[Template:Use dmy dates](/wiki/Template:Use_dmy_dates" \o "Template:Use dmy dates) [Template:Good article](/wiki/Template:Good_article) [Template:Infobox medical condition](/wiki/Template:Infobox_medical_condition) **Syphilis** is a [sexually transmitted infection](/wiki/Sexually_transmitted_infection) caused by the [bacterium](/wiki/Bacterium) [*Treponema pallidum*](/wiki/Treponema_pallidum) subspecies *pallidum*.<ref name=CDC2015Tx>[Template:Cite web](/wiki/Template:Cite_web)</ref> The signs and symptoms of syphilis vary depending in which of the four stages it presents (primary, secondary, latent, and tertiary). The primary stage classically presents with a single [chancre](/wiki/Chancre) (a firm, painless, non-itchy [skin ulceration](/wiki/Skin_ulceration)) but there may be multiple sores. In secondary syphilis a diffuse rash which frequently involves the palms of the hands and soles of the feet occurs. There may also be sores in the mouth or vagina. In latent syphilis there are little to no symptoms which can last for years.<ref name=CDC2015Fact/> In tertiary syphilis there are [gummas](/wiki/Gumma_(pathology)) (soft non-cancerous growths), neurological, or heart symptoms.<ref name=Kent08>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Syphilis has been known as "[the great imitator](/wiki/The_great_imitator)" as it may cause symptoms similar to many other diseases.<ref name=CDC2015Fact>[Template:Cite web](/wiki/Template:Cite_web)</ref><ref name=Kent08/>

Syphilis is most commonly spread through [sexual activity](/wiki/Human_sexual_activity).<ref name=CDC2015Fact/> It may also be transmitted from mother to baby during pregnancy or at birth, resulting in [congenital syphilis](/wiki/Congenital_syphilis).<ref name=CDC2015Fact/><ref name=Wood09>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Other human diseases caused by related *Treponema pallidum* include [yaws](/wiki/Yaws) (subspecies *pertenue*), [pinta](/wiki/Pinta_(disease)) (subspecies *carateum*), and [bejel](/wiki/Nonvenereal_endemic_syphilis) (subspecies *endemicum*).<ref name=Kent08/> Diagnosis is usually made by using [blood tests](/wiki/Serological_testing); the bacteria can also be detected using [dark field microscopy](/wiki/Dark_field_microscopy). The Center for Disease Control recommends all pregnant women be tested.<ref name=CDC2015Fact/>

The risk of syphilis can be decreased by [latex condom](/wiki/Latex_condom) use or not having sex.<ref name=CDC2015Fact/> Syphilis can be effectively treated with [antibiotics](/wiki/Antibiotics). The preferred antibiotic for most cases is [benzathine penicillin G](/wiki/Benzathine_benzylpenicillin) [injected into a muscle](/wiki/Intramuscular). In those who have a severe [penicillin allergy](/wiki/Penicillin_allergy), [doxycycline](/wiki/Doxycycline) or [tetracycline](/wiki/Tetracycline) may be used. In those with [neurosyphilis](/wiki/Neurosyphilis) [intravenous](/wiki/Intravenous) [penicillin G potassium](/wiki/Benzylpenicillin) or [ceftriaxone](/wiki/Ceftriaxone) is recommended. During treatment people may develop fever, headache, and [muscle pains](/wiki/Myalgia), a reaction known as [Jarisch-Herxheimer](/wiki/Jarisch-Herxheimer_reaction).<ref name=CDC2015Tx/>

In 2013 syphilis infected about 315,000 people.<ref name=GBD2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> During 2010 it caused about 113,000 deaths down from 202,000 in 1990.<ref name=Loz2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> 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](/wiki/HIV) (HIV).<ref name=Kent08/><ref name=Music08>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This is believed to be partly due to increased [promiscuity](/wiki/Promiscuity), [prostitution](/wiki/Prostitution), decreasing use of condoms, and unsafe sexual practices among [men who have sex with men](/wiki/Men_who_have_sex_with_men).[[1]](#cite_note-1)[[2]](#cite_note-2)[[3]](#cite_note-3) In 2015, [Cuba](/wiki/Cuba) became the first country in the world to eliminate mother-to-child transmission of syphilis.<ref name=WHOCUba2015>[Template:Cite web](/wiki/Template:Cite_web)</ref> [Template:TOC limit](/wiki/Template:TOC_limit)

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## Signs and symptoms[[edit](/index.php?title=(none)&action=edit&section=1)]

Syphilis can present in one of four different stages: primary, secondary, latent, and tertiary,<ref name=Kent08/> and may also occur [congenitally](/wiki/Congenital).<ref name=ST10>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> It was referred to as "the great imitator" by [Sir William Osler](/wiki/Sir_William_Osler) due to its varied presentations.<ref name=Kent08/><ref name=TUS00/>

