THE HISTOPATHOLOGICAL FEATURES OF SYPHILIS AND ITS MIMICKERS

by Indah Purnamasari

Submission date: 04-Jul-2023 10:02PM (UTC+0800)
Submission ID: 2126432633
File name: THE_HISTOPATHOLOGICAL.pdf (598.76K)
Word count: 3551
Character count: 21187

Review Article

THE HISTOPATHOLOGICAL FEATURES OF SYPHILIS AND ITS MIMICKERS

Indah Purnamasari[1,2], Afif Nurul Hidayati[2], Etty Hary Kusumastuti[3], Isaak Effendy[4]

[1]Surabaya Islamic Hospital; Darmo Hospital, Surabaya, Indonesia
[2]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga; Dr. Soetomo General Academic Hospital; Universitas Airlangga Teaching Hospital, Surabaya, Indonesia
[3]Department of Anatomical Pathology, Faculty of Medicine, Universitas Airlangga; Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[4]Department of Dermatology, Venereology, and Allergology, University Hospital; Medical School OWL University of Bielefeld, Germany

ABSTRACT

Syphilis, also known as "the great imitator," is a sexually transmitted infection with a variety of clinical symptoms and histopathological similarities to other infectious diseases. Public health concerns about syphilis have grown significantly. Since 2000, there has been an increase in syphilis prevalence in the United States, with a 17.6% increase from 2015 to 2016. From 2000 to 2019, the number of syphilis cases throughout Asia increased from 0.9% to 30.9%, whilst the number of cases in Indonesia decreased from 22.5% to 14.4%. Specific serological tests for syphilis can usually detect and confirm the diagnosis and offer follow-up care in most cases. However, in certain instances, the clinical characteristics discovered during testing can be identical to those of other diseases, which may lead to inconsistent diagnosis. Considering that the diagnostic pathology is pertinent to the clinical circumstances, a histopathological investigation may be useful for differentiating syphilis mimickers. Pathology is essential for identifying potential syphilis patients with ambiguous clinical symptoms. This study's purpose was to assist dermatologists and pathologists in identifying "mimickers" that require a biopsy and in determining the correct diagnosis and treatment coutsed based on etiology.

Keywords: Syphilis; mimickers; dermatopathology; infectious disease; sexually transmitted infection

Correspondence: Afif Nurul Hidayati, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga; Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. E-mail: afif_nurulhidayati@fk.unair.ac.id

Article history
●Submitted 10 Dec 2022 ● Revised 12 Jan 2023 ● Accepted 22 Feb 2023 ● Published 10 Mar 2023

How to cite: Purnamasari I, Hidayati AN, Kusumastuti EH, et al (2023). The histopathological features of syphilis and its mimickers. Folia Medica Indonesiana, 59 (1), 63-69. https://doi.org/10.20473/fmi.v59i1.37286

Folia Medica Indonesiana 2023:59:63-69
pISSN:2355-8393, eISSN: 2599-056x. doi: 10.20473/fmi.v59i1. 37286

Highlights:

1. The importance of having a strong suspicion for syphilis and maintaining close contact between dermatologists and pathologists cannot be understated.
2. Understanding the clinical relationship and histopathological features of syphilis is crucial for accurate diagnosis and distinction from its histopathologic mimickers.

INTRODUCTION

Syphilis is a chronic and systemic spirochete bacterial infection brought on by the *Treponema pallidum* subspecies *pallidum*. Syphilis spreads through microabrasions in the mucosa or skin, which occur almost exclusively during sexual contacts. It can spread rapidly through the bloodstream to the tissues. Additionally, syphilis can be transmitted through blood transfusions and from mother to child through the placenta (Ho & Lukehart 2011, Ali et al. 2016, Wardiana et al. 2022).

Syphilis is a global public health problem, especially in high- and middle-income countries. The World Health Organization (WHO) reported global estimates of 12 million new syphilis cases each year and one million pregnancies complicated by the disease. In recent years, the syphilis incidence has still been high, especially in Africa, Asia, and Central and South America (World Health Organization 2017, Tuddenham & Zenilman 2019).

