Doxycycline 100mg PO, twice daily (BD) for 14 days Ceftriaxone 500mg IM daily for 10 days (dependent on allergy) Azithromycin 2g PO stat or azithromycin 500mg daily for 10 days** Erythromycin 500mg QDS for 14 days**

Late (late or latent syphilis or syphilis of unknown duration), cardiovascular and gummatous syphilis in adults	Benzathine penicillin 2.4 MU IM, given weekly for three weeks (three doses)	Procaine penicillin G 600,000 units IM every day (OD) for 14 days Amoxicillin 2g PO, three times daily (TDS) plus probenecid 500mg QDS for 28 days Penicillin allergic: Doxycycline 100mg PO BD for 28 days Amoxicillin 2g PO TDS plus probenecid 500mg PO QDS for 28 days
Neurosyphilis	Benzylpenicillin 10.8–14.4g daily, given as 1.8–2.4g intravenously (IV) every 4 hours for 14 days	Penicillin allergic: Doxycycline 200mg PO BD for 28 days Ceftriaxone 2g IM or IV OD for 10–14 days (dependent on allergy)

Syphilis management in pregnancy

	First and second trimester: Benzathine penicillin 2.4 MU IM single dose	Penicillin noProcaine penicillin G 600,000 unit IM daily for 10 days non-allergic: Amoxycillin 500mg PO QDS plus probenecid 500mg PO QDS for 14 days
Early syphilis (primary, secondary or latent <2 years)	Third trimester: Benzathine penicillin 2.4 MU weekly (two doses)	Penicillin allergic: Ceftriaxone 500mg IM daily for 10 days (dependent on allergy) Erythromycin 500mg PO 14 days Azithromycin 500mg PO daily for 10 days
Late syphilis (latent syphilis or syphilis of unknown duration)	Benzathine penicillin 2.4 MU IM given weekly for three weeks (three doses)*	Procaine penicillin G 600,000 units IM OD for 14 days Amoxycillin 2g PO TDS plus probenecid 500mg QDS for 28 days

Congenital syphilis management in neonates

Congenital syphilis	Benzyl penicillin sodium IV 30mg/kg 12-hourly in the first 7 days of life and 8-hourly thereafter for 10 days	Procaine penicillin 50,000 units/kg daily IM for 10 days
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8. Treatment side effect

Penicillin use has an associated hypersensitivity risk. Patients may additionally also go through from a Jarisch-Herxheimer reaction, which manifests as a febrile illness and rash; it is hypothesised that the killed spirochaete releases a causative endotoxin. In cases of cardiovascular and neurosyphilis, steroids are co-administered to prevent atrophy of the corresponding organ through this reaction[20]. The patient need to be conscious of this reaction to prevent improper labelling as penicillin allergic. On uncommon occasions, procaine psychosis, an acute psychotic reaction, can also manifest owing to inadvertent intravenous administration, probably inflicting anxiety, hallucinations and convulsions. This can closing up to 20 minutes [28]

9. Patient counselling

Patients ought to be counselled to monitor for these signs and symptoms and have to contact a healthcare expert if they occur; they need to now not resume sexual endeavor until two weeks after treatment completion or, in the presence of any lesion(s), until all lesions have healed[14],[20]. Latex condoms might also shield in opposition to transmission from penile lesions and patients need to be suggested to sterilise any sex toys; this may also be accomplished in a dishwasher. Patients should alert preceding sexual partners, who can also be examined in accordance to the US Centers for Disease Control and Prevention guidelines[29]. As transmission is only thought

to show up in patients where lesions are present, timing of publicity is vital in determining treatment.

10. Follow-up and evaluation of syphilis treatment

Patients must be evaluated at six months and one year after treatment the usage of each scientific and serological testing[14]. Reoccurrence might also be attributed to re-infection after ample treatment. Treatment failure following appropriate antimicrobial therapy is no longer commonly owing to resistance, but as a substitute incomplete remedy or unrecognised CNS infection. Therefore, repeat CSF checking out may additionally be indicated[14],[20]. Management of recurrent infection entails weekly injections of benzathine penicillin G 2.4 million devices IM for three doses, except there is CSF involvement or the affected person is penicillin allergic (see Table 1). Those who have recurrent contamination should be tested and/or retested for the presence of HIV infection[20].

11. Epidemiology

In 2012, about 0.5% of adults have been contaminated with syphilis, with 6 million new cases.[8] In 1999, it is believed to have infected 12 million additional people, with greater than 90% of instances in the developing world.[15] It impacts between 700,000 and 1.6 million pregnancies a year, resulting in spontaneous abortions, stillbirths, and congenital syphilis.[6] During 2015, it triggered about 107,000 deaths, down from 202,000 in 1990.[5][9] In sub-Saharan Africa, syphilis contributes to approximately 20% of

perinatal deaths.[6] Rates are proportionally higher amongst intravenous drug users, these who are infected with HIV, and men who have intercourse with men.[11][12][13] In the United States, rates of syphilis as of 2007 had been six times greater in men than in women; they have been almost equal ten years earlier.[48] African Americans accounted for nearly half of all cases in 2010.[49] As of 2014, syphilis infections proceed to enlarge in the United States.[50]

Syphilis used to be very frequent in Europe at some point of the 18th and nineteenth centuries.[10] Flaubert found it regular among nineteenth-century Egyptian prostitutes.[51] In the developed world during the early twentieth century, infections declined rapidly with the sizable use of antibiotics, till the Eighties and 1990s.[10] Since 2000, charges of syphilis have been growing in the US, Canada, the UK, Australia and Europe, especially amongst guys who have sex with men.[15] Rates of syphilis among US women have remained secure during this time, while prices among UK girls have increased, but at a charge much less than that of men.[52] Increased rates among heterosexuals have took place in China and Russia since the 1990s.[15] This has been attributed to risky sexual practices, such as sexual promiscuity, prostitution, and lowering use of barrier protection.[15][52][53]

Left untreated, it has a mortality charge of 8% to 58%, with a increased demise rate amongst males.[2] The signs of syphilis have turn out to be less extreme over the nineteenth and twentieth centuries, in part due to significant availability of high quality treatment, and partly due to virulence of the bacteria.[19] With early treatment, few complications result.[18] Syphilis will increase the threat of HIV transmission with the aid of two to five times, and coinfection is frequent (30–60% in some city centers).[2][15] In 2015, Cuba grew to be the first usa in the world to eradicate mom to child transmission of syphilis.[14]

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