### Primary[[edit](/index.php?title=(none)&action=edit&section=2)]

[thumb|upright=1.4|Primary](/wiki/Image:Chancres_on_the_penile_shaft_due_to_a_primary_syphilitic_infection_caused_by_Treponema_pallidum_6803_lores.jpg) [chancre](/wiki/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.<ref name=RedBookSyphilis>[Template:Cite book](/wiki/Template:Cite_book)</ref> Approximately 3 to 90 days after the initial exposure (average 21 days) a skin lesion, called a [chancre](/wiki/Chancre), appears at the point of contact.<ref name=Kent08/> This is classically (40% of the time) a single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders between 0.3 and 3.0 cm in size.<ref name=Kent08/> The lesion may take on almost any form.<ref name=Pri2008>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In the classic form, it evolves from a [macule](/wiki/Macule) to a [papule](/wiki/Papule) and finally to an [erosion](/wiki/Erosion_(dermatopathology)#Primary_lesions) or [ulcer](/wiki/Ulcer_(dermatology)).<ref name=Pri2008/> Occasionally, multiple lesions may be present (~40%),<ref name=Kent08/> with multiple lesions more common when coinfected with HIV. Lesions may be painful or tender (30%), and they may occur outside of the genitals (2–7%). The most common location in women is the [cervix](/wiki/Cervix) (44%), the [penis](/wiki/Penis) in heterosexual men (99%), and [anally](/wiki/Anus) and [rectally](/wiki/Rectal) relatively commonly in [men who have sex with men](/wiki/Men_who_have_sex_with_men) (34%).<ref name=Pri2008/> [Lymph node](/wiki/Lymph_node) enlargement frequently (80%) occurs around the area of infection,<ref name=Kent08/> occurring seven to 10 days after chancre formation.<ref name=Pri2008/> The [lesion](/wiki/Lesion) may persist for three to six weeks without treatment.<ref name=Kent08/>

### Secondary[[edit](/index.php?title=(none)&action=edit&section=3)]

[thumb|upright=1.4|Typical presentation of secondary syphilis with a rash on the palms of the hands](/wiki/Image:Secondary_Syphilis_on_palms_CDC_6809_lores.rsh.jpg) [thumb|upright=1.4|Reddish](/wiki/Image:2ndsyphil2.jpg) [papules](/wiki/Papules) and [nodules](/wiki/Nodule_(dermatology)#Primary_lesions) over much of the body due to secondary syphilis Secondary syphilis occurs approximately four to ten weeks after the primary infection.<ref name=Kent08/> While secondary disease is known for the many different ways it can manifest, symptoms most commonly involve the skin, [mucous membranes](/wiki/Mucous_membranes), and [lymph nodes](/wiki/Lymph_nodes).<ref name=Sec2010/> There may be a symmetrical, reddish-pink, non-itchy rash on the trunk and extremities, including the palms and soles.<ref name=Kent08/><ref name=2darySyphilis>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The rash may become [maculopapular](/wiki/Maculopapular) or [pustular](/wiki/Abscess). It may form flat, broad, whitish, wart-like lesions known as [condyloma latum](/wiki/Condyloma_latum) on [mucous membranes](/wiki/Mucous_membrane). All of these lesions harbor bacteria and are infectious. Other symptoms may include [fever](/wiki/Fever), [sore throat](/wiki/Sore_throat), [malaise](/wiki/Malaise), [weight loss](/wiki/Weight_loss), [hair loss](/wiki/Hair_loss), and [headache](/wiki/Headache).<ref name=Kent08/> Rare manifestations include [liver inflammation](/wiki/Hepatitis), [kidney](/wiki/Kidney) disease, [joint inflammation](/wiki/Arthritis), [periostitis](/wiki/Periostitis), [inflammation of the optic nerve](/wiki/Optic_neuritis), [uveitis](/wiki/Uveitis), and [interstitial keratitis](/wiki/Interstitial_keratitis).<ref name=Kent08/><ref name=Eye07/> The acute symptoms usually resolve after three to six weeks;<ref name=Eye07/> about 25% of people may present with a recurrence of secondary symptoms. Many people who present with secondary syphilis (40–85% of women, 20–65% of men) do not report previously having had the classic chancre of primary syphilis.<ref name=Sec2010>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

### Latent[[edit](/index.php?title=(none)&action=edit&section=4)]

Latent syphilis is defined as having [serologic](/wiki/Serology) proof of infection without symptoms of disease.<ref name=RedBookSyphilis/> 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.<ref name=Eye07/> The United Kingdom uses a cut-off of two years for early and late latent syphilis.<ref name=Pri2008/> Early latent syphilis may have a relapse of symptoms. Late latent syphilis is [asymptomatic](/wiki/Asymptomatic), and not as contagious as early latent syphilis.<ref name=Eye07/>

