

# RELEVANCE OF DERMATOLOGICAL LESIONS IN ACQUIRED SYPHILIS

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**Abstract.** Introduction: Acquired syphilis is an infectious disease caused by the spirochete *Treponema pallidum*, transmitted through sexual intercourse or extragenital contagion. According to the World Health Organization, it is estimated that there are 12 million new cases per year, and the pathology has different stages of evolution. Objective: Control the infection and monitorate treatment through a correct diagnosis, especially in relation to dermatological lesions. Methods: Thirteen articles were collected in English and Portuguese, from 2006 to 2023, on Scielo, PubMed, Uptodate and Google Scholar platforms. In addition to these bibliographic sources, the book “Dermatologia Azulay” and Brazilian Ministry of Health protocols was also used. Results: Studies have shown an increase in the number of cases of the disease and demonstrated the epidemiological and spatial profile of the pathology. Discussion: Dermatological lesions in acquired syphilis have many details, with specific differences according to the period of chronological evolution. This chronology is divided into recent syphilis, which presents primary and secondary syphilis, with less than a year of evolution, and late syphilis, with tertiary syphilis with more than a year of evolution. It is also worth noting that the degree of infectivity reduces over time, however it can progress to more serious levels. Diagnosis is difficult due to the symptoms that are not exclusive to the disease, and detailed analysis of each phase of the disease is essential. In addition, there are screening and diagnostic tests, essential for diagnostic analysis and choosing the appropriate treatment. Conclusion: Acquired syphilis is of notable importance due to its widespread virulence and ability to generate multiple complications in humans, requiring correct diagnosis in order to control symptoms and the chain of transmission.

**Keywords.** Syphilis; *Treponema pallidum*; Dermatology; Diagnosis.

## 1. Introduction

Syphilis is an infectious disease with more than 500 years of history and prejudice related to it. The pathology became a problem in the 15th century in Europe, with widespread dissemination during the period of great navigation and wars. It was stigmatised as a venereal disease and called “Lues”. It was only in 1905 that its etiology was identified, and 35 years later, penicillin was used to treat and cure it. Despite efficient and low-cost treatment, the pathology currently remains a public health problem.

Known as “the great imitator” for its diverse facets, syphilis is caused by the spirochete *Treponema pallidum* and, in most cases, is asymptomatic, which contributes to maintaining the transmission chain. It is a parasite exclusive to humans, transmitted

mainly through sexual intercourse (oral, vaginal or anal), or, more rarely, through extragenital contagion (through blood transfusion or accidental inoculation, such as using infected utensils). The bacteria act systemically from the beginning and, without correct treatment, can progress to the chronic phase, with periods of activity interrupted by periods of latency and irreversible long-term sequels. Furthermore, the disease affects races and both sexes to an indeterminate extent and affects more young people.

According to the World Health Organization (WHO), it is estimated that there are 12 million new cases per year. In view of this, in 2010, the Brazilian Ministry of Health made the notification of new cases of acquired syphilis compulsory, starting with ordinance number 2.472, with its investigation becoming mandatory throughout the national

territory. This resulted in an increase of more than 20 times in the notification of cases per 100 thousand inhabitants from 2010 to 2016. This increase is related to the expanding coverage of available tests and the use of rapid tests, which are linked to misinformation and the reduction in the use of condoms.

The pathology has different stages of evolution, and the correct diagnosis plays a fundamental role in controlling the infection and monitoring treatment. Considering that syphilis is commonly confused with other diseases, strict attention to its dermatological expression is essential, as it may be one of the main signs observed by patients. In addition, a detailed investigation of clinical data, requesting diagnostic tests, research into previous infections, and an investigation into risky sexual exposure are essential. Therefore, taking into account the country's epidemiological situation and the complexity of acquired syphilis, this article aims to discuss general aspects of the disease caused by *Treponema pallidum* and the importance of dermatological evaluation in order to obtain an accurate diagnosis and analyse its evolution.

