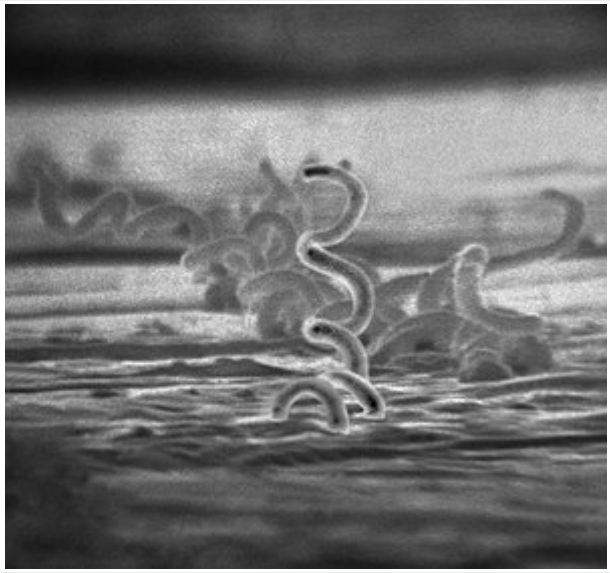
Syphilis

Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum* subspecies *pallidum*.[3] The signs and symptoms of syphilis vary depending in which of the four stages it presents (primary, secondary, latent, and tertiary).[1] The primary stage classically presents with a single chancre (a firm, painless, non-itchy skin ulceration usually between 1 cm and 2 cm in diameter) though there may be multiple sores.[1] In secondary syphilis, a diffuse rash occurs, which frequently involves the palms of the hands and soles of the feet.[1] There may also be sores in the mouth or vagina.[1] In latent syphilis, which can last for years, there are few or no symptoms.[1] In tertiary syphilis, there are gummas (soft, non-cancerous growths), neurological problems, or heart symptoms.[2] Syphilis has been known as "the great imitator" as it may cause symptoms similar to many other diseases.[1][2]

Syphilis is most commonly spread through sexual activity.[1] It may also be transmitted from mother to baby during pregnancy or at birth, resulting in congenital syphilis.[1][6] Other diseases caused by the *Treponema* bacteria include yaws (subspecies *pertenue*), pinta (subspecies *carateum*), and nonvenereal endemic syphilis (subspecies *endemicum*).[2] These three diseases are not typically sexually transmitted.[7] Diagnosis is usually made by using blood tests; the bacteria can also be detected using dark field microscopy.[1] The Centers for Disease Control and Prevention (U.S.) recommend all pregnant women be tested.[1]

Syphilis



Electron micrograph of *Treponema pallidum*

Specialty	Infectious disease
Symptoms	Firm, painless, non-itchy skin ulcer[1]
Causes	*Treponema pallidum* usually spread by sex[1]
Diagnostic method	Blood tests, dark field microscopy of infected fluid[1][2]
Differential diagnosis	Many other diseases[1]
Prevention	Condoms, not having sex[1]
Treatment	Antibiotics[3]
Frequency	45.4 million / 0.6% (2015)[4]
Deaths	107,000 (2015)[5]

The risk of sexual transmission of syphilis can be reduced by using a latex or polyurethane condom.[1] Syphilis can be effectively treated with antibiotics.[3] The preferred antibiotic for most cases is benzathine benzylpenicillin injected into a muscle.[3] In those who have a severe penicillin allergy, doxycycline or tetracycline may be used.[3] In those with neurosyphilis, intravenous benzylpenicillin or ceftriaxone is recommended.[3] During treatment people may develop fever, headache, and muscle pains, a reaction known as Jarisch-Herxheimer.[3]

