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CURRENTLY, ONE OF THE MOST RELEVANT DISEASES IS HERPES TRANSMISSION ROUTES, PATHOGENESIS AND PREVENTION

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Annotation:Herpes simplex is a viral infection caused by the herpes simplex virus. Infections are categorized based on the part of the body infected.Oral herpes involves the face or mouth. It may result in small blisters in groups often called cold sores or fever blisters or may just cause a sore throat.

Keywords:Herpes, liver, lungs, blood.

Genital herpes, often simply known as herpes, involves the genitalia. It may have minimal symptoms or form blisters that break open and result in small ulcers.[1] These typically heal over two to four weeks.[1] Tingling or shooting pains may occur before the blisters appear.[1] Herpes cycles between periods of active disease followed by periods without symptoms.[1] The first episode is often more severe and may be associated with fever, muscle pains, swollen lymph nodes and headaches.[1] Over time, episodes of active disease decrease in frequency and severity.[1]

Herpetic whitlow typically involves the fingers or thumb,[7] herpes simplex keratitis involves the eye,[8] herpesviral encephalitis involves the brain,[9] and neonatal herpes involves any part of the body of a newborn, among others.[10]

There are two types of herpes simplex virus, type 1 (HSV-1) and type 2 (HSV-2).[1] HSV-1 more commonly causes infections around the mouth while HSV-2 more commonly causes genital infections.[2] They are transmitted by direct contact with body fluids or lesions of an infected individual.[1] Transmission may still occur when symptoms are not present.[1] Genital herpes is classified as a sexually transmitted infection.[1] It may be spread to an infant during childbirth.[1] After infection, the viruses are transported along sensory nerves to the nerve cell bodies, where they reside lifelong.[2] Causes of recurrence may include: decreased immune function, stress, and sunlight exposure.[2][3] Oral and genital herpes is usually diagnosed based on the presenting symptoms.[2] The diagnosis may be confirmed by viral culture or detecting herpes DNA in fluid from blisters.[1] Testing the blood for antibodies against the virus can confirm a previous infection but will be negative in new infections.[1]

The most effective method of avoiding genital infections is by avoiding vaginal, oral, and anal sex.[1] Condom use decreases the risk.[1] Daily antiviral medication taken by someone who has the infection can also reduce spread.[1] There is no available vaccine[1] and once infected, there is no cure.[1] Paracetamol (acetaminophen) and topical lidocaine may be used to help with the symptoms.[2] Treatments with antiviral medication such as aciclovir or valaciclovir can lessen the severity of symptomatic episodes.[1][2]

Worldwide rates of either HSV-1 or HSV-2 are between 60% and 95% in adults.[4] HSV-1 is usually acquired during childhood.[1] Since there is no cure for either HSV-1 or HSV-2, rates of both inherently increase as people age.[4] Rates of HSV-1 are between 70% and 80% in populations of low socioeconomic status and 40% to 60% in populations of improved socioeconomic status.[4] An

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estimated 536 million people worldwide (16% of the population) were infected with HSV-2 as of 2003 with greater rates among women and those in the developing world.[11] Most people with HSV-2 do not realize that they are infected.[1]

HSV infection causes several distinct medical disorders. Common infection of the skin or mucosa may affect the face and mouth (orofacial herpes), genitalia (genital herpes), or hands (herpetic whitlow). More serious disorders occur when the virus infects and damages the eye (herpes keratitis), or invades the central nervous system, damaging the brain (herpes encephalitis). People with immature or suppressed immune systems, such as newborns, transplant recipients, or people with AIDS, are prone to severe complications from HSV infections. HSV infection has also been associated with cognitive deficits of bipolar disorder,[14] and Alzheimer's disease, although this is often dependent on the genetics of the infected person.

In all cases, HSV is never removed from the body by the immune system. Following a primary infection, the virus enters the nerves at the site of primary infection, migrates to the cell body of the neuron, and becomes latent in the ganglion.[15] As a result of primary infection, the body produces antibodies to the particular type of HSV involved, which can help reduce the odds of subsequent infection of that type at a different site. In HSV-1-infected individuals, seroconversion after an oral infection helps prevent additional HSV-1 infections such as whitlow, genital herpes, and herpes of the eye. Prior HSV-1 seroconversion seems to reduce the symptoms of a later HSV-2 infection, although HSV-2 can still be contracted.

Many people infected with HSV-2 display no physical symptoms—individuals with no symptoms are described as asymptomatic or as having subclinical herpes.[16] However, infection with herpes can be fatal.[17]

Other

Neonatal herpes simplex is an HSV infection in an infant. It is a rare but serious condition, usually caused by vertical transmission of HSV-1 or -2 from mother to newborn. During immunodeficiency, herpes simplex can cause unusual lesions in the skin. One of the most striking is the appearance of clean linear erosions in skin creases, with the appearance of a knife cut.[22] Herpetic sycosis is a recurrent or initial herpes simplex infection affecting primarily the hair follicles.[23]:369 Eczema herpeticum is an infection with herpesvirus in patients with chronic atopic dermatitis may result in spread of herpes simplex throughout the eczematous areas.[23]:373

Herpetic keratoconjunctivitis, a primary infection, typically presents as swelling of the conjunctiva and eyelids (blepharoconjunctivitis), accompanied by small white itchy lesions on the surface of the cornea.

