Chapter

Sexually Transmitted Infections in Pediatrics

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Abstract

Sexually transmitted diseases (STDs) disproportionately affect young people, with more than half of the infections occurring in 15- to 25-year-olds, although as an age group they constitute only 25% of the sexually active population. Adolescents have been considered as a key and vulnerable population; adolescents are considered as marginalized populations (i.e., poor access to adequate health services, social and parental acceptance, stigmatization, among others. Every year, 87 million new cases of gonorrhea are reported worldwide in the population from 15 to 49 years old. In 2016, the estimated global prevalence of CT in 15-to 49-year-old women was 3.8% and in men 2.7%, with regional values ranging from 1.5 to 7.0% in women and 1.2 to 4.0% in men. The worldwide prevalence of HSV-2 among 15–49-year old is 11.3% and for HSV-1 among 0–49-year-old is 67%. These numbers alert us about the increase in the frequency of these diseases among young populations; more open sexual behavior could be an important factor for this increase; the treatment of these diseases is challenging due to the difficulties with detection and treatment; in the case of gonorrhea, it could become a major public health problem due to the emerging antimicrobial resistance; in the case of Chlamydia, despite the effective treatment, reinfection is still a possibility and for genital herpes, the disease can be controlled but not cured. This chapter will describe the most important aspects of these three diseases for supporting the clinicians and researchers about the management of sexually transmitted diseases in the adolescent population.

Keywords: sexually transmitted diseases, chlamydia, genital herpes, HSV-1, HSV-2, gonorrhea

1. Introduction

Sexually transmitted diseases (STDs) disproportionately affect young people, with more than half of the infections occurring in 15- to 25-year-olds, although as an age group they constitute only 25% of the sexually active population [1]. Family physicians and pediatricians must be familiar with the context around STDs and mainly with the key clinical elements for diagnostic suspicion, always evaluating sexual abuse. More than 1 million sexually transmitted infections (STIs) occur every day and an estimated 376 million chlamydia, gonorrhea, syphilis, and trichomoniasis infections occur each year. STIs can have serious consequences beyond the immediate infection itself, through mother-to-child transmission of infections or conditions such as infertility and cervical cancer and some STIs can increase the risk of HIV acquisition three-fold or more. Adolescents have been considered as a key, vulnerable and marginalized population (i.e., poor access to adequate health

services, social and parental acceptance, stigmatization, among others) [2]. In this chapter, we will be describing the major clinical features of Gonorrhea, Chlamydia Trachomatis, and Genital Herpes.

2. Gonorrhea

2.1 Epidemiology

Every year, 87 million new cases of gonorrhea are reported worldwide in the population from 15 to 49 years old (2016 incidence). The median cases rates per 100,000 men from 15 to 49 years old reporting urethral discharge are 82.5 (range: 1.1–6133.7) and gonorrhea are 16.9 (range 0.0–297.1); the highest case rates were reported from the African Region, followed by the European and Western Pacific regions. In the United States, the highest peak of gonorrhea has been reported in the 20–24 years of age (720.9/100,000 in men and 702.6/100,000 in women), the second group of age with the highest incidence is the group from 15 to 19 years old (320.5/100,000 in men and 548.1/100,000 in women) [3]. Latin American countries like Colombia, Peru, and Brazil have been reported an increase in the number of cases in 2000 [4]. The highest prevalence of gonorrhea has been detected in the African Region (1.7%) followed by the Western Pacific Region (around 1.5%) [5]. One of the biggest concerns about gonorrhea is the development of antimicrobial resistance (AMR); in 2016, 57 countries reported that ≥5% of N. gonorrhea (Ng) specimens had decreased susceptibility (including azithromycin and ciprofloxacin) [6].

2.2 The pathogen

Neisseria gonorrhea (Ng) is a diplococcal gram-negative microorganism and one of the two pathogenic Neisseria species pluralism (spp); this bacterium has 80–90% of similarity to Neisseria meningitidis. Ng genome was sequenced for the first time in 2003. Ng has a high degree of genetic plasticity that enables the rapid evolution of AMR [7].

Ng has evolved mechanisms for evading innate immunity and suppressing adaptive immune responses. Ng prevents complement activation, opsonization, and bacterial killing by binding to complement proteins, sialylating its lipooligosaccharide (LOS) to hide from the complement system. Ng can bind also to the Host factor H and C4b-binding protein (C4BP), becoming serum resistant by presenting as self and by shielding itself from complement recognition [8].