In 2015, about 45.4 million people were infected with syphilis,[4] with 6 million new cases.[8] During 2015, it caused about 107,000 deaths, down from 202,000 in 1990.[5][9] After decreasing dramatically with the availability of penicillin in the 1940s, rates of infection have increased since the turn of the millennium in many countries, often in combination with human immunodeficiency virus (HIV).[2][10] This is believed to be partly due to increased promiscuity, prostitution, decreasing use of condoms, and unsafe sexual practices among men who have sex with men.[11][12][13] In 2015, Cuba became the first country to eliminate mother-to-child transmission of syphilis.[14]

Contents

Signs and symptoms

Syphilis can present in one of four different stages: primary, secondary, latent, and tertiary,[2] and may also occur congenitally.[15] It was referred to as "the great imitator" by Sir William Osler due to its varied presentations.[2][16][17]

Primary

Primary chancre of syphilis at the site of infection on the penis

Primary syphilis is typically acquired by direct sexual contact with the infectious lesions of another person.[18] Approximately 3 to 90 days after the initial exposure (average 21 days) a skin lesion, called a chancre, appears at the point of contact.[2] This is classically (40% of the time) a single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders approximately 0.3–3.0 cm in size.[2] The lesion may take on almost any form.[19] In the classic form, it evolves from a macule to a papule and finally to an erosion or ulcer.[19] Occasionally, multiple lesions may be present (~40%),[2] with multiple lesions being more common when coinfected with HIV.[19] Lesions may be painful or tender (30%), and they may occur in places other than the genitals (2–7%).[19] The most common location in women is the cervix (44%), the penis in heterosexual men (99%), and anally and rectally in men who have sex with men (34%).[19] Lymph node enlargement frequently (80%) occurs around the area of infection,[2] occurring seven to 10 days after chancre formation.[19] The lesion may persist for three to six weeks if left untreated.[2]

Secondary

Typical presentation of secondary syphilis with a rash on the palms of the hands

Secondary syphilis occurs approximately four to ten weeks after the primary infection.[2] While secondary disease is known for the many different ways it can manifest, symptoms most commonly involve the skin, mucous membranes, and lymph nodes.[20] There may be a symmetrical, reddish-pink, non-itchy rash on the trunk and extremities, including the palms and soles.[2][21] The rash may become maculopapular or pustular.[2] It may form flat, broad, whitish, wart-like lesions on mucous membranes, known as condyloma latum.[2] All of these lesions harbor bacteria and are infectious.[2] Other symptoms may include fever, sore throat, malaise, weight loss, hair loss, and headache.[2] Rare manifestations include liver inflammation, kidney disease, joint inflammation, periostitis, inflammation of the optic nerve, uveitis, and interstitial keratitis.[2][22] The acute symptoms usually resolve after three to six weeks;[22] about 25% of people may present with a recurrence of secondary symptoms.[20][23] Many people who present with secondary syphilis (40–85% of women, 20–65% of men) do not report previously having had the classical chancre of primary syphilis.[20]

Latent

Latent syphilis is defined as having serologic proof of infection without symptoms of disease.[18] 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.[22] The United Kingdom uses a cut-off of two years for early and late latent syphilis.[19] Early latent syphilis may have a relapse of symptoms in 25% of cases.[24][22] Late latent syphilis is asymptomatic, and not as contagious as early latent syphilis.[22][25]

Reddish papules and nodules over much of the body due to secondary syphilis

Tertiary

Model of a head of a person with tertiary (gummatous) syphilis, Musée de l'Homme, Paris.

Tertiary syphilis may occur approximately 3 to 15 years after the initial infection, and may be divided into three different forms: gummatous syphilis (15%), late neurosyphilis (6.5%), and cardiovascular syphilis (10%).[2][22] Without treatment, a third of infected people develop tertiary disease.[22] People with tertiary syphilis are not infectious.[2]

Gummatous syphilis or late benign syphilis usually occurs 1 to 46 years after the initial infection, with an average of 15 years.[2] This stage is characterized by the formation of chronic gummas, which are soft, tumor-like balls of inflammation which may vary considerably in size.[2] They typically affect the skin, bone, and liver, but can occur anywhere.[2]

