FEATURE ARTICLE

CE 2.0 Contact Hours

The Many Presentations of Syphilis

Brooke Ingram

ABSTRACT: Syphilis is a sexually transmitted infection caused by a spirochete, which if left untreated, transforms through four stages. Numerous cutaneous manifestations present from the time of the initial infection and evolve as the disease systemically progresses. Syphilis has been around for centuries, and we can attribute the rise of the specialty of dermatology to its prevalence and protean nature. Syphilis is on the rise again for the first time since the advent of penicillin, making it important for healthcare providers to have knowledge of its presentation in its various stages.

Key words: Dermatology History, Public Health, Sexually Transmitted Disease, Sexually Transmitted Infections (STI), Spirochete, Syphilis, *Treponema pallidum*

Syphilis is a sexually transmitted infection spread by direct contact during vaginal, anal, or oral sex (Centers for Disease Control and Prevention [CDC], 2014). Syphilis can also be spread congenitally from mother to baby via the placenta (Knott, 2014). Syphilis consists of four stages: primary, secondary, latent, and tertiary. It is caused by the spirochete (spiral-shaped bacterium; Figure 1) *Treponema* (*T.*) *pallidum* (Lebwohl, 2004). Penicillin can treat syphilis, killing *T. pallidum* and thus preventing further damage, but it will not repair damage already done. Cutaneous manifestations of the disease are present in all phases, with the exception of the latent phase (Bolognia, 2009).

The rise of the specialty of dermatology is attributed to the prevalence of syphilis in the late 1800s. Because of the numerous cutaneous manifestations of this systemic disease, syphilis helped define dermatology as a specialty beyond and distinct from general medicine. At the same time, syphilis also aided the collaboration between dermatologists and internists because of its effects on the internal organs as well (Chu & Tarbox, 2013). Other dermatological diseases have similar presentations, leading to misdiagnosis, which is why syphilis is known as "the great mimicker" (Kollipara, Guidry, & Tyring, 2015). Consequently, this required specialists who could identify specific characteristics of this disease, while at the same time keeping in mind possible differential diagnoses.

Before the emergence of penicillin in 1943 as a treatment for syphilis, earlier therapies of guaiacum, mercury, and arsenic were largely ineffective (Frith, 2015). Unfortunately, despite having penicillin readily available, syphilis is again on the rise. This is a problem for all demographics; however, according to the CDC, it is statistically highest in the homosexual male population. As of December 2014, syphilis had a 10% increase in incidence since 2012 (CDC, 2014); troubling statistics considering the CDC states that syphilis was nearly eliminated in the United States in the Year 2000 (Patton, Su, Nelson, Weinstock, & CDC, 2014). Condom usage during sex can decrease the chance of spreading the disease, if condoms are used consistently and correctly. However, abstinence is the only method that eliminates the chance of getting infected (CDC, 2013a). It is theorized the increase of syphilis in the homosexual male population may be related to "increased unsafe sexual behavior, possibly due to improved antiretroviral therapy for HIV" (Kollipara et al., 2015, p. 784).

To confirm the diagnosis of syphilis, blood tests are typically done looking for antibodies. These tests are called rapid plasma reagin and venereal disease research laboratory. The disadvantage with these tests is they detect antibodies, but not antibodies specific for *T. pallidum*, so many false positives can occur, which requires the patient to have further blood testing. There are blood tests to detect antibodies specifically to *T. pallidum* called fluorescent treponemal antibody absorption, which can detect antibodies 3–4 weeks after exposure, and *T. pallidum* particle agglutination assay. *T. pallidum* particle agglutination assay is more specific than fluorescent treponemal antibody absorption and has less false-positive results (American Association for Clinical Chemistry, 2015). Patients who do test positive for syphilis need to also be tested for HIV infection and again in 3 months if the first HIV test is negative (CDC, 2013b). Because of the patient's history of practicing unsafe sex, it would be prudent to refer the patient for testing of all sexually transmitted diseases to the local health department.

