

HERPES SIMPLEX

ICD-9 054; ICD-10 B00

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ANOGENITAL HERPESVIRAL INFECTIONS

ICD-10 A60

(Alphaherpesviral disease, Herpesvirus hominis, Human herpesviruses 1 and 2)

1. Identification—Herpes simplex is a viral infection characterized by systemic and local symptoms, latency, and a tendency to localized recurrence. The two causal agents—herpes simplex virus (HSV) types 1 and 2—generally produce distinct clinical syndromes, depending on the portal of entry. Either may infect the genital tract or oral mucosa.

Primary infection with HSV-1 may be mild and inapparent and occur in early childhood. In approximately 10% of primary infections, overt disease may appear as an illness of varying severity, marked by fever and malaise lasting a week or more; it may be associated with gingivostomatitis accompanied by vesicular lesions in the oropharynx, severe keratoconjunctivitis, a generalized cutaneous eruption complicating chronic eczema, meningoencephalitis, or some of the fatal generalized infections in newborn infants (congenital herpes simplex, ICD-9 771.2, ICD-10 P35.2).

HSV-1 causes about 2% of acute pharyngotonsillitis, usually as a primary infection.

Reactivation of latent infection commonly results in herpes labialis (fever blisters, cold sores), manifested usually on the face or lips, by superficial clear vesicles on an erythematous base that crust and heal within days. Reactivation is precipitated by various forms of trauma, fever, physiological changes or intercurrent disease, and may also involve other body tissues; it occurs in the presence of circulating antibodies, which are seldom elevated by reactivation. Severe and extensive spread of infection may occur in those who are immunodeficient or immunosuppressed. The onset of reactivation is heralded by tingling prior to the onset of vesicles; if patients learn this sign, they can prevent or shorten the clinical course of the reactivated infection through the use of antivirals.

CNS involvement may appear in association with either primary infection or recrudescence. HSV-1 is a cause of meningoencephalitis. Fever, headache, leukocytosis, meningeal irritation, drowsiness, confusion, stupor, coma and focal neurological signs may occur, and are frequently referable to one or the other temporal region. The condition may be confused with other intracranial lesions, including brain abscess and tuberculous meningitis. Because antiviral therapy may reduce case fatality, diagnostic PCR (polymerase chain reaction) for DNA of herpes virus in the CSF or biopsy of cerebral tissue should be considered early in clinically suspected cases.

Genital herpes occurs mainly in adults and is sexually transmitted. It is usually caused by HSV-2, but HSV-1 is becoming increasingly common as a cause of first episode genital herpes in some populations. Primary and recurrent infections occur, with or without symptoms of varying degree. Symptomatic primary infections often include systemic symptoms such as fever and malaise and are classically characterized by bilateral vesiculopustular or ulcerative lesions on the external genitalia in both men and women. In women, the principal sites of primary disease are the cervix and the vulva; recurrent disease generally involves the vulva, perineal skin, legs and buttocks. In men, lesions appear on the glans penis, prepuce, or penile shaft, and in the anus and rectum of those engaging in anal sex. Primary lesions may last 2-3 weeks. Recurrent disease is usually unilateral, and has a much smaller area of involvement and shorter duration than that of primary infection. Many HSV-2-infected persons do not have recognized symptoms of genital herpes, but still shed virus intermittently in the genital tract. Clinical manifestations of genital herpes may be more severe in immunocompromised persons. HSV-2 has been associated with aseptic meningitis, myelitis and radiculitis rather than meningoencephalitis. Persons with HSV-2 infection are at increased risk for acquiring HIV infection.

Neonatal infections can be divided into 3 clinical presentations: disseminated infections involving multiple organs such as the liver; encephalitides; and infections limited to the skin, eyes or mouth. The first two forms are often lethal. Infections are most frequently due to HSV-2, but HSV-1 is also common. The risk of transmission to the neonate from an infected mother depends mainly on two important maternal factors: stage of pregnancy at which the mother sheds HSV, and whether the infection is primary or recurrent. Only HSV shedding at the time of delivery is dangerous to the newborn, with the rare exception of intrauterine infections. The risk for transmission is high (30-50%) among women who acquire primary infection in late pregnancy and is low (<1%) among women with histories of recurrent herpes at term or who acquire genital HSV infection during the first half of pregnancy, in part because maternal immunity confers a degree of protection.