Neurosyphilis refers to an infection involving the central nervous system. It may occur early, being either asymptomatic or in the form of syphilitic meningitis, or late as meningovascular syphilis, general paresis, or tabes dorsalis, which is associated with poor balance and lightning pains in the lower extremities.[2] Late neurosyphilis typically occurs 4 to 25 years after the initial infection.[2] Meningovascular syphilis typically presents with apathy and seizures, and general paresis with dementia and tabes dorsalis.[2] Also, there may be Argyll Robertson pupils, which are bilateral small pupils that constrict when the person focuses on near objects (accommodation reflex) but do not constrict when exposed to bright light (pupillary reflex).

Cardiovascular syphilis usually occurs 10–30 years after the initial infection.[2] The most common complication is syphilitic aortitis, which may result in aortic aneurysm formation.[2]

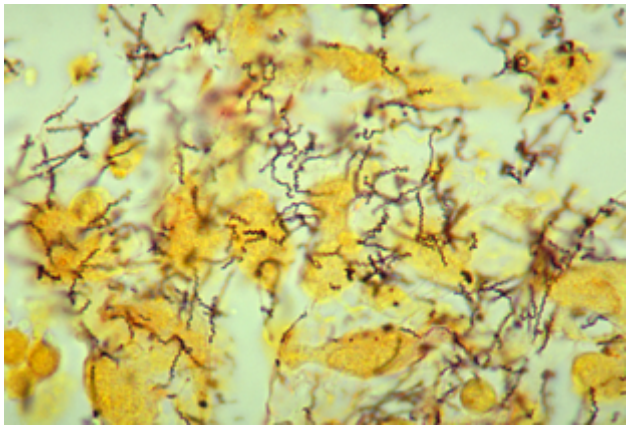
Congenital

Congenital syphilis is that which is transmitted during pregnancy or during birth.[6] Two-thirds of syphilitic infants are born without symptoms.[6] Common symptoms that develop over the first couple of years of life include enlargement of the liver and spleen (70%), rash (70%), fever (40%), neurosyphilis (20%), and lung inflammation (20%).[6] If untreated, late congenital syphilis may occur in 40%, including saddle nose deformation, Higouménakis' sign, saber shin, or Clutton's joints among others.[6] Infection during pregnancy is also associated with miscarriage.[26] The three main dental defects in congenital syphilis are Hutchinson's incisors (screwdriver shaped incisors), Moon's molars or bud molars, and Fournier's molars or mulberry molars (molars with abnormal occlusal anatomy resembling a mulberry).[27]

Cause

Bacteriology

Treponema pallidum subspecies *pallidum* is a spiral-shaped, Gram-negative, highly mobile bacterium.[10][19] Three other human diseases are caused by related *Treponema pallidum* subspecies, including yaws (subspecies *pertenue*), pinta (subspecies *carateum*) and bejel (subspecies *endemicum*).[2] Unlike subspecies *pallidum*, they do not cause neurological disease.[6] Humans are the only known natural reservoir for subspecies *pallidum*.[15] It is unable to survive more than a few days without a host.[19] This is due to its small genome (1.14Mbp) failing to encode the metabolic pathways necessary to make most of its macronutrients.[19] It has a slow doubling time of greater than 30 hours.[19] The bacterium is known for its ability to evade the immune system and its invasiveness.[28]



Histopathology of *Treponema pallidum* spirochetes using a modified Steiner silver stain

Transmission

Syphilis is transmitted primarily by sexual contact or during pregnancy from a mother to her baby; the spirochete is able to pass through intact mucous membranes or compromised skin.[2][15] It is thus transmissible by kissing near a lesion, as well as oral, vaginal, and anal sex.[2][29] Approximately 30% to 60% of those exposed to primary or secondary syphilis will get the disease.[22] Its infectivity is exemplified by the fact that an individual inoculated with only 57 organisms has a 50% chance of being infected.[19] Most (60%) of new cases in the United States occur in men who have sex with men; and in this population 20% of syphilis were due to oral sex alone.[29][2] Syphilis can be transmitted by blood products, but the risk is low due to screening of donated blood in many countries.[2] The risk of transmission from sharing needles appears limited.[2]