Data from the Centers for Disease Control and Prevention (2017) showed that there was a 52% increase of cases among men who have sex with men

(MSM), with 30-74% of them co-infected with human immunodeficiency virus (HIV). Whereas, the of syphilis prevalence in Indonesia among MSM groups showed an increase from 8.5% in 2011 to 15.7% in 2015 (Daili et al. 2015).

Syphilis is called "the great imitator" because it has widely varying clinical presentations and histopathological features that also exist in other infectious diseases (Tuddenham & Zenilman 2019). Lesions in early syphilis can be mistaken as those of other infections and conditions; therefore, syphilis should be suspected in all sexually active patients presenting with a new skin rash or an oral/genital lesion (Klausner 2019). Without treatment, syphilis can be associated with significant morbidity and mortality, especially when transmitted vertically from mother to child or in patients with advanced tertiary disease. If syphilis is left untreated, the infection may proceed through a multistage process of primary, secondary, and tertiary stages. However, it is known that an initial syphilis infection can also heal spontaneously (Klausner 2019, Tuddenham & Zenilman 2019).

Proper and reliable examination is essential for establishing the correct diagnosis of syphilis and the accuracy of the medication administration, especially in latent syphilis. Universal screening and adequate pregnancy care are important for preventing syphilis in mothers and its transmission to their children (Purnamasari et al. 2021). In addition to careful review of sexual history and physical examination, several methods can be useful in establishing the clinical diagnosis of syphilis. Today, in most cases, it can be diagnosed and followed up due to specific serological tests (RPR, VDRL, *T. pallidum*-antibody), and recently with PCR as well. In cases with atypical clinical presentations and false-negative serological laboratory results, a biopsy examination can assist in establishing clinically relevant diagnosis (Hook 2017, Tuddenham & Zenilman 2019).

OVERVIEW

The incidence of primary and secondary syphilis in the United States is at its highest level since 1994, negating the dramatic decline that was seen when HIV infection first emerged and many people's sexual habits changed as a result (Kojima & Klausner 2018). In Indonesia, syphilis is still prevalent at a high rate. Syphilis still affects 25% of transgender people. Its frequency has increased three times among MSM and injectable drug users since 2007. The prevalence of syphilis is 25% in women who sell direct sex (female sex workers/FSW), 10% in MSM, 9% in prisoners, 5% in high-risk men, and 3% in female indirect sex workers (Daili et al. 2013, Gunn & Klausner 2019). People who were infected with HIV and syphilis could improve their quality of life by actively participating in programs, such as anti-retroviral therapy and counseling, although reducing the prevalence of the disease should be of the utmost importance (Yuindartanto et al. 2022).

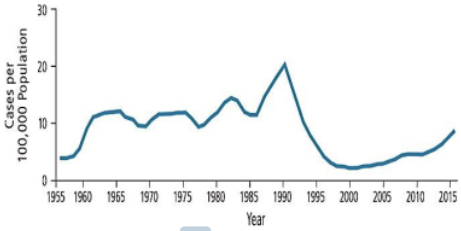

Figure 1. New cases of primary and secondary syphilis in the United States, 1956 to 2016 (Kojima & Klausner 2018).

Although syphilis can be identified based on its clinical stage, it has the ability to mimic a variety of other diseases at any stage of its development (Hook 2017). Figure 2 shows the natural stage of syphilis.

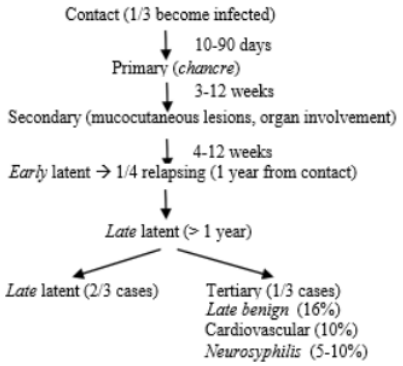

Figure 2. The progressions of syphilis related to its stages (Tuddenham & Zenilman 2019).