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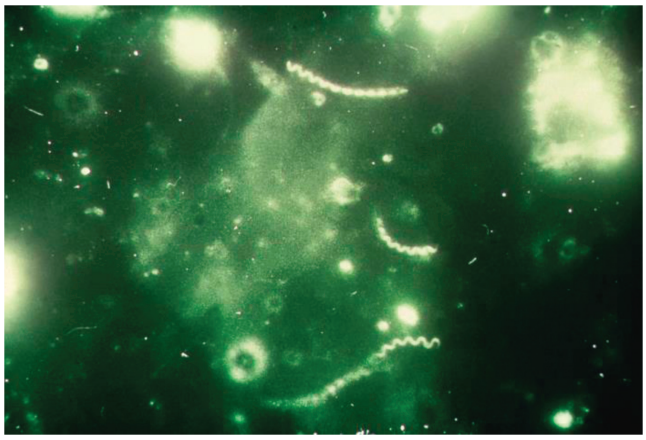

FIGURE 1. Treponema pallidum, darkfield preparation: syphilis (CDC, 1971c).

PRIMARY STAGE

The primary stage of syphilis consists of a painless, round chancre measuring 1.0–1.5 cm, on average, found on the glans penis or the cervix. These lesions can also be found on the labia, shaft of the penis, anus, fingers, or tongue (Figure 2), depending on where the spirochete entered the body. Seventy-five percent of the time, only one chancre is present. The chancre is typically painless, which is why it can go undetected, especially in the female population (Bolognia, 2009). Some individuals may also dismiss the chancre as being an ingrown hair or zipper cut (CDC, 2014). The chancre most commonly appears 2–3 weeks after exposure (Knott, 2014). A raised border and induration because of dermal involvement and moist base are the hallmark signs of the chancre. These chancres are not purulent (Bolognia, 2009), but they do ooze serum (Knott, 2014). This serum produced by the chancre is loaded with the *T. pallidum* bacterium, making it highly infectious (Knott, 2014). This fluid can be collected and examined using a dark-field microscope to confirm a diagnosis (American Association for Clinical Chemistry, 2015). According to Bolognia (2009), the borders of these chancres are not scalloped, as with ulcers seen in herpes simplex. Nearby lymph node involvement is typical in this stage (Knott, 2014). If left untreated, these chancres take approximately 4 weeks to resolve or 2 weeks with antibiotic treatment (Bolognia, 2009).

SECONDARY STAGE

Once syphilis has reached the secondary stage, bacteria have spread to many parts of the body. However, cutaneous manifestations are the most common complaint from patients in this stage. The secondary stage appears, on average, 3 weeks after the appearance of the chancre. Often, the chancre is healing, while the signs of the secondary stage are emerging. Normal duration for the secondary stage is 2–10 weeks but can last for up to 12 months (Braverman, 1998). Secondary syphilis can present in numerous forms and varies in individuals. "Some symptoms are nonspecific and are similar to those that can occur with other medical problems" (Knott, 2014, para. 18). According to Braverman (1998), typical signs and symptoms of the secondary phase include fever, malaise, lethargy, generalized lymphadenopathy, and a widespread rash that is sharply demarcated, symmetrical, nonpruritic, and nonpainful (Figure 3). Other systemic symptoms may include low-grade fever, sore throat, and joint pain (Knott, 2014).

In adults, secondary lesions can be macular, papular, and pustular, but never vesicular. Not everyone infected with syphilis will develop a macular rash. If they do, it will appear on the trunk, shoulders, and extremities and rarely on the palms and soles. It is possible that this rash may be confused with measles, rubella, drug eruptions, tinea versicolor, and seborrheic dermatitis. However, a way to identify secondary lesions of syphilis from the other diagnoses is that syphilitic lesions have a scale that flakes off easily and the macules are discrete (Braverman, 1998).

In the secondary phase, the papulosquamous rash is more common. Lesions range from 0.2 to 2 cm and can range from pink to copper red. They can appear in many areas of the body or only a few, most commonly on the face, palms (Figure 4), soles, and trunk (Knott, 2014). The rash can mimic the look of pityriasis rosea but, however, will not be distributed in the lines of cleavage typical of pityriasis rosea. The lesions "have a tendency to occur in groups or to spread peripherally to form annular, ring-shaped, or polycyclic patterns" (Braverman, 1998, p. 629). With syphilis, the patient will also be systemically ill, thus further ruling out pityriasis rosea.