It is not generally possible to contract syphilis through toilet seats, daily activities, hot tubs, or sharing eating utensils or clothing.[30] This is mainly because the bacteria die very quickly outside of the body, making transmission by objects extremely difficult.[31]

Diagnosis

Syphilis is difficult to diagnose clinically during early infection.[19] Confirmation is either via blood tests or direct visual inspection using dark field microscopy.[2][33] Blood tests are more commonly used, as they are easier to perform.[2] Diagnostic tests are unable to distinguish between the stages of the disease.[34]

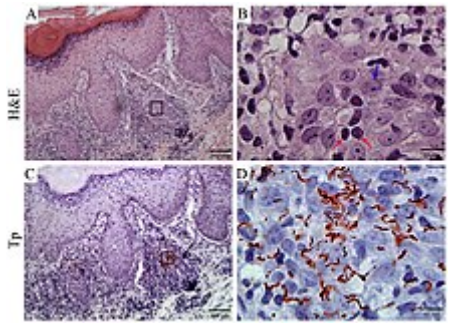
This poster acknowledges the social stigma of syphilis, while urging those who possibly have the disease to be tested (circa 1936).

Blood tests

Blood tests are divided into nontreponemal and treponemal tests.[19]

Nontreponemal tests are used initially, and include venereal disease research laboratory (VDRL) and rapid plasma reagin (RPR) tests. False positives on the nontreponemal tests can occur with some viral infections, such as varicella (chickenpox) and measles. False positives can also occur with lymphoma, tuberculosis, malaria, endocarditis, connective tissue disease, and pregnancy.[18]

Because of the possibility of false positives with nontreponemal tests, confirmation is required with a treponemal test, such as treponemal pallidum particle agglutination (TPHA) or fluorescent treponemal antibody absorption test (FTA-Abs).[2] Treponemal antibody tests usually become positive two to five weeks after the initial infection.[19] Neurosyphilis is diagnosed by finding high numbers of leukocytes (predominately lymphocytes) and high protein levels in the cerebrospinal fluid in the setting of a known syphilis infection.[2][18]



Micrograph of secondary syphilis skin lesions. (A/B) H&E stain of SS lesions. (C/D) IHC staining reveals abundant spirochetes embedded within a mixed cellular inflammatory infiltrate (shown in the red box) in the papillary dermis. The blue arrow points to a tissue histiocyte and the read arrows to two dermal lymphocytes.[32]

Direct testing

Dark field microscopy of serous fluid from a chancre may be used to make an immediate diagnosis.[19] Hospitals do not always have equipment or experienced staff members, and testing must be done within 10 minutes of acquiring the sample.[19] Sensitivity has been reported to be nearly 80%; therefore the test can only be used to confirm a diagnosis, not to rule one out.[19] Two other tests can be carried out on a sample from the chancre: direct fluorescent antibody (DFA) and polymerase chain reaction (PCR) tests.[19] DFA uses antibodies tagged with fluorescein, which attach to specific syphilis proteins, while PCR uses techniques to detect the presence of specific syphilis genes.[19] These tests are not as time-sensitive, as they do not require living bacteria to make the diagnosis.[19]

Prevention

Vaccine

As of 2018, there is no vaccine effective for prevention.[15] Several vaccines based on treponemal proteins reduce lesion development in an animal model but research continues.[35][36]