The role of biopsy in distinguishing syphilis mimickers

The diagnosis of syphilis should include the consideration of the clinical, serological, and histopathological findings (Groh & Patino 2014). The statistical data from the Centers for Disease Control and Prevention (CDC) shows that the total rate of syphilis diagnosed with biopsy increased significantly since 2003 (Figure 3). However, in most dermatopathology laboratories, only about 32% of the syphilis diagnoses were resulted from biopsy.

Biopsy examination is one of the helpful and accurate tools used in diagnosing syphilis, evaluating the course of syphilis, and confirming the correlation of the clinical morphology, serology, and histopathology (Flamm et al. 2015). Histologically, typical presentation of syphilis depends on the stage and type of lesion seen from the biopsy. Although it is not the gold standard for diagnosis, the presence of *T. pallidum* spirochetes in the histopathology can indicate syphilis. Ghaznawie (2013) stated in a study that silver staining or immunohistochemical staining can detect spirochetes. Two fundamental pathological changes in syphilis are proliferation and swelling of endothelial cells, and a perivascular infiltration of lymphoid cells and plasma cells. Treponemes are commonly seen in both primary and secondary lesions (Elder 2017).

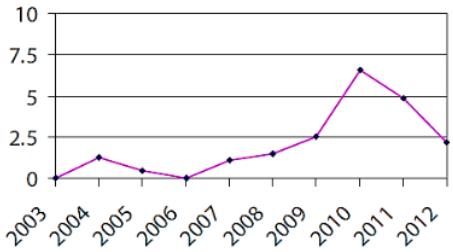

Figure 3. The total rate of biopsy diagnosis of syphilis according to the CDC data (rates per 100,000 biopsies) (Groh& Patino 2014).

Histopathological features in syphilis "the mimicker"

The classic manifestation of primary syphilis is a painless and well-circumscribed ulcer with an indurated base and raised borders, which known as "durum ulcer" (Tuddenham & Zenilman 2019). However, atypical symptoms or morphology may present, causing diagnosis challenging. Some techniques used in syphilis diagnosis are dark-field microscopy and Warthin-Starry staining. Spirochetes are found along the dermal-epidermal junction, inside and around the blood vessels, using immunofluorescent techniques and silver staining with the Levaditi stain or Warthin-Starry stain (Figure 4b). Endothelial9 swelling (endarteritis obliterans), ulceration, and a diffuse dermal infiltrate of plasma cells, lymphocytes, and histiocytes are the main histopathological findings at this stage (Figure 5a) (Johnston 2012, Elder 2014).

Many clinical symptoms of first stage syphilis have similar features as other diseases, such as chancroid or mole ulcer, genital herpes, lymphogranuloma venereum, and granuloma inguinale (Çakmak et al. 2019). Chancroid is the most similar mimicker that is difficult to distinguish from syphilis chancre. Chancroid is an acute localized genital infection caused by *Haemophilus ducreyi*, with necrotic ulcer, pain at the site of inoculation, and tender ulcer as the classic clinical symptoms (Figure 5A) (Irizarry et al. 2021). The histopathological characteristics of chancroid are solid lymphohistiocytic infiltrates with a lack of plasma cells and granulomatous vasculitis. There are three zones at the base of chancroid ulcer, i.e., an upper layer with tissue necrosis, fibrin, and neutrophils; a middle layer with vascular proliferation, prominent endothelial cells, and mixed infiltrate cells; and a deep zone with plasma cells and lymphocytes (Figure 5B, Figure 5C) (Johnston 2012).

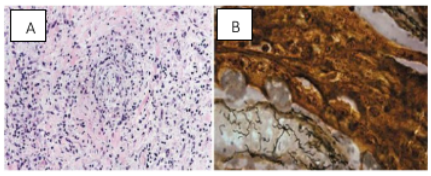

Figure 4. Primary syphilitic chancre, (a) endarteritis obliterans and diffuse dermal infiltrate of plasma cells, lymphocytes, and histiocytes; (b) the observation of *Treponema* morphology using silver stains (Johnston 2012).

