

HERPES SIMPLEX VIRUS

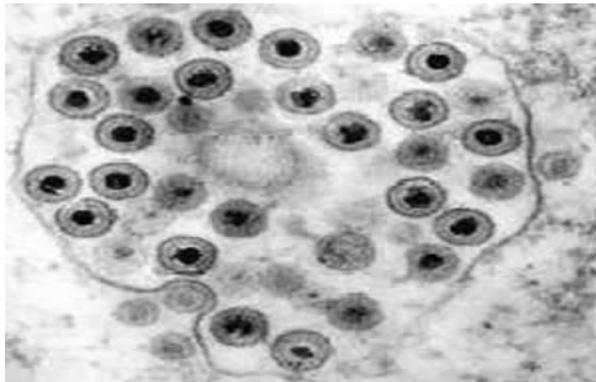
PATHOGEN SAFETY DATA SHEET - INFECTIOUS SUBSTANCES

INFECTIOUS AGENT

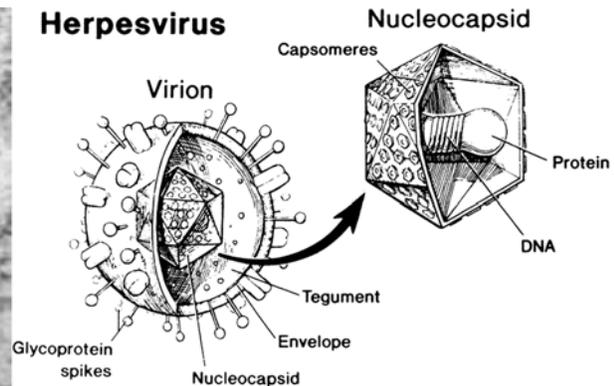
NAME: *Herpes simplex virus*

SYNONYM OR CROSS REFERENCE: HSV-1, HSV-2, HHV-1, HHV-2, *Human herpes virus 1*, *Human herpes virus 2*, cold sores, fever blisters.

CHARACTERISTICS: HSV virus, types 1 and 2, belong to the sub family *Alphaherpesviridae* in the family *Herpesviridae*, genus *Simplexvirus*. They are 120-300 nm in diameter and consist of a linear, double stranded DNA genome enclosed within an icosahedral capsid, surrounded by a phospholipid rich envelope. The lipid envelope is derived from the nuclear envelope of the infected cell.



Herpes simplex virus. Thin section of virions as they leave the nucleus of an infected cell. Magnification approximately x40,000¹⁾



Schematic drawing of an infectious virus particle (virion) of *Herpes simplex virus* type 1²⁾

HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: Although both HSV-1 and HSV-2 may infect any area, HSV-1 is associated mainly with "above the waist" infections involving the mouth, pharynx, face, eye, and central nervous system (CNS), whereas, HSV-2 is associated mainly with "below the waist" infections of the genital region.

Herpes labialis/cold sores: Caused mainly by HSV-1, there have been reported cases caused by HSV-2. Primary infections with HSV-1 are acquired usually in childhood and may be asymptomatic or subclinical. Symptomatic primary infections present mainly as gingivostomatitis (an inflammation of the oral mucosa and gums), with fever, sore throat, fetor oris, anorexia, cervical adenopathy, and mucosal edema and vesicular and ulcerative painful lesions involving the buccal mucosa, tongue, gums, and pharynx. Ulcers heal without scarring within 2-3 weeks. Recurrent infections have generally milder symptoms and clinical course. Recurrent lesions due to HSV-1 occur mainly on a specific area of the lip, and are called "cold sores" or "fever blisters". The lesions heal in approximately 8-10 days.

Herpetic whitlow: Characterized by formation of painful vesicular lesions on the nail or finger area.

Infections of the eye: Characteristic dendritic ulceration occurs on conjunctiva, and cornea. HSV infection may also cause other ocular diseases.

Encephalitis: Serious infections of the CNS, affecting both children and adolescents. It may occur due to primary or latent infection with HSV-1 virus. HSV encephalitis affects one temporal lobe, leading to focal neurologic signs and edema. The disease can be fatal (mortality rate of 70%), if left untreated.