### Tertiary[[edit](/index.php?title=(none)&action=edit&section=5)]

[thumb|left|upright=1.4|Person with tertiary (gummatous) syphilis. Bust in](/wiki/File:Tertiary_syphilis_head.JPG) [Musée de l'Homme](/wiki/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](/wiki/Neurosyphilis) (6.5%), and cardiovascular syphilis (10%).<ref name=Kent08/><ref name=Eye07/> Without treatment, a third of infected people develop tertiary disease.<ref name=Eye07/> People with tertiary syphilis are not infectious.<ref name=Kent08/>

Gummatous syphilis or late [benign](/wiki/Benignity) syphilis usually occurs 1 to 46 years after the initial infection, with an average of 15 years. This stage is characterized by the formation of chronic [gummas](/wiki/Gumma_(pathology)), which are soft, tumor-like balls of inflammation which may vary considerably in size. They typically affect the skin, bone, and liver, but can occur anywhere.<ref name=Kent08/>

[Neurosyphilis](/wiki/Neurosyphilis) refers to an infection involving the [central nervous system](/wiki/Central_nervous_system). It may occur early, being either asymptomatic or in the form of syphilitic [meningitis](/wiki/Meningitis), or late as meningovascular syphilis, [general paresis](/wiki/General_paresis), or [tabes dorsalis](/wiki/Tabes_dorsalis), which is associated with poor balance and lightning pains in the lower extremities. Late neurosyphilis typically occurs 4 to 25 years after the initial infection. Meningovascular syphilis typically presents with apathy and [seizure](/wiki/Seizure), and general paresis with [dementia](/wiki/Dementia) and [tabes dorsalis](/wiki/Tabes_dorsalis).<ref name=Kent08/> Also, there may be [Argyll Robertson pupils](/wiki/Argyll_Robertson_pupil), which are bilateral small pupils that constrict when the person focuses on near objects but do not constrict when exposed to bright light.

Cardiovascular syphilis usually occurs 10–30 years after the initial infection. The most common complication is [syphilitic aortitis](/wiki/Syphilitic_aortitis), which may result in [aneurysm](/wiki/Aortic_aneurysm) formation.<ref name=Kent08/>

### Congenital[[edit](/index.php?title=(none)&action=edit&section=6)]

[Congenital syphilis](/wiki/Congenital_syphilis) is that which is transmitted during pregnancy or during birth. Two-thirds of syphilitic infants are born without symptoms. Common symptoms that develop over the first couple of years of life include [enlargement of the liver and spleen](/wiki/Hepatosplenomegaly) (70%), rash (70%), fever (40%), neurosyphilis (20%), and [lung inflammation](/wiki/Pneumonitis) (20%). If untreated, [late congenital syphilis](/wiki/Late_congenital_syphilis) may occur in 40%, including [saddle nose](/wiki/Saddle_nose) deformation, [Higoumenakis sign](/wiki/Higoumenakis_sign), [saber shin](/wiki/Saber_shin), or [Clutton's joints](/wiki/Clutton's_joints) among others.<ref name=Wood09/>

## Cause[[edit](/index.php?title=(none)&action=edit&section=7)]

### Bacteriology[[edit](/index.php?title=(none)&action=edit&section=8)]

[thumb|upright=1.4|Histopathology of *Treponema pallidum* spirochetes using a modified Steiner silver stain](/wiki/File:Treponema_pallidum_01.png) [Template:Main](/wiki/Template:Main) *Treponema pallidum* subspecies *pallidum* is a spiral-shaped, [Gram-negative](/wiki/Gram-negative), highly mobile bacterium.<ref name=Music08/><ref name=Pri2008/> Three other human diseases are caused by related *Treponema pallidum*, including [yaws](/wiki/Yaws) (subspecies *pertenue*), [pinta](/wiki/Pinta_(disease)) (subspecies *carateum*) and [bejel](/wiki/Nonvenereal_endemic_syphilis) (subspecies *endemicum*).<ref name=Kent08/> Unlike subtype *pallidum*, they do not cause neurological disease.<ref name=Wood09/> Humans are the only known [natural reservoir](/wiki/Natural_reservoir) for subspecies *pallidum*.<ref name=ST10/> It is unable to survive without a host for more than a few days. This is due to its small genome (1.14 [MDa](/wiki/Atomic_mass_unit)) failing to encode the metabolic pathways necessary to make most of its macronutrients. It has a slow doubling time of greater than 30 hours.<ref name=Pri2008/>