Diagnosis of HSV infection can be confirmed by viral isolation, HSV DNA detection by PCR, or HSV antigen detection by enzyme immunoassay (EIA) or direct immunofluorescence (IFA). All of these methods can be used on samples from oral or genital lesions. Viral culture isolates can be typed to determine whether HSV-1 or HSV-2 is the cause of infection. HSV DNA PCR on spinal fluid has become the test of choice for diagnosing CNS infection. Brain biopsy may be considered in some cases of the latter. Cytologic detection of cellular changes (e.g. Tzanck preparation) is insensitive and nonspecific for diagnosis and should not be relied upon. Accurate type-specific HSV serologic tests based on glycoprotein G are now available and can reliably distinguish HSV-1 and HSV-2 antibodies. Antibodies to HSV may take several weeks to develop after initial infection but then persist indefinitely; false negative serologic results may occur at early stages of infection. Herpes IgM antibody tests are not reliable in determining primary infection.

2. Infectious agent—Herpes simplex virus in the virus family Herpesviridae, subfamily Alphaherpesvirinae. HSV types 1 and 2 can be differentiated immunologically (especially when highly specific or monoclonal antibodies are used), and differ with respect to their growth patterns in cell culture, embryonated eggs and experimental animals.

3. Occurrence—Worldwide; 50%–90% of adults possess circulating antibodies against HSV-1; initial infection with HSV-1 usually occurs before the fifth year of life, but more primary infections in adults are now being reported. HSV-2 infection usually begins with sexual activity and is rare before adolescence, except in sexually abused children. HSV-2 antibody occurs in approximately 20% of American adults. Seroprevalence increases with age and is higher among females, certain racial/ethnic groups, and persons with multiple sexual partners. The majority (up to 90%) of persons infected with HSV-2 have not been diagnosed with genital herpes.

4. Reservoir—Humans.

5. Mode of transmission—Contact with HSV-1 in the saliva of carriers is probably the most important mode of spread. Infection on the hands of health care personnel (e.g. dentists) from patients shedding HSV may result in herpetic whitlow. Transmission of HSV-2 is usually by sexual contact. Both types 1 and 2 may be transmitted to various sites by oral-genital, oral-anal or anal-genital contact. Transmission to the neonate usually occurs via the infected birth canal, less commonly *in utero* or postpartum.

6. Incubation period—From 2–12 days.

7. Period of communicability—HSV can be isolated for a median of about 2 weeks by culture and may continue for up to 7 weeks after primary stomatitis or primary genital lesions. Both primary and recurrent infections may be asymptomatic. After either, HSV may be shed intermittently from mucosal sites for years and possibly lifelong, in the presence or absence of clinical manifestations. Transmission of HSV can occur during asymptomatic periods. In recurrent lesions, infectivity is shorter than after primary infection, and the average duration of viral shedding from the onset of lesions is about 4 days.

8. Susceptibility—Humans are probably universally susceptible.

9. Methods of control—

A. Preventive measures:

- 1) Health education and personal hygiene directed toward minimizing the transfer of infectious material.
- 2) Avoid contaminating the skin of eczematous patients with infectious material.
- 3) Health care personnel should wear gloves when in direct contact with potentially infectious lesions.
- 4) When primary genital herpes infections occur in late pregnancy, caesarean section is often advised before the membranes rupture because of the risk of fatal neonatal infection (30%–50%). However, some specialists recommend use of antiviral medications instead of or in addition to caesarean section in this situation. The risk of neonatal infection from women with a history of recurrent genital herpes infection is much lower (<1%), and caesarean section is

advisable only when active lesions or prodromal symptoms are present at delivery. Suppressive antiviral therapy starting at 36 weeks gestation can reduce the need for caesarean delivery among women with active recurrent genital herpes.

5) Persons with genital herpes should avoid sexual activity with uninfected partners when lesions or prodromal symptoms are present. Daily use of valacyclovir by persons with genital herpes can decrease the risk of HSV-2 sexual transmission to an uninfected partner. Correct and consistent use of latex condoms in sexual practice may decrease the risk of infection.

B. Control of patient, contacts and the immediate environment:

1) Report to local health authority: Official case report in adults not ordinarily justifiable, Class 5; neonatal infections reportable in some areas, Class 3 (see *Reporting*).

2) Isolation: Contact isolation for neonatal and disseminated or primary severe lesions; for recurrent lesions, drainage and secretion precautions. Patients with herpetic lesions should have no contact with newborns, children with eczema or burns, or immunodeficient patients.