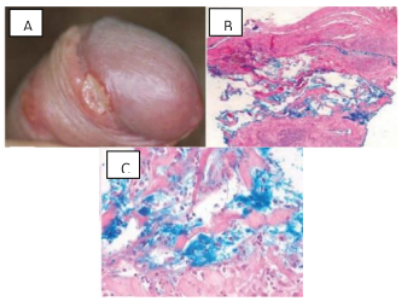

Figure 5. Chancroid ulcer with well-defined margins in the penile coronal sulcus (A); spongiform pustulation, psoriasiform changes, extensive ulceration, and three zones at the ulcer base (B, C) (Johnston 2012, Tuddenham & Zenilman 2019).

Herpes simplex virus (HSV)-induced genital herpes is an infection of the genitalia, with recurrent vesicles that cluster on an erythematous base as the characteristic symptoms. These vesicles are prone to rupture that can result in numerous erosions, ulcerations, and alterations, such as diffuse inflammation and massive necrotic ulceration (Figure 6A) (Holmes et al. 2008). The simplest

laboratory examination to distinguish HSV from a chancre is the Tzanck test with Giemsa or Wright stains, which will reveal the multinucleated giant cells. However, this test generally has a low sensitivity and specificity. The best examination of HSV is by tissue culture and enzyme linked immunosorbent assay (ELISA) (Holmes et al. 2008, Zhu & Viejo-Borbolla 2021). The histopathological features of genital herpes include ballooning degeneration of keratinocytes, multinucleated giant cells with nuclear folding, basophilic eggshell in the periphery of the nucleus as the cytopathic effect of herpes, and mild leucoclastic vasculitis (Figure 6B, Figure 6C) (Ghaznawie 2013, Elston et al. 2014, Elder 2017).

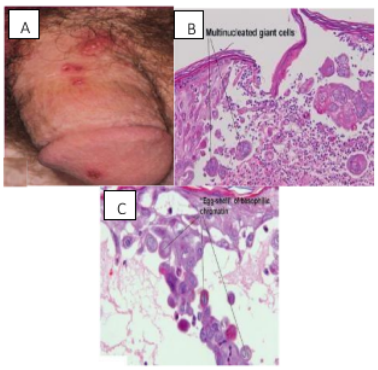

Figure 6. Clinical manifestation of genital herpes shows numerous vesicles that cluster on an erythematous base, with multiple ulcerations and necrotic ulcers (A); ballooning degeneration of keratinocytes and multinucleated giant cells (B); basophilic eggshell of chromatin at the periphery of the nucleus (C) (Elston et al. 2014, Tuddenham & Zenilman 2019).

Lymphogranuloma venereum (LGV) is a systemic sexually transmitted disease caused by *Chlamydia trachomatis* serovars L1, L2, and L3. The clinical manifestations of LGV are divided into three stages,the primary, secondary, and tertiary stages. Lesions will develop 3–30 days after infection, in the form of small herpetiform ulcers at the inoculation site and painful ulcers. Nonspecific ulceration and urethritis may occur rarely (Figure 7A). After a few weeks, primary-stage LGV will transition into a secondary stage, which is characterized by signs of lymph vessel involvement and hematogenous spread (Figure 7B) (Holmes et al. 2008). Histopathological features of the LGV mimicker show the non-specific granulation tissue. In the lymph nodes, a stellate abscess with surrounding epithelioid cells and macrophage giant cells represents the typical lesion (Figure 7C) (Johnston 2012). The prevalence of *Chlamydia trachomatis* as the most causal organism of non-specific genital infection is rare. However, the examination of the cause of non-specific genital infection is still required to register the exact treatment and not to confuse the disease as other conditions (Habibie et al. 2019).