The palms of the hands and the soles of the feet are involved in 50%–80% of cases (Kollipara et al., 2015). Because of the color (Figure 5), lesions of this type found on the palms and soles have been referred to as "copper pennies" (Bolognia, 2009). These copper penny lesions can be mistaken for rickettsial and coxsackievirus; however, if a patient has lesions on the palms and soles, always consider syphilis as a differential diagnosis (Kollipara et al., 2015).

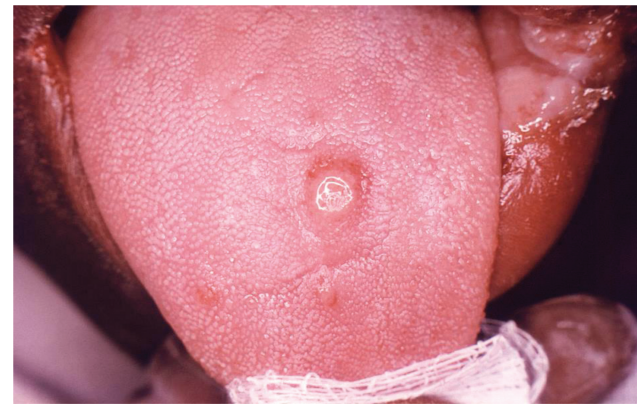

FIGURE 2. Primary syphilitic chancre (CDC, 1967b).

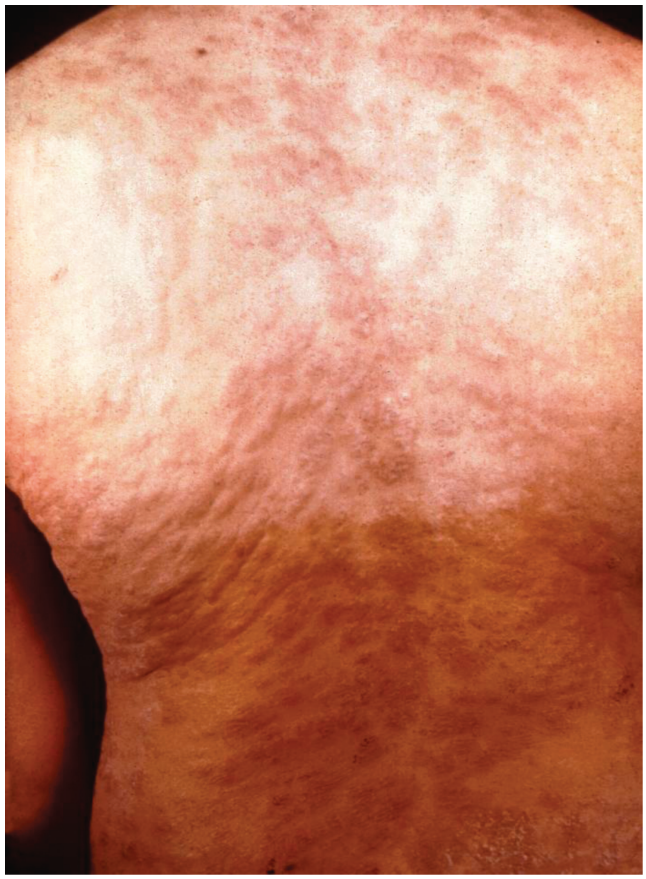

FIGURE 3. Secondary syphilis rash on the back (CDC, n.d.).

Differential diagnoses may also include psoriasis and lichen planus. However, psoriasis has a scale that does not flake off easily. The lesions may appear lichenoid, but lichen planus rarely involves the palms and soles (Braverman, 1998).

Other lesions associated with secondary syphilis can include nonscarring "moth-eaten" alopecia of the scalp, mucous patches inside the mouth (Figure 6), split papules at the oral commissures, annular plaques with central hyperpigmentation on the face, granulomatous nodules, and condyloma lata of the anogenital region (Bolognia, 2009). If left untreated, the secondary stage resolves after several weeks but can recur intermittently for up to 2 years (Knott, 2014).