### Transmission[[edit](/index.php?title=(none)&action=edit&section=9)]

Syphilis is transmitted primarily by sexual contact or during [pregnancy](/wiki/Pregnancy) from a mother to her [fetus](/wiki/Fetus); the spirochete is able to pass through intact mucous membranes or compromised skin.<ref name=Kent08/><ref name=ST10/> It is thus transmissible by [kissing](/wiki/Kissing) near a lesion, as well as oral, vaginal, and anal sex.<ref name=Kent08/> Approximately 30 to 60% of those exposed to primary or secondary syphilis will get the disease.<ref name=Eye07>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Its infectivity is exemplified by the fact that an individual inoculated with only 57 organisms has a 50% chance of being infected.<ref name=Pri2008/> Most (60%) of new cases in the United States occur in men who have sex with men. It can be transmitted by [blood products](/wiki/Blood_product). It is tested for in many countries and thus the risk is low. The risk of transmission from [sharing needles](/wiki/Sharing_needles) appears limited.<ref name=Kent08/>

It is not generally possible to contract syphilis through toilet seats, daily activities, hot tubs, or sharing eating utensils or clothing.<ref name=CDC2014>[Template:Cite web](/wiki/Template:Cite_web)</ref> This is mainly because the bacteria die very quickly outside of the body, making transmission by [objects](/wiki/Fomites) extremely difficult.[[4]](#cite_note-4)

## Diagnosis[[edit](/index.php?title=(none)&action=edit&section=10)]

[thumb|upright|alt=Poster for testing of syphilis, showing a man and a woman bowing their heads in shame|This poster acknowledges the social stigma of syphilis, while urging those who possibly have the disease to be tested (circa 1936).](/wiki/File:Syphilis_false_shame_and_fear_may_destroy_your_future.png) Syphilis is difficult to diagnose clinically early in its presentation.<ref name=Pri2008/> Confirmation is either via [blood tests](/wiki/Blood_tests) or direct visual inspection using [microscopy](/wiki/Microscopy). Blood tests are more commonly used, as they are easier to perform.<ref name=Kent08/> Diagnostic tests are unable to distinguish between the stages of the disease.<ref name= Orgin10/>

### Blood tests[[edit](/index.php?title=(none)&action=edit&section=11)]

Blood tests are divided into [nontreponemal](/wiki/Nontreponemal_tests_for_syphilis) and treponemal tests.<ref name=Pri2008/> Nontreponemal tests are used initially, and include [venereal disease research laboratory](/wiki/Venereal_disease_research_laboratory) (VDRL) and [rapid plasma reagin](/wiki/Rapid_plasma_reagin) tests. As these tests are occasionally [false positives](/wiki/False_positive#Type_I_error), confirmation is required with a treponemal test, such as [treponemal pallidum particle agglutination](/wiki/Treponemal_pallidum_particle_agglutination) (TPHA) or [fluorescent treponemal antibody absorption test](/wiki/Fluorescent_treponemal_antibody_absorption_test) (FTA-Abs).<ref name=Kent08/> False positives on the nontreponemal tests can occur with some viral infections such as [varicella](/wiki/Varicella) (chickenpox) and [measles](/wiki/Measles), as well as with [lymphoma](/wiki/Lymphoma), [tuberculosis](/wiki/Tuberculosis), [malaria](/wiki/Malaria), [endocarditis](/wiki/Endocarditis), [connective tissue disease](/wiki/Connective_tissue_disease), and [pregnancy](/wiki/Pregnancy).<ref name=RedBookSyphilis/> Treponemal antibody tests usually become positive two to five weeks after the initial infection.<ref name=Pri2008/> Neurosyphilis is diagnosed by finding high numbers of [leukocytes](/wiki/Leukocytes) (predominately [lymphocytes](/wiki/Lymphocytes)) and high protein levels in the [cerebrospinal fluid](/wiki/Cerebrospinal_fluid) in the setting of a known syphilis infection.<ref name=Kent08/><ref name=RedBookSyphilis/>

### Direct testing[[edit](/index.php?title=(none)&action=edit&section=12)]

[Dark ground microscopy](/wiki/Dark_field_microscopy) of [serous fluid](/wiki/Serous_fluid) from a chancre may be used to make an immediate diagnosis. Hospitals do not always have equipment or experienced staff members, whereas testing must be done within 10 minutes of acquiring the sample. [Sensitivity](/wiki/Sensitivity_and_specificity) has been reported to be nearly 80%, thus can only be used to confirm a diagnosis but not rule one out. Two other tests can be carried out on a sample from the chancre: [direct fluorescent antibody](/wiki/Direct_fluorescent_antibody) testing and [nucleic acid amplification](/wiki/Polymerase_chain_reaction) tests. Direct fluorescent testing uses [antibodies](/wiki/Antibodies) tagged with [fluorescein](/wiki/Fluorescein), which attach to specific syphilis proteins, while nucleic acid amplification uses techniques, such as the [polymerase chain reaction](/wiki/Polymerase_chain_reaction), to detect the presence of specific syphilis genes. These tests are not as time-sensitive, as they do not require living bacteria to make the diagnosis.<ref name=Pri2008/>