## 2. Material and methods

The methodology used to carry out this literature review is the analysis and selection of published articles relevant to acquired syphilis. The system used to collect the analysed articles was a search on the platforms Google Scholar, Scientific Electronic Library Online (SciELO), National Library of Medicine (PubMed) and UpToDate, using the descriptors "syphilis", "treponema pallidum", "dermatology" and "diagnosis", in line with the Health Sciences Descriptors (DeCS). From this bibliographic search, 13 articles were selected between 2006 and 2023. In addition to these bibliographic sources, the book *Dermatologia Azulay* (AZULAY, R.D.) and Brazilian Ministry of Health protocols was also used.

## 3. Results

Due to the heterogeneity of the disease, its diagnosis can be complex, and it is essential to track and detect syphilis to carry out correct and effective treatment in order to prevent the progression of the disease to extensive lesions and the unbridled spread of the parasite. Data from the Brazilian Notifiable Diseases Information System (Sinan) show an increase in the detection of syphilis cases in the country, from 59.1 cases per 100,000 inhabitants in 2017 to 78.5 cases per 100,000 inhabitants in 2021.

In a cross-sectional epidemiological study carried out by Amaral et al. (2022), it was demonstrated that the majority of affected individuals are male (60.5%), dark-skinned (76.7%), with complete secondary education (47%), residents of urban areas (97.7%), and young people between 20 and 29 years old (44%).

Another study carried out by Holzmann et al. (2022) demonstrates that single and younger men are the groups that most seek health services for syphilis testing and treatment, possibly due to greater exposure to risk situations.

Based on these studies, an epidemiological and spatial profile of the pathology can be analysed, observing the magnitude of this public health problem and targeting the factors with the highest incidence that must be combatted through public policies aimed at accurate syphilis screening and diagnosis.

## 4. Discussion

*Treponema pallidum* has a helical morphology with a spiral, thin shape and movement in its longitudinal axis, facilitating its penetration into the host's tissues. This results in a broad virulence and invasiveness of the microorganism. This parasite penetrates the entire mucosa or submucosa of the genitalia or through microscopic lesions of the skin and invades the blood and/or lymphatic pathways within the first few hours.

The incubation period lasts around 21 days, and after this period the first lesion may appear, which is a hard chancre with lymph node repercussions in the surrounding area, and is related to primary syphilis. After 2 or 3 months, the agent spreads to all organs and tissues, and generalised lesions (syphilides) may occur, defining secondary syphilis. The initial years of the disease can be characterised by clinical silence (latent syphilis), but with a high concentration of antibodies, or by the presence of few but infectious lesions (recent recurrent syphilis). In the second year of the disease, circumscribed and non-infectious lesions may appear, thus entering the tertiary phase of syphilis.

Therefore, the infection is divided chronologically into two subclassifications (Table 1): recent syphilis, with infectious, non-destructive lesions and spontaneous involution (includes primary and secondary syphilis), lasting less than 1 year; and late syphilis, with more than 1 year of evolution, few lesions, non-contagious, however destructive (referring to tertiary syphilis). Between these phases, a latency period may occur with the absence of symptoms and the presence of positive serological reactions.

**Tab. 1 - Chronology of the disease**

Chronological division of acquired syphilis		
Recent syphilis	primary secondary	less than 1 year of evolution
Late syphilis	tertiary	more than 1 year of evolution

Therefore, it is observed that in the natural history of the disease, the transmission of the agent gradually reduces over time. However, it is essential

to emphasise that initial symptoms vary and disappear, regardless of the treatment used. Therefore, the disease is difficult to diagnose since the clinical manifestations are not exclusive to syphilis, requiring research for differential diagnoses. Based on that, it is important to analyse in detail the events that may appear in each period of the disease.