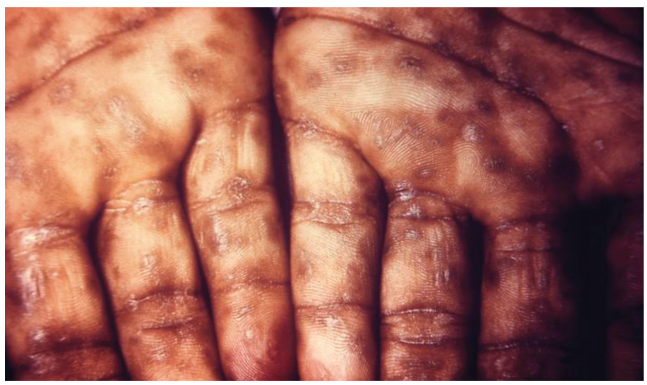

FIGURE 4. Palmar lesions of secondary stage syphilis (CDC, 1971b).

LATENT STAGE

The infected person is considered to be in the latent stage of syphilis when the symptoms of the primary and secondary syphilis have disappeared. In the latent stage of syphilis, laboratory testing is the only way to confirm diagnosis, as there are no cutaneous manifestations.

The latent stage is divided into two phases: early latent and late latent. Early latent syphilis is defined as seropositive on laboratory testing, with no symptoms, and is less than 1 year since contracting the infection. The patient will be considered to have late latent syphilis if the patient contracted the syphilis greater than 1 year ago or if the duration is unknown (Lo, 2015).

TERTIARY STAGE

The final stage is tertiary syphilis. This can happen many years after the initial infection and may lead to death (Knott, 2014). Tertiary syphilis can affect any organ but most commonly presents with skin, bone, liver, heart, and brain lesions (Braverman, 1998).

The cutaneous manifestation of the tertiary phase of syphilis is the formation of gumma. Gummas are rubbery, painless tumors that typically show up in areas of trauma secondary to the inflammation because of a deep granulomatous reaction.

Gumma can occur in any organ, but most common are the skin, mucous membranes, and bones. Gumma developing on organs can affect the function of the organ (Knott, 2014). The gummas eventually cause tissue destruction with central necrosis and an oozing kidney-shaped ulcer (Figure 7). The discharge from these ulcers is characteristically thick and stringy. There may be one or multiple tumors and can be as large as several centimeters. Gumma on the bones can cause bone pain at night, and the chronic inflammation can cause fevers and anemia (Knott, 2014).

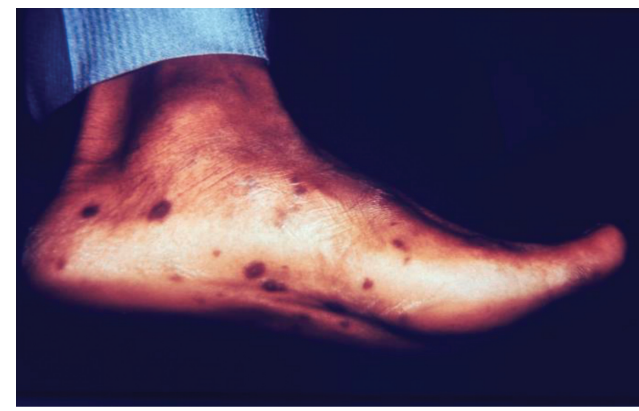

FIGURE 5. Plantar lesions of secondary stage syphilis (CDC, 1972).