## Prevention[[edit](/index.php?title=(none)&action=edit&section=13)]

### Vaccine[[edit](/index.php?title=(none)&action=edit&section=14)]

[Template:As of](/wiki/Template:As_of), there is no vaccine effective for prevention.<ref name=ST10/> Several vaccines based on treponemal proteins reduce lesion development in an animal model, and research is ongoing.[[5]](#cite_note-5)

### Sex[[edit](/index.php?title=(none)&action=edit&section=15)]

Abstinence from intimate physical contact with an infected person is effective at reducing the transmission of syphilis, as is the proper use of a [latex condom](/wiki/Latex_condom). Condom use does not completely eliminate the risk.[[6]](#cite_note-6)[[7]](#cite_note-7) Thus, the [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention) recommends a long-term, mutually monogamous relationship with an uninfected partner and the avoidance of substances such as [alcohol](/wiki/Alcoholic_beverage) and other drugs that increase risky sexual behavior.[[6]](#cite_note-6)

### Congenital disease[[edit](/index.php?title=(none)&action=edit&section=16)]

Congenital syphilis in the newborn can be prevented by screening mothers during early pregnancy and treating those who are infected.<ref name=Screening04>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The [United States Preventive Services Task Force](/wiki/United_States_Preventive_Services_Task_Force) (USPSTF) strongly recommends universal screening of all pregnant women,[[8]](#cite_note-8) while the [World Health Organization](/wiki/World_Health_Organization) recommends all women be tested at their first antenatal visit and again in the [third trimester](/wiki/Third_trimester).<ref name=Lancet11/> If they are positive, they recommend their partners also be treated.<ref name=Lancet11>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Congenital syphilis is still common in the developing world, as many women do not receive [antenatal care](/wiki/Antenatal_care) at all, and the antenatal care others receive does not include screening,<ref name=Screening04/> and it still occasionally occurs in the developed world, as those most likely to acquire syphilis (through drug use, etc.) are least likely to receive care during pregnancy.<ref name=Screening04/> Several measures to increase access to testing appear effective at reducing rates of congenital syphilis in low- to middle-income countries.<ref name=Lancet11/> Point-of-care testing to detect syphilis appeared to be good although more research is needed to assess its effectiveness and into improving outcomes in mothers and babies.[[9]](#cite_note-9)

### Screening[[edit](/index.php?title=(none)&action=edit&section=17)]

The CDC recommends that sexually active men who have sex with men be tested at least yearly.[[10]](#cite_note-10) The USPSTF also recommends screening among those at high risk.[[11]](#cite_note-11) Syphilis is a [notifiable disease](/wiki/Notifiable_disease) in many countries, including Canada[[12]](#cite_note-12) the European Union,[[13]](#cite_note-13) and the United States.[[14]](#cite_note-14) This means health care providers are required to notify [public health](/wiki/Public_health) authorities, which will then ideally provide [partner notification](/wiki/Partner_notification) to the person's partners.[[15]](#cite_note-15) Physicians may also encourage patients to send their partners to seek care.[[16]](#cite_note-16) Several strategies have been found to improve follow-up for STI testing including email and text messaging as reminders of appointments.[[17]](#cite_note-17)

## Treatment[[edit](/index.php?title=(none)&action=edit&section=18)]

### Early infections[[edit](/index.php?title=(none)&action=edit&section=19)]

The first-choice treatment for uncomplicated syphilis remains a single dose of intramuscular [benzathine penicillin G](/wiki/Benzathine_benzylpenicillin).<ref name=CDC2015a/> [Doxycycline](/wiki/Doxycycline) and [tetracycline](/wiki/Tetracycline) are alternative choices for those allergic to penicillin; due to the risk of birth defects these are not recommended for pregnant women.<ref name=CDC2015a>[Template:Cite web](/wiki/Template:Cite_web)</ref> [Resistance](/wiki/Antibiotic_resistance) to [macrolides](/wiki/Macrolide), [rifampin](/wiki/Rifampin), and [clindamycin](/wiki/Clindamycin) is often present.<ref name=ST10/> [Ceftriaxone](/wiki/Ceftriaxone), a third-generation [cephalosporin](/wiki/Cephalosporin) [antibiotic](/wiki/Antibiotic), may be as effective as penicillin-based treatment.<ref name=Kent08/> It is recommended that a treated person avoid sex until the sores are healed.<ref name=CDC2014/>

### Late infections[[edit](/index.php?title=(none)&action=edit&section=20)]

For neurosyphilis, due to the poor penetration of penicillin G into the [central nervous system](/wiki/Central_nervous_system), those affected are recommended to be given large doses of intravenous penicillin for a minimum of 10 days.<ref name=Kent08/><ref name=ST10/> If a person is allergic, ceftriaxone may be used or penicillin desensitization attempted. Other late presentations may be treated with once-weekly intramuscular penicillin G for three weeks. If allergic, as in the case of early disease, doxycycline or tetracycline may be used, albeit for a longer duration. Treatment at this stage limits further progression but has only slight effect on damage which has already occurred.<ref name=Kent08/>