Herpetic sycosis is a recurrent or initial herpes simplex infection affecting primarily the hair follicle.[23]:369[24]

Bell's palsy

Although the exact cause of Bell's palsy—a type of facial paralysis—is unknown, it may be related to the reactivation of HSV-1.[25] This theory has been contested, however, since HSV is detected in large numbers of individuals having never experienced facial paralysis, and higher levels of antibodies for HSV are not found in HSV-infected individuals with Bell's palsy compared to those without.[26] Antivirals may improve the condition slightly when used together with corticosteroids in those with severe disease.[27]

Alzheimer's disease

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HSV-1 has been proposed as a possible cause of Alzheimer's disease.[28][29] In the presence of a certain gene variation (APOE-epsilon4 allele carriers), HSV-1 appears to be particularly damaging to the nervous system and increases one's risk of developing Alzheimer's disease. The virus interacts with the components and receptors of lipoproteins, which may lead to its development.[30][31]

Pathophysiology

Herpes shedding[32]	
HSV-2 genital	15–25% of days
HSV-1 oral	6–33% of days
HSV-1 genital	5% of days
HSV-2 oral	1% of days

Herpes is contracted through direct contact with an active lesion or body fluid of an infected person.[33] Herpes transmission occurs between discordant partners; a person with a history of infection (HSV seropositive) can pass the virus to an HSV seronegative person. Herpes simplex virus 2 is typically contracted through direct skin-to-skin contact with an infected individual, but can also be contracted by exposure to infected saliva, semen, vaginal fluid, or the fluid from herpetic blisters.[34] To infect a new individual, HSV travels through tiny breaks in the skin or mucous membranes in the mouth or genital areas. Even microscopic abrasions on mucous membranes are sufficient to allow viral entry.

HSV asymptomatic shedding occurs at some time in most individuals infected with herpes. It can occur more than a week before or after a symptomatic recurrence in 50% of cases.[35] Virus enters into susceptible cells by entry receptors[36] such as nectin-1, HVEM and 3-O sulfated heparan sulfate.[37] Infected people who show no visible symptoms may still shed and transmit viruses through their skin; asymptomatic shedding may represent the most common form of HSV-2 transmission.[35] Asymptomatic shedding is more frequent within the first 12 months of acquiring HSV. Concurrent infection with HIV increases the frequency and duration of asymptomatic shedding.[38] Some individuals may have much lower patterns of shedding, but evidence supporting this is not fully verified; no significant differences are seen in the frequency of asymptomatic shedding when comparing persons with one to 12 annual recurrences to those with no recurrences.[35]

Antibodies that develop following an initial infection with a type of HSV can reduce the odds of reinfection with the same virus type.[39] In a monogamous couple, a seronegative female runs a greater than 30% per year risk of contracting an HSV infection from a seropositive male partner.[40] If an oral HSV-1 infection is contracted first, seroconversion will have occurred after 6 weeks to provide protective antibodies against a future genital HSV-1 infection.[39] Herpes simplex is a double-stranded DNA virus.[41]

Examination

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Primary orofacial herpes is readily identified by examination of persons with no previous history of lesions and contact with an individual with known HSV infection. The appearance and distribution of sores is typically presents as multiple, round, superficial oral ulcers, accompanied by acute gingivitis.[42] Adults with atypical presentation are more difficult to diagnose. Prodromal symptoms that occur before the appearance of herpetic lesions help differentiate HSV symptoms from the similar symptoms of other disorders, such as allergic stomatitis. When lesions do not appear inside the mouth, primary orofacial herpes is sometimes mistaken for impetigo, a bacterial infection. Common mouth ulcers (aphthous ulcer) also resemble intraoral herpes, but do not present a vesicular stage.[42]

Genital herpes can be more difficult to diagnose than oral herpes, since most people have none of the classical symptoms.[42] Further confusing diagnosis, several other conditions resemble genital herpes, including fungal infection, lichen planus, atopic dermatitis, and urethritis.[42]

Laboratory testing

Laboratory testing is often used to confirm a diagnosis of genital herpes. Laboratory tests include culture of the virus, direct fluorescent antibody (DFA) studies to detect virus, skin biopsy, and polymerase chain reaction to test for presence of viral DNA. Although these procedures produce highly sensitive and specific diagnoses, their high costs and time constraints discourage their regular use in clinical practice.[42]

Until the 1980s serological tests for antibodies to HSV were rarely useful to diagnosis and not routinely used in clinical practice.[42] The older IgM serologic assay could not differentiate between antibodies generated in response to HSV-1 or HSV-2 infection. However, a glycoprotein G-specific (IgG) HSV test introduced in the 1980s is more than 98% specific at discriminating HSV-1 from HSV-2.[43]

Differential diagnosis

It should not be confused with conditions caused by other viruses in the *herpesviridae* family such as herpes zoster, which is caused by varicella zoster virus. The differential diagnosis includes hand, foot and mouth disease due to similar lesions on the skin. Lymphangioma circumscriptum and dermatitis herpetiformis may also have a similar appearance.