2.3 The disease

Ng is an obligated human pathogen that is primarily transmitted through genital, oral, and anal sexual contact, infecting mucosal surfaces at these sites leading to the various symptoms associated with gonorrhea. Transmission is highly efficient (a substantial proportion of people become infected after a single exposure); can be asymptomatic or symptomatic (all sites), both can lead to additional Sexual Reproductive Health (SRH) complications (infection itself or inflammatory response); it can be also transmitted to neonates from infected mothers during childbirth infecting the conjunctival mucosa [9].

The asymptomatic infection is frequently unrecognized and is accountable for the larger proportion of all infections, this is the most frequent presentation in women; the acute symptomatic syndrome is the most common presentation in men [8, 9].

In women, as already mentioned, most of the infections have no or mild symptoms like vaginal discharge, it is frequently mistaken for other reproductive conditions and the coinfection with Chlamydia trachomatis (CT) is common. In men, gonorrhea is presented as an acute lower genital tract infection with urethritis with purulent discharge or dysuria within 5 days of infection. Among both sexes, extragenital infections of the oropharynx and rectum are usually asymptomatic but can cause symptomatic pharyngitis and proctitis [8, 9].

Ng infections have potential adverse sexual reproductive health outcomes like pelvic inflammatory disease (PID), tubo-ovarian abscesses, infertility, epididymo-orchitis, ectopic pregnancy, chronic pelvic pain, urethral stricture in men, and adverse pregnancy outcomes. In the neonate can cause vision loss due by neonatal conjunctivitis. Ng also increases the risk of HIV, finally, the infection can be disseminated (i.e., arthritis, gonococcemia, endocarditis, and meningitis). Ng also generates important psychosocial consequences like stigmatization and negative effects on sexual relationships [7–10].

A recent increase in gonorrhea incidence has been reported, one of the main reasons is the change in sexual behavior in the era of antiretroviral treatment for HIV infection; it seems that people are less cautious and have sex with new and casual partners without condoms [7], this is of particular importance in the adolescent population that is considered a vulnerable group.

Gonorrhea infections are more common in adolescents, followed by neonatal infections; in children between these two periods, sexual abuse should be always considered [10].

2.4 Diagnosis

The most recent definition of a gonorrhea case is the one published by the Centers for Disease Control and Prevention (CDC). This definition includes laboratory criteria for diagnosis and case classification [11]. Observation of Ng in a urethral smear (gram-negative diplococci) from men or an endocervical smear from a female indicates Ng infection; also the isolation by culture can make the diagnosis; finally and more recently, the demonstration of Ng in a clinical specimen by detection of antigen or nucleic acid can also make Gonorrhea diagnosis. A case is confirmed when Ng is isolated by culture or N. gonorrhea is demonstrated in a clinical specimen by detection of antigen or detection of nucleic acid via nucleic acid amplification (e.g., PCR or hybridization with a nucleic acid probe).

For practical purposes, we can consider two types of diagnosis: Clinical gonorrhea defined by a confirmed case and clinical signs and symptoms; and asymptomatic gonorrhea, defined as a confirmed case without clinical signs and symptoms.

2.5 Gonorrhea in children and sexual abuse

In general, gonococcal infections in children and adolescents can occur in three different age groups [9]:

- In the newborn, in which the most frequent clinical manifestation is conjunctivitis; other manifestations include scalp abscess, disseminated disease, vaginitis, and urethritis. Infection in the newborn normally occurs due to vertical transmission.

- In children beyond this period, gonorrhea has been considered as "proof" of sexual abuse, vaginitis is the most common manifestation in pre-pubertal females. Sexual transmission should be considered always in these cases; it

is mandatory to suspect and manage sexual abuse in the applicable legal and medical context [9, 10].

- In adolescents with active sexual life, in which the infection is often asymptomatic; in female adolescents the Fitz-Hugh-Curtis syndrome and be seen (perihepatitis).