### Jarisch-Herxheimer reaction[[edit](/index.php?title=(none)&action=edit&section=21)]

One of the potential side effects of treatment is the [Jarisch-Herxheimer reaction](/wiki/Jarisch-Herxheimer_reaction). It frequently starts within one hour and lasts for 24 hours, with symptoms of fever, muscle pains, headache, and a [fast heart rate](/wiki/Tachycardia).[[18]](#cite_note-18) It is caused by [cytokines](/wiki/Cytokines) released by the immune system in response to lipoproteins released from rupturing syphilis bacteria.<ref name=Radolf2006>[Template:Cite book](/wiki/Template:Cite_book)</ref>

### Pregnancy[[edit](/index.php?title=(none)&action=edit&section=22)]

Penicillin is an effective treatment for syphilis in pregnancy[[19]](#cite_note-19) but there is no agreement on which dose or way of giving it is most effective.<ref name=Walk2001/> More research is needed into how much antibiotic to give and when to give it.<ref name=Walk2001>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=23)]

[Template:Main](/wiki/Template:Main) [thumb|upright=1.5|](/wiki/Image:Syphilis_world_map_-_DALY_-_WHO2004.svg)[Age-standardized](/wiki/Age_adjustment) death from syphilis per 100,000 inhabitants in 2004[[20]](#cite_note-20)[Template:Multicol](/wiki/Template:Multicol) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-break](/wiki/Template:Multicol-break) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-end](/wiki/Template:Multicol-end) In 2013 syphilis infected about 315,000 people.<ref name=GBD2013/> Syphilis is believed to have infected 12 million additional people in 1999, with greater than 90% of cases in the [developing world](/wiki/Developing_world).<ref name=ST10/> It affects between 700,000 and 1.6 million pregnancies a year, resulting in [spontaneous abortions](/wiki/Spontaneous_abortion), [stillbirths](/wiki/Stillbirth), and congenital syphilis.<ref name=Wood09/> During 2010 it caused about 113,000 deaths down from 202,000 in 1990.<ref name=Loz2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In [sub-Saharan Africa](/wiki/Sub-Saharan_Africa), syphilis contributes to approximately 20% of [perinatal deaths](/wiki/Perinatal_death).<ref name=Wood09/> Rates are proportionally higher among [intravenous drug users](/wiki/Recreational_drug_use), those who are infected with HIV, and men who have sex with men.[[1]](#cite_note-1)[[2]](#cite_note-2)[[3]](#cite_note-3) In the United States, rates of syphilis as of 2007 were six times greater in men than women; they were nearly equal in 1997.[[21]](#cite_note-21) [African Americans](/wiki/African_American) accounted for almost half of all cases in 2010.[[22]](#cite_note-22) As of 2014, syphilis infections continue to increase in the United States.[[23]](#cite_note-23) Syphilis was very common in Europe during the 18th and 19th centuries.<ref name=Music08/> Flaubert found it universal among nineteenth-century Egyptian prostitutes.[[24]](#cite_note-24) In the developed world during the early 20th century, infections declined rapidly with the widespread use of [antibiotics](/wiki/Antibiotic), until the 1980s and 1990s.<ref name=Music08/> Since 2000, rates of syphilis have been increasing in the USA, Canada, the UK, Australia and Europe, primarily among [men who have sex with men](/wiki/Men_who_have_sex_with_men).<ref name=ST10/> Rates of syphilis among American women have remained stable during this time, and rates among UK women have increased, but at a rate less than that of men.<ref name=AOP08>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Increased rates among heterosexuals have occurred in China and Russia since the 1990s.<ref name=ST10/> This has been attributed to unsafe sexual practices, such as sexual promiscuity, prostitution, and decreasing use of barrier protection.<ref name=ST10/><ref name=AOP08/>[[25]](#cite_note-25) Untreated, it has a mortality of 8% to 58%, with a greater death rate in males.<ref name=Kent08/> 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 decreasing [virulence](/wiki/Virulence) of the spirochaete.<ref name=Sec2010/> With early treatment, few complications result.<ref name=Pri2008/> Syphilis increases the risk of HIV transmission by two to five times, and coinfection is common (30–60% in some urban centers).<ref name=Kent08/><ref name=ST10/> In 2015 Cuba became the first country in the world to eradicate mother to child transmission of syphilis.<ref name=WHOCUba2015/>

## History[[edit](/index.php?title=(none)&action=edit&section=24)]

[Template:Main](/wiki/Template:Main) [thumb|Portrait of](/wiki/Image:Rembrandt_Harmensz._van_Rijn_095.jpg) [Gerard de Lairesse](/wiki/Gerard_de_Lairesse) by [Rembrandt van Rijn](/wiki/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.[[26]](#cite_note-26)