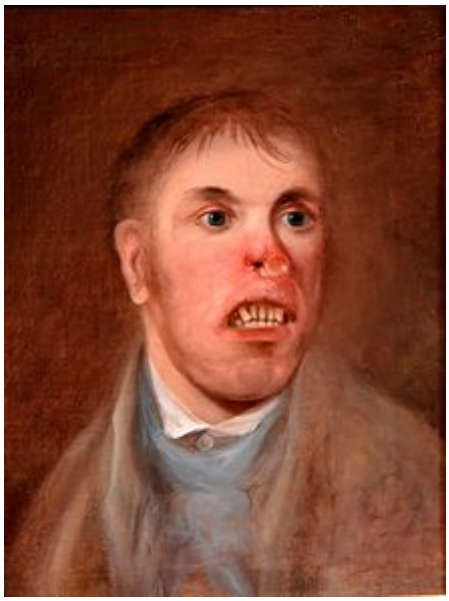
Sex

Condom use reduces the likelihood of transmission during sex, but does not completely eliminate the risk.[37] The Centers for Disease Control and Prevention (CDC) states, "Correct and consistent use of latex condoms can reduce the risk of syphilis only when the infected area or site of potential exposure is protected.[38] However, a syphilis sore outside of the area covered by a latex condom can still allow transmission, so caution should be exercised even when using a condom."[39]

Abstinence from intimate physical contact with an infected person is effective 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 mutually monogamous relationship with a partner who has been tested and is known to be uninfected."[39]

Congenital disease

Congenital syphilis in the newborn can be prevented by screening mothers during early pregnancy and treating those who are infected.[41] The United States Preventive Services Task Force (USPSTF) strongly recommends universal screening of all pregnant women,[42] while the World Health Organization (WHO) recommends all women be tested at their first antenatal visit and again in the third trimester.[43][44] If they are positive, it is recommend their partners also be treated.[43] Congenital syphilis is still common in the developing world, as many women do not receive antenatal care at all, and the antenatal care others receive does not include screening.[41][45] It still occasionally occurs in the developed world, as those most likely to acquire syphilis are least likely to receive care during pregnancy.[41] Several measures to increase access to testing appear effective at reducing rates of congenital syphilis in low- to middle-income countries.[43] Point-of-care testing to detect syphilis appeared to be reliable although more research is needed to assess its effectiveness and into improving outcomes in mothers and babies.[46]



Portrait of Mr. J. Kay, affected with what is now believed to have been congenital syphilis c. 1820[40]

Screening

The CDC recommends that sexually active men who have sex with men be tested at least yearly.[47] The USPSTF also recommends screening among those at high risk.[48]

Syphilis is a notifiable disease in many countries, including Canada[49] the European Union,[50] and the United States.[51] This means health care providers are required to notify public health authorities, which will then ideally provide partner notification to the person's partners.[52] Physicians may also encourage patients to send their partners to seek care.[53] Several strategies have been found to improve follow-up for STI testing, including email and text messaging of reminders for appointments.[54]

Treatment

Early infections

The first-line treatment for uncomplicated syphilis remains a single dose of intramuscular benzathine benzylpenicillin.[55] Doxycycline and tetracycline are alternative choices for those allergic to penicillin; due to the risk of birth defects, these are not recommended for pregnant women.[55] Resistance to macrolides, rifampicin, and clindamycin is often present.[15] Ceftriaxone, a third-generation cephalosporin antibiotic, may be as effective as penicillin-based treatment.[2] It is recommended that a treated person avoid sex until the sores are healed.[30]

Late infections

For neurosyphilis, due to the poor penetration of benzathine penicillin into the central nervous system, those affected are given large doses of intravenous penicillin for a minimum of 10 days.[2][15] If a person is allergic to penicillin, ceftriaxone may be used or penicillin desensitization attempted.[2] Other late presentations may be treated with once-weekly intramuscular benzathine penicillin for three weeks.[2] Treatment at this stage solely limits further progression of the disease and has a limited effect on damage which has already occurred.[2]