2.6 Treatment

Since the discovery of the sulfonamides in the 1930's decade followed by Penicillin G, Spectinomycin, 3rd generation cephalosporins, macrolides, and finally fluoroquinolones; Ng has been developed evolutive mechanisms for antimicrobial resistance. The first Ng strain with high-level resistance to ceftriaxone was isolated in 2009 in Japan, same findings occurred in France and Spain 2 years later; other countries like Japan, China, Australia, Singapore, Canada, and Argentina also reported treatment failures with ceftriaxone. In 2014, the first failure of ceftriaxone–azithromycin dual therapy for gonorrhea was verified in the United Kingdom. Since 2015, an international spread of one ceftriaxone-resistant gonococcal strain, initially described in Japan, has been confirmed and the first strain with resistance to ceftriaxone plus high-level azithromycin resistance was isolated in 2018 in the UK and Australia [7–12].

2.6.1 Uncomplicated gonococcal infections treatment beyond the neonatal period and adolescents

Considering that older children normally acquire the infection through sexual abuse, it is very important to reduce the traumatic impact of treatment; in these cases, a single dose oral regimen is preferred [10]. The recommended regimens for Ng treatment depend on the location of the infection.

For uncomplicated vulvovaginitis, cervicitis, urethritis, proctitis, or pharyngitis, the primary recommendation is for children who weigh less than 45 kg: ceftriaxone 125 mg IM in a single dose; and for children who weigh 45 kg or more: 250 mg IM in a single dose plus azithromycin, 1 g orally in a single dose. In the case of uncomplicated infections that involve the anal region, dual treatment with cefixime (400 mg orally) and azithromycin may be used if ceftriaxone is not available. For infections located in the pharynx, the primary treatment recommended is ceftriaxone; cefixime should not be used [9, 13]. In the case of cephalosporin allergy, a consultation with a pediatric allergologist or an allergy expert consultation should be performed.

Tests-of-cure are not needed; these are recommended only for pharyngeal locations (test-of-cure 7–14 days after using NAAT or culture).

In the case of persistent infections, other causes must be considered: recurrent Ng infection can be seen among sexually active adolescents previously treated with gonorrhea mostly related to reinfection (i.e., sexual partners did not receive the treatment). It is recommended that this population that has been treated for Ng, should be retested 3 months after treatment [13–15].

2.6.2 Complicated gonococcal infections treatment beyond the neonatal period and adolescents

Complicated gonococcal infections include arthritis-dermatitis syndrome, meningitis, endocarditis, conjunctivitis, and epididymitis [9, 13–15].

- For disseminated infection, the recommendation is:

- In children who weigh less than 45 kg: Ceftriaxone (50 mg/kg/day; maximum 1 g/day, intravenous or intramuscular, once a day for 7 days) AND Erythromycin base or ethylsuccinate (50 mg/kg/day; maximum 2 g, orally divided into 4 doses every day for 14 days.

- In children who weigh 45 kg or more: Ceftriaxone (1 g, intravenous or intramuscular, once a day for 7 days) AND Azithromycin (1 g, orally in a single dose).

- For meningitis or endocarditis, the recommendation is:

  - In children who weigh less than 45 kg: Ceftriaxone (50 mg/kg/day; maximum 2 g/day, intravenous or intramuscular, every 12–24 hours. For meningitis: 10 to 14 days. For Endocarditis: at least 28 days; AND Erythromycin base or ethylsuccinate (50 mg/kg/day; orally divided into 4 doses every day for 14 days.

  - In children who weigh 45 kg or more: Ceftriaxone (1–2 g, intravenous or intramuscular, every 12–24 hours. For meningitis: 10–14 days. For endocarditis: at least 28 days; AND Azithromycin (1 g, orally in a single dose).

- For conjunctivitis, the recommendation is:

  - In children who weigh less than 45 kg: Ceftriaxone 1 g, intramuscular in a single dose.

  - In children who weigh 45 kg or more: Ceftriaxone, 1 g, intramuscular in a single dose; AND Azithromycin 1 g, orally in a single dose.

- For epididymitis the recommendation is:

  - Ceftriaxone, 250 mg intramuscular in a single dose AND doxycycline, 100 mg orally twice daily for 10 days.

2.7 Prevention and patient counseling

The patient should be counseled about the importance of routine screening for gonorrhea to prevent reproductive health complications of untreated infections, especially in young women; the asymptomatic nature of most gonococcal infections in females, whereas males often present with symptoms; the importance of treating partners and the high risk of repeated infection; the need to abstain from intercourse after completion of treatment for both partners for at least 7 days and while symptomatic; and the risk reduction strategies, including consistent condom use [16].