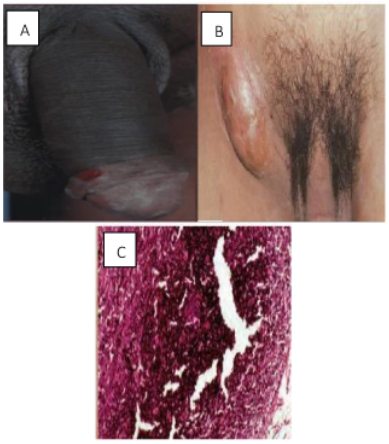

Figure 7. Clinical primary stage with small herpetiform ulceration (A); secondary stage with lymph involvement, hematogenous spread (B); a stellate abscess with surrounding epithelioid cells and macrophage giant cells (C) (Johnston 2012).

Granuloma inguinale (donovanosis) is a sexually transmitted infection caused by *Klebsiella granulomatis* (*Calymatobacterium granulomatis*). The disease is characterized by beefy red lesion in the form of ulcer filled with abundant granulation tissue, that bleeds easily. The boundaries of the ulcer are clear and have serpiginous lines (Figure 8A). The histopathological figures of a granuloma inguinale mimicker show pseudopitheliomatous hyperplasia with neutrophilic abscess (Figure 8B) and organisms in histiocytes of the dermis (Donovan bodies) (Figure 8C). Electron microscopy showed that the organisms were very thin with big green leafy veggie appearance (Johnston 2012, Elder 2017).

Secondary syphilis is known clinically as the "great imitator" because it resembles a variety of skin conditions and manifest itself anywhere on the body, including the palms of the hands and soles of the feet. Significant symptoms that are important to note in distinguishing syphilis from other diseases are skin conditions in the secondary stage, which are generally not itchy, often accompanied by generalized lymphadenitis, and also occur on the palms and soles (Johnston 2012, Elder 2017, Tuddenham & Zenilman 2019). Histopathological features of secondary syphilis lesions (such as macular, papular, and papulosquamous types) often overlap. However, epidermal changes are rare in the clinical form of

macular and papulosquamous lesions (Elder 2017).

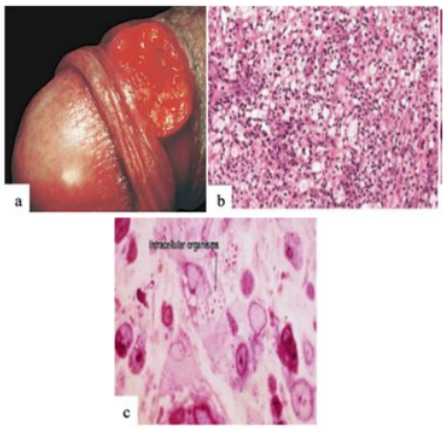

Figure 8. Neutrophilic abscess cells mixed with foamy macrophages (A); Donovan bodies with pseudoepitheliomatous hyperplasia; (B) clinical manifestation of ulcer characterized by a beefy appearance (C) (Elston et al. 2014).

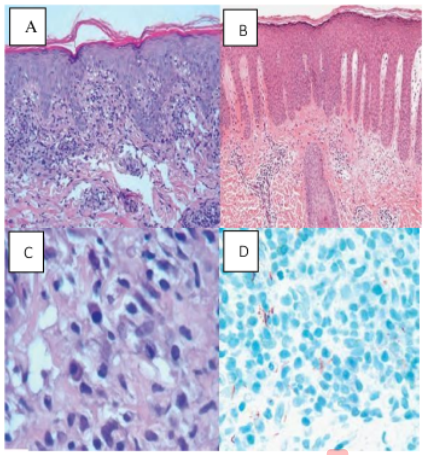

Figure 9. Histopathological features of psoriasis: neutrophils in the epidermis, regular acanthosis, prominent papillary blood vessels (x5) (A); pityriasis rubra pilaris: checkerboard-pattern hyperkeratosis, parakeratosis, and follicular blockage (x10) (B); secondary syphilis: acanthosis with slender rete, lichenoid inflammation, endothelial cell swelling, plasma cells occasionally seen (x5) (C); chronic spongiotic dermatitis: parakeratosis and spongiosis, irregular acanthosis (x5) (D) (Ko & Barr 2017).