Jarisch-Herxheimer reaction

Jarisch-Herxheimer reaction in a person with syphilis and human immunodeficiency virus[56]

One of the potential side effects of treatment is the Jarisch-Herxheimer reaction.[2] It frequently starts within one hour and lasts for 24 hours, with symptoms of fever, muscle pains, headache, and a fast heart rate.[2] It is caused by cytokines released by the immune system in response to lipoproteins released from rupturing syphilis bacteria.[57]

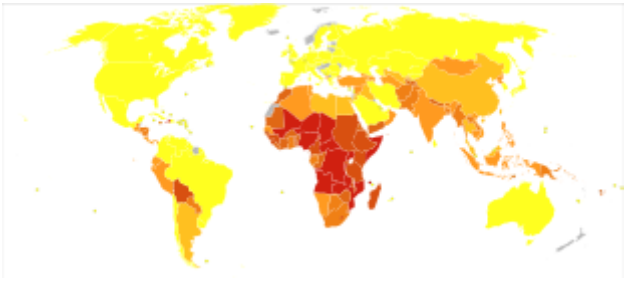
Pregnancy

Penicillin is an effective treatment for syphilis in pregnancy[58] but there is no agreement on which dose or route of delivery is most effective.[59]

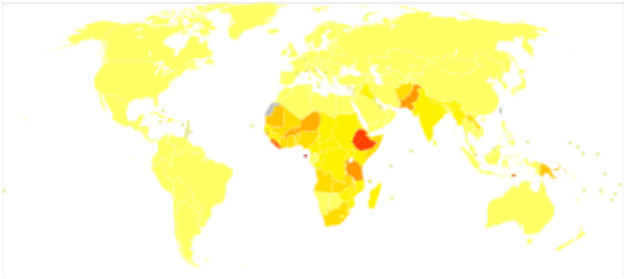
Epidemiology

In 2012, about 0.5% of adults were infected 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 cases in the developing world.[15] It affects between 700,000 and 1.6 million pregnancies a year, resulting in spontaneous abortions, stillbirths, and congenital syphilis.[6] During 2015, it caused 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 among intravenous drug users, those who are infected with HIV, and men who have sex with men.[11][12][13] In the United States about 55,400 people are newly infected each year.[61] In the United States, rates of syphilis as of 2007 were six times greater in men than in women; they were nearly equal ten years earlier.[62] African Americans accounted for almost half of all cases in 2010.[63] As of 2014, syphilis infections continue to increase in the United States.[64][65]



Syphilis was very common in Europe during the 18th and 19th centuries.[10] Flaubert found it universal among nineteenth-century Egyptian prostitutes.[66] In the developed world during the early 20th century, infections declined rapidly with the widespread use of antibiotics, until the 1980s and 1990s.[10] Since 2000, rates of syphilis have been increasing in the US, Canada, the UK, Australia and Europe, primarily among men who have sex with men.[15] Rates of syphilis among US women have remained stable during this time, while rates among UK women have increased, but at a rate less than that of men.[67] Increased rates among heterosexuals have occurred in China and Russia since the 1990s.[15] This has been attributed to unsafe sexual practices, such as sexual promiscuity, prostitution, and decreasing use of barrier protection.[15][67][68]



Left untreated, it has a mortality rate of 8% to 58%, with a greater death rate among males.[2] The symptoms of syphilis have become less severe over the 19th and 20th centuries, in part due to widespread availability of effective treatment, and partly due to virulence of the bacteria.[20] With early treatment, few complications result.[19] Syphilis increases the risk of HIV transmission by two to five times, and coinfection is common (30–60% in some urban centers).[2][15] In 2015, Cuba became the first country in the world to eradicate mother to child transmission of syphilis.[14]