Genital herpes: It is a sexually transmitted disease. Genital herpes is caused mainly by HSV-2, although HSV-1 has become as common as HSV-2 in primary genital infections in developed countries. Primary genital herpes is characterized by formation of multiple, bilateral, painful, and extensive genital ulcers, which heal without scarring within 12 days. Patients also present with tender enlarged lymph nodes, fever, malaise, and myalgia. Rarely, the disease may also cause aseptic meningitis with neck rigidity and severe headache. Recurrent genital herpes disease is of shorter duration, is milder and does not have systemic symptoms. The main manifestation of the disease is prodromal paresthesias in the perineum, genitalia or buttocks, followed by formation of grouped lesions on the external genital area. The lesions heal without scarring in 2-5 days.

Neonatal Herpes: Neonatal herpes is an extremely severe disease with a very high mortality rate. Neurological complications may occur in infants who survive the infection. Clinical manifestations of the disease are variable and can be classified into three groups: disseminated disease, involving multiple visceral organs, such as lung, liver, adrenal glands, skin, eye, and the brain (25%); CNS disease with listlessness and seizures (~ 30% of total cases; including 60 to 75% of those cases displaying disseminated disease); and disease limited to the skin, eyes, and/or mouth (SEM) (45%).

EPIDEMIOLOGY: Worldwide. HSV infections occur worldwide without any specific seasonal distribution. The prevalence of HSV-1 infection is greater than HSV-2 infection in most geographic areas. HSV-1 causes mainly oral infections in children and has a seroprevalence in adults of 70% in developed countries and 100% in developing countries. Orolabial herpes has an infection rate of approximately 33% in developing countries and 20% in developed countries. Genital herpes, caused mainly by HSV-2, is the main cause of genital ulcers worldwide. Neonatal herpes is an uncommon but serious complication of genital herpes with occurrence rates ranging from 1/3,000 to 1/20,000 live births, resulting in an estimated incidence of 1,500 new cases of neonatal HSV infection annually in the United States. Corneal diseases due to HSV infection are an important cause of blindness, and account for an estimated 500,000 cases annually in the United States. *Herpes simplex* encephalitis (HSE), caused by HSV infection, is one of the most severe CNS infections, accounting for approximately 10–20% of all encephalitic viral infections of the CNS, in the United States.

HOST RANGE: Humans, but non-human primates in captivity can be accidentally infected. Rabbits and rodents can be infected experimentally.

INFECTIOUS DOSE: Unknown

MODE OF TRANSMISSION: Direct contact with infected secretions or mucous membranes/skin with lesions from an asymptomatic or symptomatic patients shedding the virus, is the main mode of transmission of HSV. Transmission of HSV-1 can also occur by respiratory droplets. Genital herpes is transmitted sexually. Neonatal herpes can be acquired at different times: intrauterine (*in utero*) in 5% of the cases, peripartum (perinatal) in 85% of the cases, and postpartum (postnatal) in 10% of the cases.

INCUBATION PERIOD: Incubation period generally ranges from 1-26 days. Incubation period for orolabial HSV infection is 2 to 12 days, with an average of 4 days. Genital herpes is acquired within 5 days. Oral and genital lesions appear approximately 19 and 24 days following transplantation organ of an infected organ.

COMMUNICABILITY: HSV viruses are passed through close personal contact and mainly oral-genital or genital-genital contact. Vertical transmission can also occur in symptomatic and asymptomatic women. Transfer may be *in utero*, intrapartum, or postnatal.

DISSEMINATION

RESERVOIR: Humans

ZOONOSIS: None

VECTOR: None

STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Antiviral drugs like acyclovir, foscarnet, valacyclovir, famciclovir, and penciclovir can inhibit viral replication. Foscarnet is used for acyclovir-resistant HSV cases.

DRUG RESISTANCE: Acyclovir resistant strains have been isolated from immunocompromised patients, particularly acquired immunodeficiency syndrome (AIDS) patients with persistent/recurrent lesions.

SUSCEPTIBILITY TO DISINFECTANTS: HSV virus is easily inactivated by lipid solvents. It can be inactivated by 0.5% Lysol in 5 min; by Listerine (1:1 mixtures) in 5 min; by 2,000 ppm (2,000 µl/liter) of bleach in 10 min; by rubbing alcohol (1:1 mixtures). HSV is also susceptible to quaternary ammonium compounds. Most herpes viruses are also susceptible to 30% ethanol and isopropanol, 0.12% orthophenyl phenol, and 0.04% glutaraldehyde.