As with almost all sexually transmitted infections, women are more susceptible to acquiring genital HSV-2 than men.[44] On an annual basis, without the use of antivirals or condoms, the transmission risk of HSV-2 from infected male to female is about 8–11%.[40][45] This is believed to be due to the increased exposure of mucosal tissue to potential infection sites. Transmission risk from infected female to male is around 4–5% annually.[45] Suppressive antiviral therapy reduces these risks by 50%.[46] Antivirals also help prevent the development of symptomatic HSV in infection scenarios, meaning the infected partner will be seropositive but symptom-free by about 50%. Condom use also reduces the transmission risk significantly.[47][48] Condom use is much more effective at preventing male-to-female transmission than *vice versa*.[47] Previous HSV-1 infection may reduce the risk for acquisition of HSV-2 infection among women by a factor of three, although the one study that states this has a small sample size of 14 transmissions out of 214 couples.[49]

However, asymptomatic carriers of the HSV-2 virus are still contagious. In many infections, the first symptom people will have of their own infections is the horizontal transmission to a sexual partner or the vertical transmission of neonatal herpes to a newborn at term. Since most asymptomatic individuals are unaware of their infection, they are considered at high risk for spreading HSV.[50]

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In October 2011, the anti-HIV drug tenofovir, when used topically in a microbicidal vaginal gel, was reported to reduce herpes virus sexual transmission by 51%.[51]

Barrier methods

Condoms offer moderate protection against HSV-2 in both men and women, with consistent condom users having a 30%-lower risk of HSV-2 acquisition compared with those who never use condoms.[52] A female condom can provide greater protection than the male condom, as it covers the labia.[53] The virus cannot pass through a synthetic condom, but a male condom's effectiveness is limited[54] because herpes ulcers may appear on areas not covered by it. Neither type of condom prevents contact with the scrotum, anus, buttocks, or upper thighs, areas that may come in contact with ulcers or genital secretions during sexual activity. Protection against herpes simplex depends on the site of the ulcer; therefore, if ulcers appear on areas not covered by condoms, abstaining from sexual activity until the ulcers are fully healed is one way to limit risk of transmission.[55] The risk is not eliminated, however, as viral shedding capable of transmitting infection may still occur while the infected partner is asymptomatic.[56] The use of condoms or dental dams also limits the transmission of herpes from the genitals of one partner to the mouth of the other (or *vice versa*) during oral sex. When one partner has a herpes simplex infection and the other does not, the use of antiviral medication, such as valaciclovir, in conjunction with a condom, further decreases the chances of transmission to the uninfected partner.[15] Topical microbicides that contain chemicals that directly inactivate the virus and block viral entry are being investigated.[15]

Antivirals, Antivirals may reduce asymptomatic shedding; asymptomatic genital HSV-2 viral shedding is believed to occur on 20% of days per year in patients not undergoing antiviral treatment, versus 10% of days while on antiviral therapy.[35]

Pregnancy, The risk of transmission from mother to baby is highest if the mother becomes infected around the time of delivery (30% to 60%),[57][58] since insufficient time will have occurred for the generation and transfer of protective maternal antibodies before the birth of the child. In contrast, the risk falls to 3% if the infection is recurrent,[59] and is 1–3% if the woman is seropositive for both HSV-1 and HSV-2,[59][60] and is less than 1% if no lesions are visible.[59] Women seropositive for only one type of HSV are only half as likely to transmit HSV as infected seronegative mothers. To prevent neonatal infections, seronegative women are recommended to avoid unprotected oral-genital contact with an HSV-1-seropositive partner and conventional sex with a partner having a genital infection during the last trimester of pregnancy. Mothers infected with HSV are advised to avoid procedures that would cause trauma to the infant during birth (e.g. fetal scalp electrodes, forceps, and vacuum extractors) and, should lesions be present, to elect caesarean section to reduce exposure of the child to infected secretions in the birth canal.[15] The use of antiviral treatments, such as aciclovir, given from the 36th week of pregnancy, limits HSV recurrence and shedding during childbirth, thereby reducing the need for caesarean section.[15]

Aciclovir is the recommended antiviral for herpes suppressive therapy during the last months of pregnancy. The use of valaciclovir and famciclovir, while potentially improving compliance, have less-well-determined safety in pregnancy.

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