3. Chlamydia Trachomatis

3.1 Epidemiology

Chlamydia trachomatis (CT) is one of the most reported diseases; however, case reports likely underestimate the burden of disease because most infections are asymptomatic and are neither diagnosed nor reported. Case report data are strongly

influenced by screening activity, for these reasons, case report data are not reliable indicators of either population incidence or population prevalence [16]. In 2016 the estimated global prevalence of CT was 3.8% in women (95% UI: 3.3–4.5) and 2.7% in men (95% UI:1.9–3.7) in the group from 15 to 49-year-old [17]. A total of 1,758,668 cases of CT infection were reported in 2018 in the United States. Among females aged 15–24 years, the cases reported by chlamydia screening, increased 11.8% from 2014 to 2018; in men, the cases increased 37.8% from 2014 to 2018; this may reflect an increased number of men being tested and diagnosed due to increased availability of screening tests; this could also reflect increased transmission. Among sexually active women aged 16–24 years, CT screening has been increased [3].

3.2 The pathogen

CT is a gram-negative obligate intracellular bacterium; humans are its exclusive natural host. CT serovars include Agents of preventable blindness (serovars A–C), the most common bacterial sexually transmitted infections worldwide (serovars D–K), and lymphatic system infections (serovars L1–L3). Some distinctive features include its ability to avoid destruction by the host's innate and adaptive immune system. By autophagy, CT migrates to the upper genital tract and establishes a chronic infection. Without treatment, up to 50% of infected women continue to be infected for greater than 1 year [18, 19].

The life cycle of CT consists of 2 main phases, the elementary body (EB) and the reticulate body (RB). EBs are present in the semen from infected males and are also released from infected female genital tract epithelial cells. The EB represents the infectious extracellular form and the RB is the non-infectious replicative form; RBs can convert back to EBs as required. CT can enter the 3rd stage when it is exposed to certain stressors, like interferon-gamma, penicillin, or iron-depletion, the organism is metabolically active but does not divide and continues to increase in size [20].

3.3 The disease

In the pediatric population, CT is associated with several clinical conditions, these include conjunctivitis, nasopharyngitis, and pneumonia in young infants; and in the case of children and adolescents: genital tract infection, lymphogranuloma venereum, and trachoma.

Neonatal conjunctivitis is vertically transmitted, the neonate usually shows ocular congestion, edema, and discharge; these could last 1 to 2 weeks after birth. Pneumonia can be seen in young infants, normally occurs between 2 and 19 weeks after birth; could be afebrile and it is associated with hyperinflation of the lungs, nasal stuffiness, and otitis media; its presence could indicate immunosuppression.

Clinical manifestations in children and adolescents with genitourinary CT include vaginitis in prepubertal females and the post-pubertal females can present the Fitz-Hugh-Curtis syndrome (urethritis, cervicitis, endometritis, salpingitis, proctitis, and perihepatitis); also described for gonorrhea infections. In males, the most frequent manifestations are urethritis, epididymitis, and proctitis; also, Reiter syndrome can be seen (reactive arthritis, urethritis, and bilateral conjunctivitis) [20]. Lymphogranuloma venereum is another clinical manifestation of CT infection in adolescents; this is an invasion of the lymphatic nodes that generates an ulcerative lesion in the genital area plus inguinal or femoral or both lymphadenopathies, typically unilateral.

Young age is a strong predictor of CT infection, particularly prevalent in individuals younger than 25 years. CT infection is normally asymptomatic in both men and women (routine screening is essential for the detection); this situation increases the transmission between partners (rates are greater than 50%); also, it is important to highlight that transmission is more efficient from men to women. The incubation period ranges from 7 to 21 days after exposure. In the case of neonates, at least 60–70% acquire conjunctivitis when exposed to CT during passage through the birth canal [18]. The most common clinical presentations are described in **Figure 1**.

CT extra-genitourinary manifestations include rectal and oropharyngeal infections. Rectal infection is presented as proctitis; this can be acquired by sexual anal intercourse and due to autoinoculation in women. In the case of the oropharynx, the infection is usually asymptomatic, sometimes it can be presented as pharyngitis or cervical lymphadenopathy.

Finally, trachoma is a form of chronic keratoconjunctivitis, follicular with neovascularization of the cornea; blindness occurs in 1–15% of the affected population.