History

The origin of syphilis is disputed.[2] Syphilis was present in the Americas before European contact,[70] and it may have been carried from the Americas to Europe by the returning crewmen from Christopher Columbus's voyage to the Americas, or it may have existed in Europe previously but gone unrecognized until shortly after Columbus's return.[34] These are the *Columbian* and *pre-Columbian* hypotheses, respectively, with the *Columbian* hypothesis better supported by the evidence.[34][71][72]

The first written records of an outbreak of syphilis in Europe occurred in 1494 or 1495 in Naples, Italy, during a French invasion (Italian War of 1494–98).[10][34] Since it was claimed to have been spread by French troops, it was initially called the "French disease" by the people of Naples.[73] In 1530, the pastoral name "syphilis" (the name of a character) was first used by the Italian physician and poet Girolamo Fracastoro as the title of his Latin poem in dactylic hexameter describing the ravages of the disease in Italy.[74][75] It was also called the "Great Pox".[76][77]

Portrait of Gerard de Lairesse by Rembrandt van Rijn, circa 1665–67, oil on canvas - De Lairesse, himself a painter and art theorist, had congenital syphilis that deformed his face and eventually blinded him.[69]

In the 16th through 19th centuries, syphilis was one of the largest public health burdens in prevalence, symptoms, and disability,[78]:208–209[79] although records of its true prevalence were generally not kept because of the fearsome and sordid status of sexually transmitted diseases in those centuries.[78]:208–209 At the time the causative agent was unknown but it was well known that it was spread sexually and also often from mother to child. Its association with sex, especially sexual promiscuity and prostitution, made it an object of fear and revulsion and a taboo. The magnitude of its morbidity and mortality in those centuries reflected that, unlike today, there was no adequate understanding of its pathogenesis and no truly effective treatments. Its damage was caused not so much by great sickness or death early in the course of the disease but rather by its gruesome effects decades after infection as it progressed to neurosyphilis with tabes dorsalis. Mercury compounds and isolation were commonly used, with treatments often worse than the disease.[76]

The causative organism, *Treponema pallidum*, was first identified by Fritz Schaudinn and Erich Hoffmann, in 1905.[80] The first effective treatment for syphilis was Arsphenamine, discovered by Sahachiro Hata in 1909, during a survey of hundreds of newly synthesized organic arsenical compounds led by Paul Ehrlich. It was manufactued and marketed from 1910 under the trade name Salvarsan by Hoechst AG.[81] This organoarsenic compound was the first modern chemotherapeutic agent.

During the 20th century, as both microbiology and pharmacology advanced greatly, syphilis, like many other infectious diseases, became more of a manageable burden than a scary and disfiguring mystery, at least in developed countries among those people who could afford to pay for timely diagnosis and treatment. Penicillin was discovered in 1928, and effectiveness of treatment with penicillin was confirmed in trials in 1943,[76] at which time it became the main treatment.[82]

Many famous historical figures, including Franz Schubert, Arthur Schopenhauer, Édouard Manet,[10] Charles Baudelaire,[83] and Guy de Maupassant are believed to have had the disease.[84] Friedrich Nietzsche was long believed to have gone mad as a result of tertiary syphilis, but that diagnosis has recently come into question.[85] It has been proposed that this was a posthumous smear campaign by anti-Nazis.[86]

Arts and literature

The earliest known depiction of an individual with syphilis is Albrecht Dürer's *Syphilitic Man*, a woodcut believed to represent a Landsknecht, a Northern European mercenary.[87] The myth of the *femme fatale* or "poison women" of the 19th century is believed to be partly derived from the devastation of syphilis, with classic examples in literature including John Keats' *La Belle Dame sans Merci*.[88][89]

The Flemish artist Stradanus designed a print called *Preparation and Use of Guayaco for Treating Syphilis*, a scene of a wealthy man receiving treatment for syphilis with the tropical wood guaiacum sometime around 1590.[90]

An early medical illustration of people with syphilis, Vienna, 1498

Tuskegee and Guatemala studies

A Work Projects Administration poster about syphilis c. 1940.