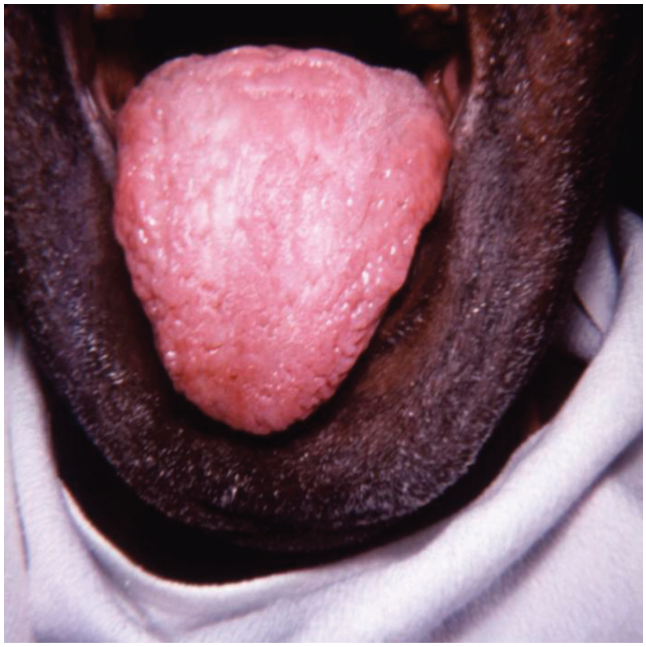

FIGURE 6. Mucous patches on the tongue of secondary syphilis (CDC, 1967a).

Cutaneous gummas heal leaving atrophic, noncontractile scars. The characteristic of the scar being noncontractile is key to distinguishing it from tuberculosis scars, which are typically contractile causing deformities (Braverman, 1998).

Other complications of the tertiary stage can include aortic aneurysms, heart murmurs, heart failure, loss of mental function, changes in personality, stroke, meningitis, blindness, deafness, dementia, memory loss, confusion, depression, hallucinations, difficulty walking, incoordination, and foot numbness (Knott, 2014).

CONGENITAL SYPHILIS

Pregnant women can pass syphilis through the placenta to the fetus (Kaneshiro, 2013). This is called congenital syphilis. In this case, this is a blood-borne infection, so the infants will not have a primary phase (Bolognia, 2009). Statistically, approximately 50% of babies infected with syphilis will die in utero or shortly after birth (Kaneshiro, 2013). Babies infected with syphilis who survive are more likely to be premature and of low birth weight (CDC, 2014).

Congenital syphilis is divided into two stages: early and late. In early congenital syphilis, the infant presents with symptoms before 2 years old (Knott, 2014). If the infection occurs early on in pregnancy, the baby can present with a weeping eczematous rash on the mouth (Figure 8), neck, genitals, and anus (Braverman, 1998). Fissuring is common with this rash and can cause scarring around the mouth. The newborn may present with small blisters on the palms of the hands and soles of the feet, which later change into the "copper penny" lesions (Kaneshiro, 2013). If the infection is contracted later on in pregnancy, the baby will present with dermatologic signs similar to adults who have been infected (Braverman, 1998). Other signs may include swollen liver and spleen, failure to thrive, fever, irritability, inflammation of the bones, anemia, lymphedema, jaundice, saddle nose (no bridge), and rhinorrhea (Kaneshiro, 2013; Knott, 2014).

Late congenital syphilis, with symptoms presenting after 2 years old, includes symptoms similar to the tertiary stage seen in adults. Older infants/young children do not present with as many dermatological signs but may show gray, mucous-like patches and/or scarring on the anus and outer vagina. Nondermatological signs are notched, widely

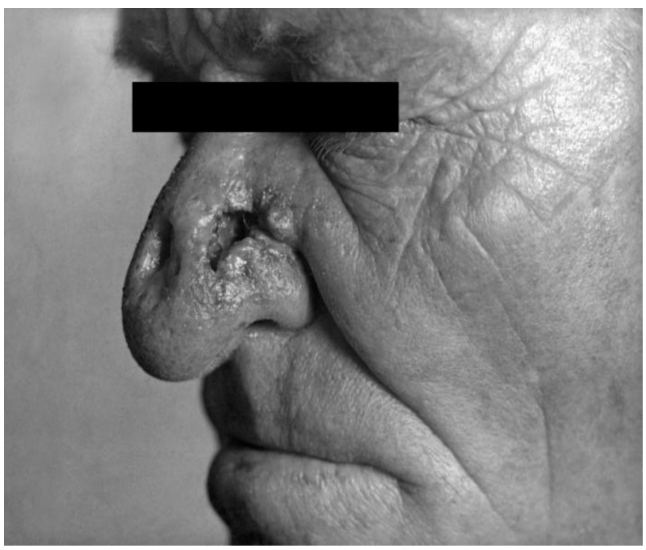

FIGURE 7. Gumma of the tertiary stage (CDC, 1971a).