3.4 Diagnosis

Untreated CT infections can lead to complications like infertility (20%), life-threatening tubal pregnancy (9%), and debilitating chronic pain (18%). Currently, the best method for CT infection detection is the Nucleic acid amplification tests (NAATs). NAATs offer greatly expanded sensitivities of detection, usually well above 90%, while maintaining very high specificity, usually ≥99%. Currently, NAATs are the approved tests by international regulatory organisms for the detection of genital tract infections caused by CT in men and women with and without symptoms. Acceptable samples for NAATs are vaginal swabs in women and first catch urine from men. The performance of NAATs for overall sensitivity, specificity, and ease of specimen transport is better than that of any of the other tests available for the diagnosis of chlamydial infections NAATs are cost-effective in preventing sequelae due to CT [21].

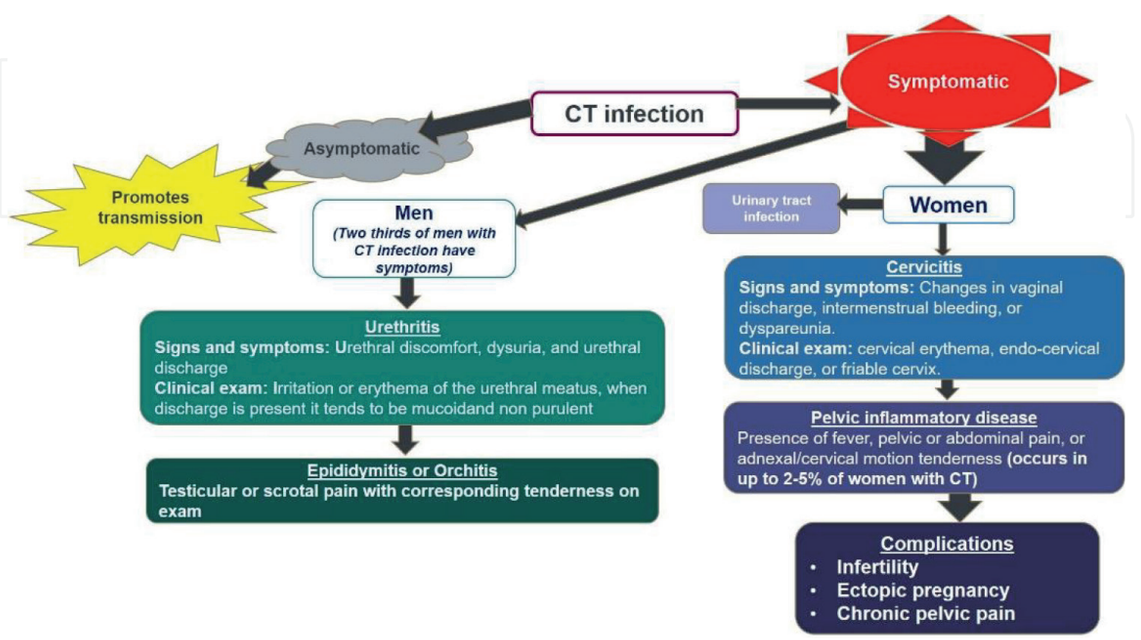

Figure 1.
Chlamydia trachomatis clinical manifestations and evolution.

3.4.1 Screening tests in the adolescent population

3.4.1.1 Genitourinary CT detection

As mentioned above, for female screening, samples from vaginal swabs are the preferred ones; these areas are sensitive as cervical swabs with similar specificity; for clinical and research settings it is also important to know that self-collected vaginal swabs are equivalent in sensitivity and specificity to those collected by health care personnel. Cervical samples could be done as part of pelvic examinations but not as routine tests; in general, cervical samples should be avoided; vaginal swabs should be preferred in all cases [21].

Currently, there are no specific recommendations for CT screening in heterosexual men. Recommendations are recommended only in specific settings such as sexually active heterosexual men in clinical settings with a high prevalence of C. trachomatis (i.e., sexually transmitted diseases clinics, adolescent clinics, detention and prisons, persons entering the armed forces. Etc).

3.5 Treatment

Treatment can be classified depending on the type of clinical manifestations that are frequently associated with the group of age. In infants with conjunctivitis or pneumonia, the treatment is oral erythromycin base or ethylsuccinate (50 mg/kg/day in 4 divided doses daily for 14 days) or with azithromycin (20 mg/kg, single daily dose for 3 days). When CT infection is detected in an infant, the mother and her sexual partner(s) must receive treatment. In the neonates, the presence of CT infection must alert the physician for also detecting Ng. Any infant younger than 6 weeks and treated with oral erythromycin or azithromycin must be monitored for any signs or symptoms of hypertrophic pyloric stenosis [20].