#### 4.1 Primary syphilis

Initially, primary syphilis may have the appearance of hard chancre (or protosyphiloma) and micro polyadenopathy, between 9 and 90 days after infection (on average, 21 days). This hard chancre is marked by treponema inoculation and is a lesion that initially appears as a small macule or papule that erodes and becomes an ulcerative lesion. It is normally single and painless — however, this symptom is subjective — with ramped edges, an infiltrated base with a cartilaginous consistency, and a clean, reddish and discreetly serous base. In women, the lesion is more common in the cervix and vulva (labia minora and majora), and in men, it occurs more in the balanopreputial groove and the glans. It is also possible to cause extragenital lesions depending on the site of inoculation of the bacteria, such as the anus, lips, fingers, tongue and other places on the integument. The lesion described is highly contagious and regresses spontaneously within 3 to 6 weeks, normally without leaving a scar.

In relation to hard cancer, there are still some peculiarities that may appear. There is the possibility of giant chancre, phagedenic chancre, decapitated syphilis, mixed chancre and redux chancre. Giant cancer has a lesion larger than the classic form, and fadegenic cancer has more destructive characteristics, normally associated with immunosuppressed patients (malnourished, elderly, and alcoholics). Decapitated syphilis is observed in the absence of chancre, and can occur in transfusion infections or patients who, during contagion, used antibiotics capable of masking the lesion, but not eradicating the pathology. Mixed chancre (or mixed chancre) presents an association between syphilitic chancre and chancroid (it starts with chancroid and, after 2 weeks, evolves to hard cancer). Finally, cancer redux presents a single gummy lesion that reappears in the place of the old cancer, representing a recurrence of the cancer.

Another relevant sign is micro polyadenopathy, defined by nodulations with increased size and number of lymph nodes or nodes in the local neighbourhood of the hard chancre, commonly present in the inguinal region, with a “rubbery” consistency. This set of lymph nodes is called “Pleide of Ricord”. The adenopathy present at this stage of the disease is usually painless, multiple, without phlogistic signs, symmetrical and bilateral, appearing about 10 days after the cancer.

#### 4.2 Secondary syphilis

In a second moment, on average 8 weeks after the

disappearance of the cancer, secondary syphilis begins, which can present various cutaneous and systemic manifestations in addition to painless generalised adenopathy. At this stage, the lesions appear chronologically: the first manifestation is a non-pruritic macular eruption (syphilitic roseolas), erythematous and/or hyperpigmented, small and well-defined, with spontaneous resolution in 20 to 40 days. After weeks, the appearance of papular or papulosquamous (psoriasiform) and, rarely, pustular syphilides is observed, often with palmoplantar and scrotal involvement; these sites are of great diagnostic value but are not pathognomonic. Itching in the lesions is not common, which is an important symptom for investigating differential diagnoses. There may also be a discrete peripheral desquamation called the Biett collarette.

Other findings of secondary syphilis are, in the oral mucosa, mucous plaques — erosive, multiple, asymptomatic and measuring around 1 cm in a rounded or oval shape — and a decapitated tongue, called Cornell sign. In areas of friction, such as the intergluteal groove, inguinofemoral region and around the anus and vulva, flat condyloma can occur with a large, raised, greyish skin rash that may show signs of irritation and inflammation. These lesions are considered the most contagious at this stage of the disease. In the black race, annular syphilis lesions and withcircinations in natural orifices (such as mouths, fingers and anuses) are called “elegant lesions”.

Furthermore, this phase can appear with lesions around the neck (necklace of Venus), but this is rare, occurring later and mainly in women, with the possibility of remaining hypochromic macules limited by hyperpigmented skin even after adequate treatment. Faneros can also be affected, presenting as alopecia, madarosis, paronychia and anonychia, and this condition is temporary and reversible after controlling the infection. Furthermore, general manifestations may occur: generalised micro-polyadenopathy, myalgias, arthralgias, headaches, meningitis, fever, weight loss, asthenia, iridocyclitis, hepatitis, splenomegaly, gastritis and periostitis. The lesions regress spontaneously after a few months, thus beginning the pathology silent latency period.