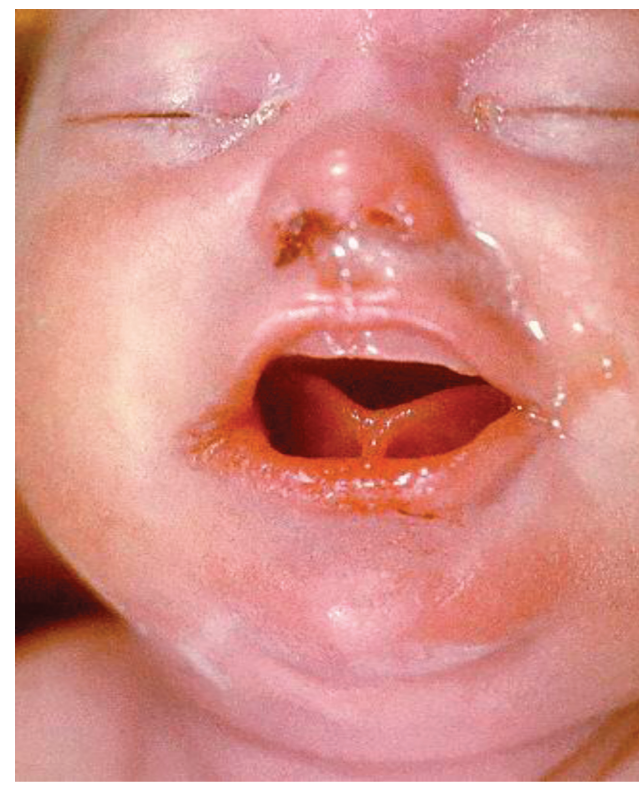

FIGURE 8. Congenital syphilis (CDC, 1963).

TABLE 1. Treatment of Choice

	Primary	Secondary	Early Latent	Late Latent	Tertiary
Benzathine penicillin G 2.4 million units IM	X	X	X		
Peds: benzathine penicillin G 50,000 units/kg IM, maximum dose of 2.4 million units	X	X	X		
Benzathine penicillin G 2.4 million units IM once a week for 3 weeks				X	X
Peds: benzathine penicillin G 50,000 units/kg IM, maximum dose of 2.4 million units once a week for 3 weeks				X	X

Lo, 2015.

spaced permanent front teeth (Hutchinson teeth); bone pain; blindness; cornea clouding; hearing impairments or deafness; and swelling of the joints. As with adults, congenital syphilis is treated with penicillin (Kaneshiro, 2013).

NEUROSYPHILIS

Neurosyphilis, syphilis infection affecting the nervous system can occur early in untreated syphilis. Symptoms of neurosyphilis include personality changes, memory loss, difficulty speaking, numbness or tingling of the hands or feet, and muscle pain (Knudsen, 2016). Neurosyphilis is not a distinct and separate phase of syphilis, but the possibility of neurosyphilis is important to consider with regard to treatment.

TREATMENT

As mentioned, the treatment drug of choice for syphilis is penicillin, to the extent that the CDC recommends that patients with penicillin allergies should have allergy skin testing to determine if penicillin desensitization is necessary (CDC, 2011). "No proven alternatives to penicillin are available for treating neurosyphilis, congenital syphilis, or syphilis in pregnant women" (CDC, 2011, para. 1). HIV-positive patients should also be treated with penicillin, if at all possible. The severe reactions to penicillin causing urticarial, angioedema, or anaphylaxis are an immunoglobulin-E-mediated response. "Although an estimated 10% of persons who report a history of severe allergic reactions to penicillin continue to remain allergic their entire lives, with the passage of time, most persons who have had a severe reaction to penicillin stop expressing penicillin- specific IgE" (CDC, 2011, para. 2). Therefore, 90% of these people can be treated with penicillin safely. The skin testing for this population needs to include major and minor determinants of penicillin. The patients who test allergic should be desensitized. Because the skin tests may possibly miss 10% of the patients who could still present with a severe reaction to penicillin, the patients who test negative to the skin tests can be addressed in one of two ways. These patients could also go through the desensitization process or be given gradual doses of penicillin in a setting where their medical needs could be addressed, should they have a severe allergic reaction (CDC, 2011). Allergic patients undergoing desensitization should be in a setting like this as well.