The exact origin of syphilis is disputed.<ref name=Kent08/> Syphilis was indisputably present in the Americas before European contact. The dispute is over whether or not syphilis was also present elsewhere in the world at that time. One of the two primary hypotheses proposes that syphilis was carried from the Americas to Europe by the returning crewmen from [Christopher Columbus's](/wiki/Christopher_Columbus) voyage to the [Americas](/wiki/Americas). The other hypothesis says that syphilis existed in Europe previously, but went unrecognized until shortly after Columbus' return. These are referred to as the *Columbian* and *pre-Columbian* hypotheses, respectively.<ref name=Orgin10>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The Columbian hypothesis is best supported by the available evidence.[[27]](#cite_note-27)[[28]](#cite_note-28) The first written records of an outbreak of syphilis in Europe occurred in 1494 or 1495 in [Naples, Italy](/wiki/Naples), during a French invasion ([Italian War of 1494–98](/wiki/Italian_War_of_1494–98)).<ref name=Music08/><ref name=Orgin10/> As it was claimed to have been spread by French troops, it was initially known as the "French disease" by the people of Naples.[[29]](#cite_note-29) In 1530, the pastoral name "syphilis" (the name of a character) was first used by the Italian physician and poet [Girolamo Fracastoro](/wiki/Girolamo_Fracastoro) as the title of his [Latin](/wiki/Latin) poem in dactylic hexameter describing the ravages of the disease in Italy.[[30]](#cite_note-30)[[31]](#cite_note-31) It was also known historically as the "Great Pox".<ref name=Old05>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Euro04>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The causative organism, *Treponema pallidum*, was first identified by [Fritz Schaudinn](/wiki/Fritz_Schaudinn) and [Erich Hoffmann](/wiki/Erich_Hoffmann) in 1905.<ref name=Music08/> The first effective treatment ([Salvarsan](/wiki/Salvarsan)) was developed in 1910 by [Paul Ehrlich](/wiki/Paul_Ehrlich), which was followed by trials of [penicillin](/wiki/Penicillin) and confirmation of its effectiveness in 1943.<ref name=Music08/><ref name=Old05/> Before the discovery and use of antibiotics in the mid-twentieth century, [mercury](/wiki/Mercury_(element)) and isolation were commonly used, with treatments often worse than the disease.<ref name=Old05/>

Many famous historical figures, including [Franz Schubert](/wiki/Franz_Schubert), [Arthur Schopenhauer](/wiki/Arthur_Schopenhauer), and [Édouard Manet](/wiki/Édouard_Manet), are believed to have had the disease.<ref name=Music08/> [Friedrich Nietzsche](/wiki/Friedrich_Nietzsche) was long believed to have gone mad as a result of [tertiary syphilis](/wiki/Tertiary_syphilis), but that diagnosis has recently come into question.[[32]](#cite_note-32)

### Arts and literature[[edit](/index.php?title=(none)&action=edit&section=25)]

[Template:See also](/wiki/Template:See_also) [thumb|The earliest known medical illustration of people with syphilis, Vienna, 1498](/wiki/File:400Behandlung_der_Syphilis.jpg) The earliest known depiction of an individual with syphilis is [Albrecht Dürer's](/wiki/Albrecht_Dürer) *Syphilitic Man*, a woodcut believed to represent a [Landsknecht](/wiki/Landsknecht), a Northern European [mercenary](/wiki/Mercenary).[[33]](#cite_note-33) The myth of the [*femme fatale*](/wiki/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'](/wiki/John_Keats) [*La Belle Dame sans Merci*](/wiki/La_Belle_Dame_sans_Merci).[[34]](#cite_note-34)[[35]](#cite_note-35) The artist [Jan van der Straet](/wiki/Jan_van_der_Straet) painted a scene of a wealthy man receiving treatment for syphilis with the tropical wood [guaiacum](/wiki/Guaiacum) sometime around 1580.[[36]](#cite_note-36) The title of the work is "Preparation and Use of Guayaco for Treating Syphilis". That the artist chose to include this image in a series of works celebrating the New World indicates how important a treatment, however ineffective, for syphilis was to the European elite at that time. The richly colored and detailed work depicts four servants preparing the concoction while a physician looks on, hiding something behind his back while the hapless patient drinks.[[37]](#cite_note-37)