#### 4.3 Early malignant syphilis

Subsequently, it is important to discuss early malignant syphilis, an uncommon variant of syphilis that is more recurrent in immunocompromised individuals. This is characterised by the presence of erythematous squamous papules that evolve into ulcerated and painful plaques and nodules, covered by hemorrhagic crusts rupioids. The most affected regions are the face, scalp and mucosa. They are commonly accompanied by a feeling of malaise, fever, lack of appetite and myalgia, this is the severe evolutionary form of the disease. These lesions appear at the beginning of secondary syphilis and do not heal spontaneously.

#### 4.4 Recent recurrent syphilis

Another form that occurs is recent relapsing syphilis, which occurs between the secondary and tertiary phases. This presents papular and papulonodular lesions with little quantity, circumscribed, regressing spontaneously.

#### 4.5 Recent recurrent syphilis

The last phase is tertiary syphilis, defined as late syphilis, which appears after more than 1 year of contamination and can appear from 2 to 40 years after infection. Studies carried out from 1891 to 1958 by Boeck and Gjestland, in a period when there was still an absence of antibiotics to treat this disease, demonstrate the natural history of syphilis, in which around 60% of patients do not progress to this late phase, presenting a spontaneous cure even without treatment. However, a third of treated patients develop late complications: 16% develop integumentary lesions, 10% have cardiovascular issues, 6% have neurosyphilis, and 10% die.

This phase has three general categories: integumentary, cardiovascular and neurological manifestations. In relation to skin lesions and their appendages, there are gums, tubercles and juxta articular nodules, and they are characterised by lesions that are normally few, asymmetrical, located in defined and destructive regions, and the development of atrophic scars. These lesions can be painful, are not contagious and do not regress spontaneously, but they respond well to treatment. Initially, the gum corresponds to an immune reaction that forms granulomas with a necrotic centre and a "rubbery" texture, which can affect the skin, bones, mucosa, muscles and other organs. Tubercular circinate lesions have plaques and nodules (which may be ulcerated), are brownish-red in colour and scaly, with central scarring, and an annular, serpiginous or polycyclic shape, mainly affecting the back face and extensor surfaces of the limbs. Juxta articular nodules are painless, mobile nodules with a soft consistency that especially affect the elbows.

As already mentioned, in addition to integumentary changes, there are also cardiovascular and neurological manifestations. Among cardiovascular diseases, it is worth highlighting coronary stenosis, aortitis, ascending aortic aneurysm and aortic insufficiency. Neurological complications can be classified as asymptomatic or symptomatic. Asymptomatic conditions are the most common, with cerebrospinal fluid (CSF) changes without the presence of clinical manifestations. Among the symptomatic ones, we can mention syphilitic meningitis, cerebrovascular or spinal syphilis, optic nerve atrophy, damage to the seventh cranial nerve, tabes dorsalis and dementia.

#### 4.6 Diagnostic tests

Associated with the investigation of dermatological lesions are screening and diagnostic tests. Among them is direct research for *Treponema pallidum*,

treponemal and non-treponemal serological reactions, CSF examination and histopathological examination. These tests must be requested appropriately according to the evolutionary phase of the disease.

Screening is carried out with the aim of diagnosing asymptomatic people to obtain an early diagnosis and interrupt the chain of transmission of the etiological agent, using the VDRL non-treponemal serological test. Data from the Brazilian Ministry of Health demonstrate an increasing trend in case notifications between 13 and 29 years of age in the country, with annual screening recommended among sexually active people up to 30 years of age. Above this age, it is recommended in Brazil for the risk groups presented in Table 2:

**Tab. 2 - Brazilian protocol for syphilis**

Protocol with risk groups for syphilis in Brazil	
Groups	Screening time
Young people under 30	Annually
Pregnant women	At the 1st consultation (1st trimester), 3rd trimester (28 weeks), at birth and in case of miscarriage/stillbirth
Gays, transvestites, transsexuals, sex workers and alcohol or drug abuse	Semiannual
People diagnosed with STI	At the time of diagnosis and 4 to 6 weeks after diagnosis
People with receptive sexual practices without using condoms	Semiannual
PVHIV	Semiannual
Persons deprived of liberty	Semiannual
Sexual violence	At initial care and 4 to 6 weeks after exposure
People using PrEP	Quarterly
People with PeP indication	At initial care and 4 to 6 weeks after exposure