The most common histopathological sign of secondary syphilis is psoriasiform hyperplasia, which is frequently accompanied by spongiosis and vacuolar alterations. Other features may vary, including the presence of parakeratosis, abundant plasma cells, edema of the papillary dermis, lichenoid, and granulomatous. *Treponema pallidum* can be identified by silver staining, such as the Warthin-Starry stain or immunoperoxidase technique (Elston et al. 2014, Elder 2017). Various mimickers in secondary syphilis lesions that have psoriasiform histopathological features are difficult or impossible to distinguish, including psoriasis, pityriasis rubra pilaris, and chronic dermatitis (Johnston 2012, Elston et al. 2014, Ko & Barr 2017).

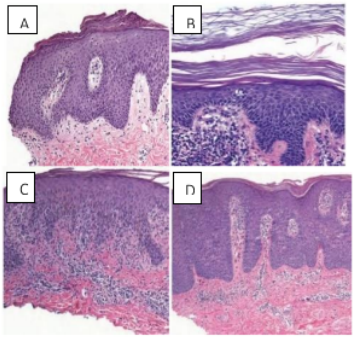

Figure 10. Psoriasiform hyperplasia seen mainly in the epidermis; orthohyperkeratosis, parakeratosis, and papillary dermal edema (x5) (A, B); vacuolar alterations with an abundance of neutrophils and barely perceptible plasma cells are observed (C); *T. pallidum* is visible in a silver-staining with 100x oil immersion (D) (Johnston 2012, Ko & Barr2017).

Strength and limitations

This review article discusses the histopathological characteristics that help distinguish syphilis from its common clinical and histological mimickers at each stage. However, because each research article analyzed in this study presented diverse cases with various symptoms, it was tricky to synthesize the distinguishing criteria. Therefore, universal screening and adequate pregnancy care must be a priority. It is recommended that future studies be discussed in greater detail with regard to the description of a number of additional syphilis mimickers, so that case recognition is better understood to aid in the diagnosis of syphilis.

CONCLUSION

High suspicion of syphilis and close communication between dermatologists and pathologists remain of the utmost importance. Dermatologists and pathologists should take the variety of clinical and

histologic presentations into account when making a differential diagnosis. The independent value of numerous syphilis histologic characteristics may have been overstated.[17] Endothelial swelling (endarteritis obliterans), interstitial inflammation, irregular acanthosis, and elongated rete ridge combinations raise the probability of syphilis. Vacuolar interface dermatitis and lymphocytes with visible cytoplasm also raise syphilis probability. Understanding of syphilis's clinical correlation and the histological appearance is crucial to correctly diagnosing the disease and distinguishing it from the histologic mimickers.

Acknowledgment

The authors would like to thank the Department of Anatomical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

Conflict of interest

None.

Funding disclosure

None.

Author contribution

IP, ANH, and EHK contributed to the conception of the study, and drafted the manuscript. IE gave final approval for the manuscript to be published, and agreed to be accountable for all aspects of the work.

REFERENCES

Ali R, Perez-Downes J, Baidoun F, et al (2016). Challenges in treating secondary syphilis osteitis in an immunocompromised patient with a penicillin allergy: Case report and review of the literature. Case Reports in Infectious Diseases 2016, 1–6. doi:10.1155/2016/4983504.

Çakmak SK, Tamer E, Karadağ AS, et al (2019). Syphilis: A great imitator. Clinics in Dermatology 37, 182–91. doi: 10.1016/j.clindermatol.2019.01.007.