### Tuskegee and Guatemala studies[[edit](/index.php?title=(none)&action=edit&section=26)]

[Template:See also](/wiki/Template:See_also) [thumb|A](/wiki/File:Stop_syphilis_LCCN98509573.jpg) [Work Projects Administration](/wiki/Work_Projects_Administration) poster about syphilis circa 1940. One of the most infamous United States cases of questionable [medical ethics](/wiki/Medical_ethics) in the 20th century was the [Tuskegee syphilis study](/wiki/Tuskegee_syphilis_study).[[38]](#cite_note-38) The study took place in [Tuskegee, Alabama](/wiki/Tuskegee,_Alabama), and was supported by the [U.S. Public Health Service](/wiki/U.S._Public_Health_Service) (PHS) in partnership with the [Tuskegee Institute](/wiki/Tuskegee_Institute).<ref name=CDCTime>[Template:Cite web](/wiki/Template:Cite_web)</ref> The study began in 1932, when syphilis was a widespread problem and there was no safe and effective treatment.<ref name=TUS00>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The study was designed to measure the progression of untreated syphilis. By 1947, penicillin had been shown to be an effective cure for early syphilis and was becoming widely used to treat the disease.<ref name=CDCTime/> Its use in later syphilis was still unclear.[[39]](#cite_note-39) Study directors continued the study and did not offer the participants treatment with penicillin.<ref name=CDCTime/> This is debated, and some have found that penicillin was given to many of the subjects.[[39]](#cite_note-39) In the 1960s, [Peter Buxtun](/wiki/Peter_Buxtun) sent a letter to the [CDC](/wiki/Centers_for_Disease_Control_and_Prevention), who controlled the study, expressing concern about the ethics of letting hundreds of black men die of a disease that could be cured. The CDC asserted that it needed to continue the study until all of the men had died. In 1972, Buxton went to the mainstream press, causing a public outcry. As a result, the program was terminated, a lawsuit brought those affected nine million dollars, and Congress created a commission empowered to write regulations to deter such abuses from occurring in the future.<ref name=CDCTime/>

On 16 May 1997, thanks to the efforts of the Tuskegee Syphilis Study Legacy Committee formed in 1994, survivors of the study were invited to the White House to be present when President Bill Clinton apologized on behalf of the United States government for the study.[[40]](#cite_note-40) Syphilis experiments were also carried out in [Guatemala](/wiki/Guatemala) from 1946 to 1948. They were [United States](/wiki/United_States)-sponsored [human experiments](/wiki/Human_subject_research), conducted during the government of [Juan José Arévalo](/wiki/Juan_José_Arévalo) with the cooperation of some Guatemalan health ministries and officials. Doctors infected soldiers, prisoners, and [mental patients](/wiki/Mental_patient) with syphilis and other [sexually transmitted diseases](/wiki/Sexually_transmitted_diseases), without the [informed consent](/wiki/Informed_consent) of the subjects, and then treated them with [antibiotics](/wiki/Antibiotic). In October 2010, the U.S. formally apologized to Guatemala for conducting these experiments.[[41]](#cite_note-41) [Template:Clear](/wiki/Template:Clear)

## References[[edit](/index.php?title=(none)&action=edit&section=27)]

[Template:Research help](/wiki/Template:Research_help) [Template:Reflist](/wiki/Template:Reflist)

## Further reading[[edit](/index.php?title=(none)&action=edit&section=28)]

* Bliss, Katherine Elaine. "The Science of Redemption: Syphilis, Sexual Promiscuity, and Reformism in Revolutionary Mexico City" *Hispanic American Historical Review* 79:1 1999, pp. 1–40.
* Parascandola, John. *Sex, Sin, and Science: A History of Syphilis in America* (Praeger, 2008) 195 pp. ISBN 978-0-275-99430-3 [excerpt and text search](http://www.amazon.com/Sex-Sin-Science-Syphilis-Medicine/dp/0275994309/)
* Shmaefsky, Brian, Hilary Babcock and David L. Heymann. *Syphilis* (Deadly Diseases & Epidemics) (2009)
* Stein, Claudia. *Negotiating the French Pox in Early Modern Germany* (2009)

## External links[[edit](/index.php?title=(none)&action=edit&section=29)]

[Template:Sister project links](/wiki/Template:Sister_project_links)

* ["Syphilis - CDC Fact Sheet"](http://www.cdc.gov/std/Syphilis/STDFact-Syphilis.htm) [Centers for Disease Control and Prevention](/wiki/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)

[Template:Diseases of the skin and appendages by morphology](/wiki/Template:Diseases_of_the_skin_and_appendages_by_morphology) [Template:STD/STI](/wiki/Template:STD/STI) [Template:Gram-negative non-proteobacterial bacterial diseases](/wiki/Template:Gram-negative_non-proteobacterial_bacterial_diseases) [Template:Diseases of maternal transmission](/wiki/Template:Diseases_of_maternal_transmission)

[Template:Authority control](/wiki/Template:Authority_control)

[Category:Bacterial diseases](/wiki/Category:Bacterial_diseases) [Category:Bacterium-related cutaneous conditions](/wiki/Category:Bacterium-related_cutaneous_conditions) [Category:Infections with a predominantly sexual mode of transmission](/wiki/Category:Infections_with_a_predominantly_sexual_mode_of_transmission) [Category:Spirochaetes](/wiki/Category:Spirochaetes) [Category:Syphilis](/wiki/Category:Syphilis) [Category:RTT(full)](/wiki/Category:RTT(full))