The "Tuskegee Study of Untreated Syphilis in the Negro Male" was an infamous, unethical, and racist clinical study conducted between 1932 and 1972 by the U.S. Public Health Service.[91][92] The purpose of this study was to observe the natural history of untreated syphilis; the African-American men in the study were told they were receiving free health care from the United States government.[93]

The Public Health Service started working on this study in 1932 in collaboration with Tuskegee University, a historically black college in Alabama. Investigators enrolled in the study a total of 600 impoverished, African-American sharecroppers from Macon County, Alabama. Of these men, 399 had previously contracted syphilis before the study began, and 201 did not have the disease.[92] The men were given free medical care, meals, and free burial insurance for participating in the study. The men were told that the study was only going to last six months, but it actually lasted 40 years.[92] After funding for treatment was lost, the study was continued without informing the men that they would never be treated. None of the men infected were ever told that they had the disease, and none were treated with penicillin even after the antibiotic was proven to successfully treat syphilis. According to the Centers for Disease Control, the men were told that they were being treated for "bad blood", a colloquialism that described various conditions such as syphilis, anemia, and fatigue. "Bad blood"—specifically the collection of illnesses the term included—was a leading cause of death within the southern African-American community.[92]

The 40-year study was controversial for reasons related to ethical standards. Researchers knowingly failed to treat patients appropriately after the 1940s validation of penicillin was found as an effective cure for the disease that they were studying. The revelation in 1972 of study failures by a whistleblower, Peter

Buxtun, led to major changes in U.S. law and regulation on the protection of participants in clinical studies. Now studies require informed consent,[94] communication of diagnosis, and accurate reporting of test results.[95]

Similar experiments were carried out in Guatemala from 1946 to 1948. It was done during the administration of American President Harry S. Truman and Guatemalan President Juan José Arévalo with the cooperation of some Guatemalan health ministries and officials.[96] Doctors infected soldiers, prostitutes, prisoners and mental patients with syphilis and other sexually transmitted diseases, without the informed consent of the subjects, and treated most subjects with antibiotics. The experiment resulted in at least 83 deaths.[97][98] In October 2010, the U.S. formally apologized to Guatemala for the ethical violations that took place. Clinton and Sebelius stated "Although these events occurred more than 64 years ago, we are outraged that such reprehensible research could have occurred under the guise of public health. We deeply regret that it happened, and we apologize to all the individuals who were affected by such abhorrent research practices."[99] The experiments were led by physician John Charles Cutler who also participated in the late stages of the Tuskegee syphilis experiment.[100]

Preparation and Use of Guayaco for Treating Syphilis, after Stradanus, 1590

Names

First called *grande verole* or the "great pox" by the French. Other historical names have included "button scurvy", sibbens, frenga and dichuchwa, among others.[101][102]

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External links

- "Syphilis - CDC Fact Sheet" (https://www.cdc.gov/std/Syphilis/STDFact-Syphilis.htm) Centers for Disease Control and Prevention (CDC)
- UCSF HIV InSite Knowledge Base Chapter: Syphilis and HIV (http://hivinsite.ucsf.edu/InSite?page=kb-05-01-04)
- Recommendations for Public Health Surveillance of Syphilis in the United States (https://www.cdc.gov/std/syphsurvreco.pdf)

Classification	**ICD-10**: A50 (http://apps.who.int/classifications/icd10/browse/2016/en#/A50)-A53 (http://apps.who.int/classifications/icd10/browse/20 D

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External resources	**MedlinePlus**: 000861 (https://www.nlm.nih.gov/medlineplus/ency/article/000861.htm) · **eMedicine**: med/2224 (https://emedicine.medscape.com/med/2224-overview) emerg/563 (http://www.emedicine.com/emerg/topic563.htm#) derm/413 (http://www.emedicine.com/derm/topic413.htm#) · **Patient UK**: Syphilis (https://patient.info/doctor/syphilis-pro)