In primary syphilis, the tests requested are *Treponema pallidum* research and serological tests. The research is carried out by collecting directly from the hard chancre, which can be carried out using dark field microscopy, staining using the Fontana-Tribondeau method, or direct

immunofluorescence. Serological tests vary in the period for the emergence of antibodies in each individual; however, after 10 days of the development of hard cancer, it is possible to obtain reactivity with FTA-abs (treponemal) being performed. In addition, the VDRL (non-treponemal) serological test can be performed 2 or 3 weeks after the onset of the cancer disease; however, it may be negative in primary syphilis (to be considered positive, the value must be greater than or equal to 1/8).

Secondary syphilis has tests related to the research for the etiological agent directly in mucocutaneous lesions using dark field microscopy, staining using the Fontana-Tribondeau method, or direct immunofluorescence. Serology for VDRL and FTA-abs is also performed. It is worth highlighting the possibility of false negatives at this stage due to excess antibodies, called the prostatic, requiring the use of higher dilutions of serum. False positives should also be observed, which occur in cases of malaria, pregnancy, viruses, lepromatous leprosy, and autoimmune diseases.

The tests requested in tertiary syphilis are serological VDRL and FTA-abs and histopathological with evidence of vascular changes, granulomatous infiltrate with lymphocytes, plasma cells, and giant epithelioid cells, with or without central necrosis.

Cerebrospinal fluid examination is only indicated in the diagnosis of recent or late syphilis with neural symptoms and patients with a high titer of serological reactions, even after correct treatment.

#### 4.7 Treatment

Regarding the treatment of the disease, penicillin is the drug used in all forms of syphilis, and resistance to this medication has not been reported to date. Immediate treatment with benzathine penicillin is indicated after a positive result in cases of pregnancy, sexual violence and individuals with a chance of losing treatment follow-up.

For primary, secondary and recent latent syphilis, a single dose of benzathine penicillin G of 2.400,000 IU is indicated. In tertiary and late latent syphilis (more than 1 year of evolution) or latent syphilis of unknown period, the administration of 7.200,000 IU of benzathine penicillin G is indicated, given in 3 weekly doses of 2.400,000 IU.

Oral medications can also be used, with at least 10 days of administration: doxycycline, tetracycline and ceftriaxone. However, these drugs do not have data to confirm their treatment, make adherence difficult, and are recommended in cases of penicillin allergy. Furthermore, the choice of these drugs must be careful due to resistant strains, especially in patients with HIV.

For serological monitoring of the treatment with benzathine penicillin, a non-treponemal VDRL test is requested every 3 months in the first year, every 6 months in the second year, or until the patient

presents two negative tests. In primary and secondary syphilis, there should be a drop of two dilutions from 3 months onward (for example, 1/64 to 1/16) and three dilutions from 6 months onward. If negative results occur after 6 to 9 months, it shows that the infection has been cured. It is worth noting that the earlier the diagnosis and treatment, the greater the chances of being negative. However, if the diagnosis occurs after secondary syphilis, you may have a serological scar with a low positive titer ( $\frac{1}{4}$ ) for the rest of your life. With two negative or low and stable tests after two years, the patient is discharged. However, in cases where values rise between tests, reinfection or therapeutic failure occurs, requiring treatment again.

## 5. Conclusion

Acquired syphilis is an infectious disease of significant importance in Brazil due to its widespread virulence and the multiple complications it can generate in humans. This pathology requires thorough investigation in order to prevent progression to more serious forms, which can result in irreversible sequelae. Therefore, accurate knowledge about the dermatological manifestations of the disease is essential, as these are diverse and essential for diagnosis, carrying out diagnostic tests, and appropriate treatment. It is worth highlighting the importance of being a compulsory notification problem, aiming to reduce personal and collective damage by interrupting the transmission chain through correct screening and treatment.

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