PHYSICAL INACTIVATION: HSV virus is easily inactivated by exposure to pH <4, temperatures >56°C for 30 min, pasteurization (60°C for 10 h), and microwave heating for 4 min. HSV-2 is more thermolabile than HSV-1.

SURVIVAL OUTSIDE HOST: HSV virus survives for short periods of time outside the host. It can survive on dry inanimate surfaces (survival ranges from few hours to 8 weeks). They survive longer at lower humidity.

FIRST AID / MEDICAL

SURVEILLANCE: Monitor for symptoms, including lesions in or around the oral cavity. Viral culture or PCR is used to detect presence of viral infection. Culture in cells can show multinucleated giant cells, desquamated epithelial cells with intranuclear inclusions. Direct examination of virus in clinical samples can also be done using fluorescent antibody test to detect viral antigens present within a tissue or smear specimen, Tzanck test, Enzyme immunoassay (EIA). Polymerase chain reaction (PCR) can be used to detect viral deoxyribonucleic acid (DNA) in cerebrospinal fluid in the case of encephalitis or in blood in cases of neonatal HSV infection.

FIRST AID/TREATMENT:

Genital herpes: Treated with antiviral drugs such as acyclovir, valacyclovir, famciclovir, and penciclovir. Valacyclovir, famciclovir are approved for chronic suppression of genital herpes.

Herpes labialis: Primary infection in children is treated with oral acyclovir. N-docosanol, a non-prescription topical medication, or topical acyclovir reduces time to healing and duration of pain by approximately half a day. Oral acyclovir and valacyclovir can be used for recurrent infections.

Herpes simplex encephalitis: Treated with Acyclovir.

Neonatal HSV infection: Treated with intravenous acyclovir for 21 days for disseminated infection or CNS infection, and 14 days for SEM infection.

Eye infections associated with HSV infection can be treated either with topical trifluridine, idoxuridine, and vidarabine; or with oral acyclovir, valacyclovir, famciclovir.

IMMUNIZATION: None

PROPHYLAXIS: Acyclovir can be used as a prophylactic drug to prevent reactivation of *Herpes labialis* after exposure to ultraviolet radiation, facial surgery, or exposure to sun and wind during skiing. Prophylaxis with oral acyclovir is recommended to suppress genital HSV recurrences near the end of pregnancy. Suppressive therapy with Valcyclovir may be used to prevent frequent recurrences of genital herpes.

LABORATORY HAZARD

LABORATORY-ACQUIRED INFECTIONS: No infections reported.

SOURCE/SPECIMENS: Virus is shed from saliva, cervix, and urethra.

PRIMARY HAZARDS: Direct contact with clinical material or viral isolates, inhalation of concentrated aerosolized materials, droplet exposure of mucous membranes of the eyes, nose, or mouth, ingestion, accidental parenteral inoculation are the primary hazards associated with herpes viruses including HSV 1 and 2.

SPECIAL HAZARDS: None

EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 2.

CONTAINMENT REQUIREMENTS: Containment Level 2 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials, animals, or cultures.

PROTECTIVE CLOTHING: Lab coat. Gloves when direct skin contact with infected materials or animals is unavoidable. Eye protection must be used where there is a known or potential risk of exposure to splashes.

OTHER PRECAUTIONS: All procedures that may produce aerosols, or involve high concentrations or large volumes should be conducted in a biological safety cabinet (BSC). The use of needles, syringes, and other sharp objects should be strictly limited. Additional precautions should be considered with work involving animals or large scale activities.

HANDLING AND STORAGE

SPILLS: Allow aerosols to settle and, wearing protective clothing, gently cover spill with paper towels and apply an appropriate disinfectant, starting at the perimeter and working towards the centre. Allow sufficient contact time before clean up.

DISPOSAL: Decontaminate all wastes that contain or have come in contact with the infectious organism before disposing by autoclave, chemical disinfection, gamma irradiation, or incineration.

STORAGE: The infectious agent should be stored in leak-proof containers that are appropriately labeled.

REFERENCE

Pathogen Safety Data Sheet (PSDS) for *Herpes simplex* virus has been modified from the ones produced by the Public Health Agency of Canada as educational and informational resources for laboratory personnel working with infectious substances.

- 1) Picture: Micrograph from F. A. Murphy, University of Texas Medical Branch, Galveston, Texas.
- 2) Picture: www.oculist.net