Centers for Disease Control and Prevention (2017). Sexually transmitted disease surveillance 2016. Atlanta. [Web Page]

Chandrasekar PH (2017). Syphilis. Medscape. [Web Page]

Daili SF, Indriatmi W, Wiweko SN, et al (2013). Pedoman tata laksana sifilis untuk pengendalian sifilis di layanan kesehatan dasar. [Web Page]

Daili SF, Indriatmi W, Zubier F, et al (2015). Infeksi menular seksual: Pedoman praktis diagnosis & tatalaksana. Kementerian Kesehatan Republik Indonesia, Jakarta. [Web Page]

Elder DE (2017). Lever's Histopathology of the Skin, 11th edn. Lippincott Williams & Wilkins. [Web Page]

Elston D, Ferringer T, Ko C, et al (2014). Dermatopathology. [Web Page]

Flamm A, Parikh K, Xie Q, et al (2015). Histologic features of secondary syphilis: A multicenter retrospective review. Journal of the American Academy of Dermatology 73, 1025–30. doi: 10.1016/j.jaad.2015.08.062.

Ghaznawie M (2013). Peran dermatopatologi pada diagnosis berbagai kelainan kulit.

Groh J, Patino WD (2014). Increased frequency of histologic diagnosis of syphilis in older individuals during the last five years. Journal of the American Osteopathic College of Dermatology 30, 44–7. [Journal]

Gunn RA, Klausner JD (2019). Enhancing the control of syphilis among men who have sex with men by focusing on acute infectious primary syphilis and core transmission groups. Sexually Transmitted Diseases 46, 629–36. doi:10.1097/olq.0000000000001039.

Habibie DP, Murtiastutik D, Rahmadewi R (2019). Polymerase chain reaction chlamydia trachomatis examination in nonspecific genital infection patients. Dermatology Reports. doi: 10.4081/dr.2019.8055.

Ho EL, Lukehart SA (2011). Syphilis: Using modern approaches to understand an old disease. Journal of Clinical Investigation 121, 4584–92. doi: 10.1172/JCI57173.

Holmes KK, Sparling PF, Stamm WE, et al (2008). Sexually transmitted disease. McGraw-Hill, New York. [Web Page]

Hook EW (2017). Syphilis. Lancet 389, 1550–7. doi: 10.1016/S0140-6736(16)32411-4.

Irizarry L, Velasquez J, Wray AA (2021). Chancroid. StatPearls. [Journal]

Johnston R (2012). Spirochetal infections. In Weedon's skin pathology essentials, pp. 435–9. Elsevier. [Web Page]

Klausner JD (2019). The great imitator revealed: Syphilis. Topics in Antiviral Medicine 27, 71–4. [Journal]

Ko CJ, Barr RJ (2017). Dermatopathology: Diagnosis by first impression, 3rd edn. John Wiley & Sons. [Website]

Kojima N, Klausner JD (2018). An update on the global epidemiology of syphilis. Current Epidemiology Reports 5, 24–38. doi: 10.1007/s40471-018-0138-z.

Liu XK, Li J (2020). Histologic features of secondary syphilis. Dermatology 236, 145–50. doi: 10.1159/000502641.

Purnamasari I, Barakbah J, Martodiharjo S, et al (2021). Secondary syphilis during pregnancy: The importance of screening and clinical management.

Berkala Ilmu Kesehatan Kulit dan Kelamin 33, 145. doi: 10.20473/bikk.V33.2.2021.145-149.

Tuddenham SA, Zenilman JM (2019). Syphilis. In Fitzpatrick's Dermatology, ed. Kang S, Amagai M, Bruckner A, Enk A, Margolis D, McMichael A & Orringer J. McGraw Hill. [Web Page]

Wardiana M, Prakoeswa CRS, Sawitri S, et al (2022). Dealing with tests and treatments for HIV, syphilis, and hepatitis B infection to prevent mother-to-child transmission (MTCT) from a tertiary hospital in Indonesia. Bali Medical Journal 11, 334–40. doi: 10.15562/bmj.v11i1.3376.