3) Concurrent disinfection: Not applicable.

4) Quarantine: Not applicable.

5) Immunization of contacts: Not applicable. Vaccine trials are ongoing.

6) Investigation of contacts and source of infection: Seldom of practical value.

7) Specific treatment: The acute manifestations of herpetic keratitis and early dendritic ulcers may be treated with trifluridine, vidarabine, acyclovir or ganciclovir as an ophthalmic ointment or solution. Corticosteroids for ocular involvement should only be administered by an experienced ophthalmologist. Acyclovir used orally or intravenously has been shown to reduce shedding of virus, diminish pain, and accelerate healing time in primary and recurrent genital herpes, rectal herpes, stomatitis, and herpetic whitlow. Valacyclovir and famciclovir are more recently licensed congeners of acyclovir that are also efficacious. Oral preparations of these three antiviral drugs are most convenient to use and can provide benefit even with extensive anogenital infection. Prophylactic daily administration of these drugs (suppressive therapy) can reduce the frequency of both clinical and sub-clinical HSV recurrences in adults. Strains of herpes virus resistant to antivirals have been reported, though these are uncommon in infections of immunocompetent persons. Intravenous acyclovir should be provided for patients with severe HSV disease, disseminated infection, or CNS complications (e.g., meningitis or encephalitis). Neonatal infections should be treated with high-dose intravenous acyclovir. Topical creams are not effective in genital herpes.

C. Epidemic measures: Not applicable.

D. Disaster implications: None.

E. International measures: None.

MENINGOENCEPHALITIS DUE TO CERCOPITHECINE HERPES VIRUS 1

ICD-9 054.3; ICD-10 B00.4

(B-virus, Simian B disease)

B-virus infection is a CNS disease caused by cercopithecine herpesvirus 1, a zoonotic virus closely related to HSV. B-virus infections in humans are rare and cause an ascending encephalomyelitis seen in veterinarians, laboratory workers and others in close contact with macaque monkeys or their secretions or tissues. After an incubation of three days to three weeks, there is acute febrile onset with headache, often local vesicular lesions, lymphocytic pleocytosis, and variable neurological patterns, ending in death in an estimated 80% of untreated cases, one day to three weeks after onset of symptoms. Occasional recoveries have been associated with considerable residual disability; a few cases, treated with acyclovir, have recovered completely. The virus causes a natural infection of macaque monkeys analogous to HSV infection in humans; 30%–80% of rhesus monkeys (*Macaca mulatta*) are seropositive. On a given day, ~2% of seropositive rhesus monkeys shed B virus, but shedding increases during periods of stress (e.g. shipping and handling). The ocular, oral, and genital secretions, CNS tissues and CSF, and cell cultures from macaque monkeys are potentially infectious. Human illness, rare but highly fatal, has been acquired through monkey bites and scratches or exposure of naked skin or mucous membrane to infected saliva or monkey cell cultures, exposure to tissue culture or autopsy material, needlestick injuries, cage scratches and, in one case, mucosal splash. Prevention depends on proper use of protective gauntlets, eyewear and masks, and care taken to minimize exposure to monkeys. All bite or scratch wounds or other exposure to potentially infectious material from macaques or from cages possibly contaminated with macaque secretions and that result in bleeding must be immediately and thoroughly scrubbed and cleaned for at least 15 minutes. Eyes and mucous membranes should be flushed with sterile saline or water. Skin should be washed preferably with a solution containing detergent soap (e.g., chlorhexidine or povidone-iodine). Prophylactic treatment with an antiviral agent such as valacyclovir, acyclovir or famciclovir is recommended when an animal handler sustains a deep, penetrating wound, a wound that was not adequately cleaned, a laceration of the head, neck or torso, an exposure from a high-risk source (e.g. a macaque that is ill or objects contaminated with fluids likely to contain B virus), or when a post-cleansing culture is positive for B virus. Prophylaxis should be considered for other exposures involving a mucosal splash or skin laceration or puncture. It is not recommended for skin exposures in which the skin remains intact or exposures from non-macaque species. The B-virus status of the monkey should be determined to evaluate the risk. The appearance of any skin lesions or neurological symptoms, such as itching, pain, or numbness near the site of the wound, calls for expert medical consultation for diagnosis and possible treatment. In addition, because B virus infection has occurred in macaque handlers who did not recall obvious exposures, such workers should report episodes of fever >48 hours or symptoms compatible with B virus infection to appropriate health care personnel.