The type and dose of penicillin are based on the stage of syphilis in which the patient presents (Table 1). Primary, secondary, and early latent syphilis is treated with benzathine penicillin G 2.4 million units of intramuscular (IM) injection. In pediatrics, benzathine penicillin G is dosed at 50,000 units/kg IM, with a maximum dose of 2.4 million units per dose.

TABLE 2. Penicillin Allergy

	Primary	Secondary	Early Latent	Late Latent	Tertiary
Doxycycline 100 mg PO BID × 14 days	X	X	X		
Tetracycline 500 mg PO QID × 14 days	X	X	X		
Azithromycin 2000 mg one-time dose	X	X	X		
Ceftriaxone 250 mg IM or IV daily for 10–14 days	X	X	X		
Doxycycline 100 mg PO BID × 28 days				X	
Tetracycline 500 mg PO QID × 28 days				X	

Lo, 2015.

TABLE 3. Follow-up Guidelines

	Primary	Secondary	Latent	HIV Infected
3 months				X
6 months	X	X	X	X
9 months				X
12 months	X	X	X	X
24 months			X	X

CDC, 2013.

Late latent and tertiary syphilis is treated with benzathine penicillin G 2.4 million units IM once a week for 3 weeks, and in pediatrics, benzathine penicillin G is dosed at 50,000 units/kg IM, up to 2.4 million units weekly for 3 weeks (Lo, 2015).

If skin testing and penicillin desensitization are not feasible, substitutes are available for nonpregnant patients but are not as effective, so use with caution. These patients will need, and be willing to commit to, close clinical and laboratory follow-up to ensure the treatment has been successful (CDC, 2015). Alternative options are doxycycline, tetracycline, azithromycin, or ceftriaxone for primary, secondary, or early latent syphilis (Table 2)—doxycycline 100 mg by mouth (PO) twice a day (BID) for 14 days, tetracycline 500 mg PO four times a day (QID) for 14 days, azithromycin 2000 mg PO single dose, or ceftriaxone 250 mg IM or intravenous daily for 10–14 days. For patients in the late latent phase, the recommended treatment is doxycycline 100 mg PO BID for 28 days or tetracycline 500 mg PO QID for 28 days (Lo, 2015). The effectiveness of nonpenicillin antibiotics in the tertiary stage is not well documented, and the patient should be referred to an infectious disease specialist.

PATIENT FOLLOW-UP

Patients who received treatment for syphilis need to be followed up by their family doctor or an infectious disease specialist for both physical examination and repeat blood testing according to the guidelines outlined in Table 3. Patients treated in the primary and secondary phases require follow-up in 6 and 12 months, where patients treated in the latent phase need an additional follow-up in 24 months. Patients treated for syphilis who are also HIV positive need close follow-up at 3, 6, 9, 12, and 24 months (CDC, 2013b).

PATIENT EDUCATION

It is important to educate patients with syphilis to have no sexual contact until the antibiotics are complete and all sores are completely healed. Patients with syphilis are the most contagious during the primary and secondary stages when lesions or rashes are present (CDC, 2013b). It is also vital that the patients notify past sexual partners of their disease status so they can receive testing and treatment. "Presumptive treatment should be given to those persons who were exposed within the 90 days preceding a sex partner's diagnosis of primary, secondary, or early latent syphilis, because they might be infected, even if seronegative" (CDC, 2013b, p. 17, para. 4). Referral of patients to the local health department sexually transmitted infection program can help them with this process. Laws vary from state to state on the mandatory reporting of infected patients. Providers should contact their local or state health department for guidance.

Patients also need to be educated on the prevention of future exposure. Options of prevention strategies include abstinence, mutual monogamy with an uninfected partner, use of condoms consistently and correctly, and limiting the number of sex partners (CDC, 2013b).

CONCLUSION

Syphilis is a dynamic sexually transmitted or congenital disease with various presentations, often mimicking other dermatology disorders. Syphilis is on the rise again, and it is important that nurses are aware of the signs and symptoms of syphilis. Nurses are the drivers for educating patients and the public on disease prevention. Dermatology nurses have an advantage over other nurses by appreciating the subtleties of various dermatologic presentations. The more knowledge nurses have about this disease and how it is treated, the more effective nurses will be with public education on prevention and early detection. ■

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