World Health Organization (2011). Prevalence and incidence of selected sexually transmitted infections, Chlamydia trachomatis, Neisseria gonorrhoeae, syphilis and trichomonas vaginalis: Methods and results used by WHO to generate 2005 estimates. [Web Page]

World Health Organization (2017). Kajian nasional respon HIV di bidang kesehatan Republik Indonesia. [Web Page]

Yuindartanto A, Hidayati AN, Indramaya DM, et al (2022). Risk factors of syphilis and HIV/AIDS coinfection. Berkala Ilmu Kesehatan Kulit dan Kelamin 34, 114–9. doi: 10.20473/bikk.V34.2.2022.114-119.

Zhu S, Viejo-Borbolla A (2021). Pathogenesis and virulence of herpes simplex virus. Virulence 12, 2670–702. doi: 10.1080/21505594.2021.1982373.

THE HISTOPATHOLOGICAL FEATURES OF SYPHILIS AND ITS MIMICKERS

ORIGINALITY REPORT

16%	12%	12%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Christine J. Ko, Ronald J. Barr. "Dermatopathology", Wiley, 2022 Publication	1%
2	blog.balimedicaljournal.org Internet Source	1%
3	safeaccess.unboundmedicine.com Internet Source	1%
4	www.pagepress.org Internet Source	1%
5	ijbnpa.biomedcentral.com Internet Source	1%
6	Alexandra Flamm, Kruti Parikh, Qiang Xie, Eun Ji Kwon, Dirk M. Elston. "Histologic features of secondary syphilis: A multicenter retrospective review", Journal of the American Academy of Dermatology, 2015 Publication	1%
7	www.bbc.com Internet Source	1%

8	www.jurnal.syntaxliterate.co.id Internet Source	1 %
9	"Hospital-Based Dermatopathology", Springer Science and Business Media LLC, 2020 Publication	1 %
10	docplayer.net Internet Source	1 %
11	Katrice M. Karanfilian, Amer Ali Almohssen, Rajendra Kapila, Robert A. Schwartz. "Malignant syphilis: a new and revised definition", International Journal of Dermatology, 2022 Publication	1 %
12	www.frontiersin.org Internet Source	1 %
13	Dirk M. Elston. "Viral infections, helminths, and arthropods", Elsevier BV, 2009 Publication	1 %
14	sciencescholar.us Internet Source	<1 %
15	www.unsv.com Internet Source	<1 %
16	jurnal.uii.ac.id Internet Source	<1 %
17	www.em-consulte.com Internet Source	<1 %

18	api.crossref.org Internet Source	<1 %
19	repository.unair.ac.id Internet Source	<1 %
20	sandiegohealth.org Internet Source	<1 %
21	vdoc.pub Internet Source	<1 %
22	Ana S. Oliveira, Ana R. Ferrão, Filomena Martins Pereira, José Martinez-de-Oliveira, Ana Palmeira-de-Oliveira. "Trichomonas vaginalis: An Updated Overview Towards Diagnostic Improvement", Acta Parasitologica, 2016 Publication	<1 %
23	Diogo Goulart Corrêa, Simone Rachid de Souza, Tomás de Andrade Lourenção Freddi, Ana Paula Alves Fonseca et al. "Imaging features of Neurosyphilis", Journal of Neuroradiology, 2023 Publication	<1 %
24	epdf.pub Internet Source	<1 %
25	univmed.org Internet Source	<1 %

26	www.statpearls.com Internet Source	<1%
27	www.verywellhealth.com Internet Source	<1%
28	"New and Emerging Entities in Dermatology and Dermatopathology", Springer Science and Business Media LLC, 2021 Publication	<1%
29	Alexandra Flamm, Veronica Merelo Alcocer, Viktoryia Kazlouskaya, Eun Ji Kwon, Dirk Elston. "Histopathologic features distinguishing secondary syphilis from its mimickers", Journal of the American Academy of Dermatology, 2020 Publication	<1%
30	Jerome B. Taxy, Thomas Cibull. "Syphilis", American Journal of Surgical Pathology, 2020 Publication	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	On		

THE HISTOPATHOLOGICAL FEATURES OF SYPHILIS AND ITS MIMICKERS

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7