In adolescents with uncomplicated anogenital CT, the recommendation is doxycycline 100 mg, twice daily for 7 days; or azithromycin 1 g oral in a single dose. In affected children who weigh less than 45 kg the recommendation is oral erythromycin base or ethylsuccinate 50 mg/kg/day divided into 4 doses, daily for 14 days. For children younger than 8 years but weighing 45 kg or more, the recommendation is azithromycin 1 g orally in a single dose. In the case of 8 years and older children, the recommendation is azithromycin 1 g orally in a single dose; or doxycycline 100 mg orally 2 times a day for 7 days. Test of cure is not recommended; repeating the test 3 or 4 weeks after therapy to detect treatment failures can be done only if: adherence is in question, symptoms persist, or reinfection is suspected [17, 19, 20].

The treatment for lymphogranuloma venereum is with doxycycline 100 mg, orally twice daily for 21 days. Trachoma can be treated with oral azithromycin, a single dose of 20 mg/kg (maximum dose of 1 g) is recommended [20].

4. Genital herpes

4.1 Epidemiology

Genital herpes caused by HSV-2 and HSV-1 has been considered prevalent worldwide. The estimated global prevalence of these 2 pathogens is:

- HSV-2 among 15–49-year olds: 11.3% averaged across all ages [22]
- HSV-1 infection among 0–49-year-old: 67% averaged across all ages [23, 24]

A comparison between the most important epidemiological features is presented in **Figure 2**.

In several developed settings (e.g., the USA, Western Europe, Australia, and New Zealand) there is evidence that the proportion of first-episode genital herpes that is due to HSV-1 has increased, particularly among young people [25, 26]. Characteristics related to the first episode, latency site, viral shedding, and subsequent recurrence are presented in **Figure 3**.

Complications in HSV-2 are rare besides genital herpes; in HSV-1, the most common identified complications are sporadic encephalitis and ophthalmic disease in children and adults. HSV-2 rarely causes neonatal herpes, but these types of infections have a much more severe neurologic outcome. HSV-1 in the neonate, even rare can cause a devastating illness with high morbidity and mortality; when mothers shed genital HSV at delivery, HSV-1 may be more likely to be transmitted to the neonate [26].

4.2 The pathogen

Herpes simplex is a large DNA virus (150–200 nm) from the genus Simplex virus, subfamily Alphaherpesvirinae, and family Herpesviridae. It is a neurotropic virus with an envelope and depending on the protein coat, it can be named HSV-1 or HSV-2. HSV-2 shares>80% identity on the amino acid level with HSV-1. Both types can infect the oral or genital skin or mucosa and cause recurrent ulcerations.

	HSV-2	HSV-1
Age	Usually acquired through sexual contact; therefore, antibodies to virus are rarely found before ages of onset of sexual activity.	Occur during childhood and infection is never cleared
Most affected gender	Women	Women
Highly infectious	✓	✓
Primarily transmitted by	Almost entirely sexually transmitted, and is therefore most closely associated with genital herpes	Oral-oral contact (respiratory droplets or saliva, and most often by kissing) and causes orolabial herpes (notably "cold sores"). Potential to be transmitted through oral sex to cause genital infection
Worlwide highly prevalent and endemic	417 million ✓	3.7 billion ✓
Annual incidence (2012)	19 million ✓	118 million ✓

Figure 2.
Comparison between HSV-1 and HSV-2 in terms of age of onset, most affected gender, infectivity, transmission, prevalence, and incidence.

	HSV-2	HSV-1
First episode	Genital herpes, clinically indistinguishable	Oropharyngeal involvement occurs in the primary HSV-1 infection Primary infection is often more symptomatic and severe than reactivations Genital herpes, clinically indistinguishable
Latency site	Dorsosacral roots	Trigeminal Ganglia
Latency with reactivation periods	Normally benign, important feature of the infection.	
Viral shedding	Lifelong potential for symptomatic or asymptomatic viral shedding episodes	
Subsequent recurrences	**Severe and frequent**	**Milder and much less frequent.**

Figure 3.
Comparison between HSV-1 and HSV-2 based on the first episode, latency site, viral shedding, and subsequent recurrences.

The HSV genome consists of two covalently linked components, designated as L (long) and S (short). Each component is formed by unique sequences (UL and US, respectively) flanked by regions of repeated and inverted sequences that facilitate replication of the genome. The DNA molecular weight is estimated to be approximately 150 kbp, with a G + C content of 68% for HSV-1 and 69% for HSV-2. The viral composition is important for generating an immunogenic response, some of the most important proteins are in the capsid including VP5, VP19C, VP23, VP24, VP26, and the protein encoded by the UL6 gene. Another important component of the virion is the envelope, which consists of a lipid bilayer with approximately 11 viral glycoproteins, four of which (gB, gD, gH, and gL) are essential for virus entry into cells.

4.3 The disease

Once the virus replicates in the host, the intact virion is transported through a retrograde axonal flow to the sensory or autonomic ganglia, where the virus can remain in a latent form in the trigeminal ganglia for HSV-1 and the dorsosacral roots for HSV-2. Recurrences can occur when the latent virus is reactivated, being carried by anterograde axonal flow to the region of the primary infection. This reactivation is triggered by local stimuli (i.e., injury to the innervated tissue harboring latent HSV, systemic factors as physical or emotional stress, fever, exposure to ultraviolet light, menstruation, and hormonal imbalance).

Genital herpes is presented with one or more vesicles, or small blisters, on or around the genitals, rectum, or mouth. The average incubation period for an initial herpes infection is 4 days, ranging from 2 to 12 days after exposure. The vesicles then break leaving painful ulcers that may take 2–4 weeks to heal after the initial herpes infection; this is known as "outbreak" or genital herpes episode.

There are differences between the first and recurrent outbreaks. The first outbreaks have a longer duration of herpetic lesions, the viral shedding is increased (this makes HSV transmission more likely) and the patients experience more systemic symptoms like fever, body aches, swollen lymph nodes, or headache. In the case of the recurrent outbreaks, the duration is shorter and these episodes are less severe than the first outbreak; recurrent outbreaks are very common and normally have prodromal symptoms, either localized genital pain or tingling or shooting pains in the legs, hips, or buttocks, which occur hours to days before the eruption of herpetic lesions. The number of symptomatic recurrent outbreaks may decrease over time.

It is important to highlight that recurrences and subclinical shedding are much less frequent for genital HSV-1 infection than for genital HSV-2 infection.

Another important clinical manifestation in children and adolescents is HSV encephalitis, this can occur because of a primary or recurrent HSV-1 infection. The most common sign and symptoms include fever, alterations in the state of consciousness, personality changes, seizures, and other neurological symptoms. A form of self-limited aseptic meningitis has been associated with genital HSV-2 infection. HSV can cause other unusual central nervous system manifestations such as Bell's palsy, ascending and transverse myelitis, postinfectious encephalomyelitis, and recurrent meningitis.

4.4 Treatment

Currently, there is no treatment able to definitively cure genital herpes; some antiviral chemotherapy offers control and relief to the most symptomatic patients; also, recurrences can be reduced but not eradicated. For these patients, Acyclovir

can be used for initial episodes, in the case of recurrences, 45, 52 and 63% of patients remain free of recurrences in the first, second and third year of treatment. Valacyclovir is also used for the initial episode and as suppressive therapy, it has been considered as the gold standard therapy; after 6 months of using valacyclovir almost 55% of the patients remain without recurrences and 34% one year after.

For a first episode, oral acyclovir is recommended 400 mg three times a day for 7–10 days or acyclovir 200 mg five times a day for 7–10 days or valacyclovir 1 g orally twice a day for 7–10 days. For suppressive treatment, valacyclovir can be used 1 g once daily; or acyclovir 400 mg orally twice a day.

5. Vaccines for Gonorrhea, Chlamydia trachomatis and genital herpes

In the last 10 years, several efforts have been done for developing vaccines for these pathogens. The most important challenges are related to the immunological pathways (i.e., local mucosal immunity involved, the need of cellular immune responses plus neutralizing antibodies induction); currently, there is new hope for the development of efficacious vaccines for these targets; mRNA technology and the recently discovered effectiveness against gonorrhea using Men B vaccines are showing some light at the end of the road.

Conflict of interest

Diana Leticia Coronel Martínez is a employee of Sanofi Pasteur.

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