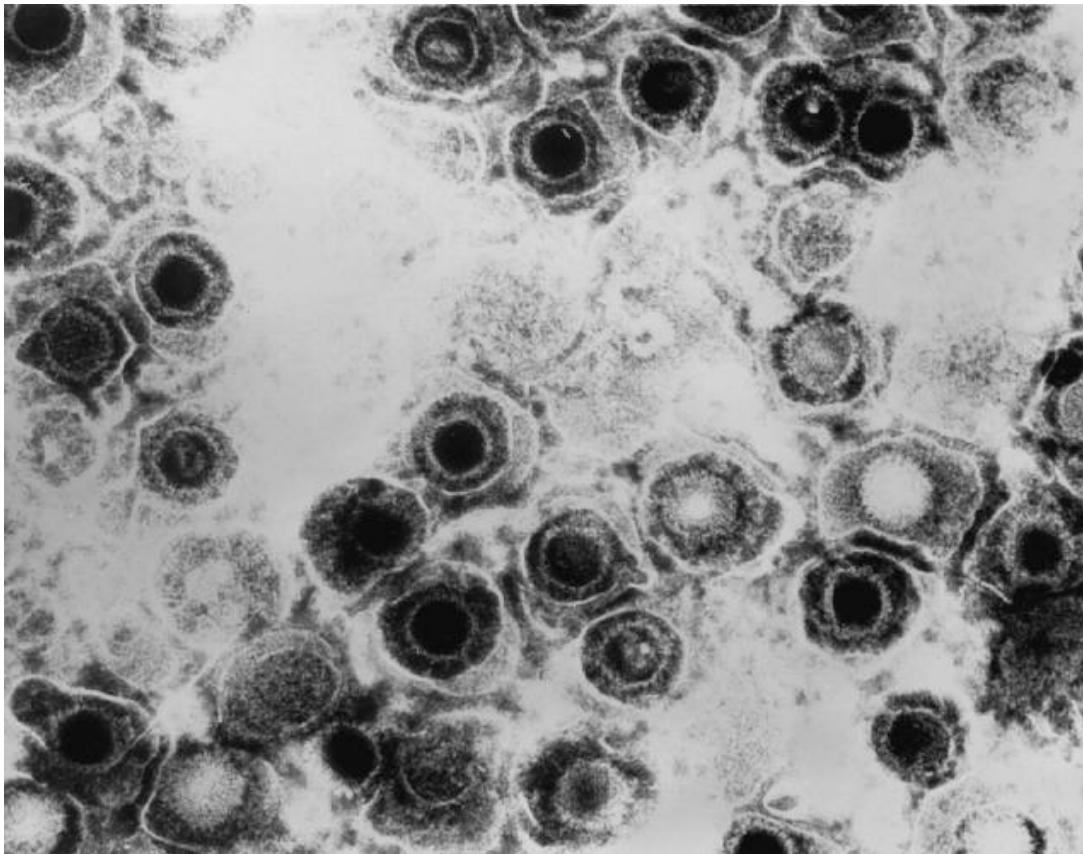


Congenital Herpes Simplex Virus (HSV) — Signs and Symptoms

[See online here](#)

Intrauterine and perinatal transmission of herpes simplex virus (HSV) to the fetus or the newborn is a possible cause of neonatal sepsis. The main clinical manifestations of congenital HSV infection are skin scars, chorioretinitis, and microcephaly. The three main forms of neonatal HSV infection are skin, eye and mouth disease diagnosed in 45 % of the cases, central nervous system disease diagnosed in 30 % of the cases and disseminated disease recognized in 25 % of the cases.



Overview of HSV Infections in Neonates

Congenital HSV infection is a debatable entity and has been reported only a few times in the medical literature. In this article, we will discuss the **three types of neonatal herpes simplex virus infections, which are named after the extent of the disease and the major organs involved.**

The acquisition of **HSV type 1 or type 2** without prior exposure to the virus in the mother is known as a **primary infection**. A **non-primary infection** refers to the

acquisition of an HSV type in a subject with previous exposure to another HSV type. For example, a neonate who had HSV type 1 will have pre-formed antibodies against it when s/he is exposed to HSV type 2.

HSV reactivation occurs when the same type appears in skin lesions in a patient with documented antibodies against that type, also known as previous exposure. Symptomatic HSV shedding is defined as the presence of genital herpes by detecting HSV-1 or HSV-2 in the lesions, either by culturing or polymerase chain reaction testing.

Transmission of Neonatal HSV infection

Neonatal HSV infection can be acquired in three distinct periods:

1. Rarely intrauterine, accounting for 1 in 250,000 deliveries
2. Most (85%) neonatal HSV infections are acquired perinatally, especially in maternal HSV infection, longer membrane rupture duration, and the use of a fetal scalp monitor.
3. HSV can also be acquired postnatally in 10% of cases, especially when the infant comes in contact with a caretaker with herpes labialis infection.

Epidemiology of Neonatal HSV Infections

To study the epidemiology of HSV infections in neonates, it is helpful to consider the epidemiology of genital HSV infections during pregnancy and the perinatal period.

Up to 20% of pregnant women in the United States are seropositive for HSV-2. **Most genital herpes infections are asymptomatic.** Up to two-thirds of pregnant women who acquire HSV-1 or HSV-2 during pregnancy develop no symptoms.

Women with a documented history of HSV before pregnancy have a 70% chance of developing a recurrence during pregnancy. Another 14% of those women are likely to develop prodromal symptoms suggestive of HSV reactivation at the time of delivery.

Neonatal HSV infection is reported in up to 60% of the newborns of mothers who developed a primary HSV infection around the time of delivery. However, only 3% of the newborns of women who develop a recurrent HSV infection around the time of delivery develop neonatal HSV infection.

The estimated incidence of neonatal HSV infections is around **1 in 3200 deliveries**. In the United States, up to 1500 new cases of neonatal HSV infection are diagnosed each year.

Risk Factors

Neonatal HSV infections occur only if the mother is shedding the virus at the time of delivery. Being symptomatic is not related to the risk of neonatal HSV infection; shedding is the more critical factor. Approximately 1.4 % of women with a prior history of recurrent genital herpes shed the virus at the time of delivery.

Another important risk factor for neonatal transmission is whether the maternal infection was a primary infection or a recurrent one. **Primary maternal HSV infections near the time of delivery are associated with a significantly higher risk of virus shedding at the time of delivery** and, potentially, neonatal HSV infection.

The other **risk factors** for neonatal HSV infection are **vaginal delivery** in a mother who is shedding the virus, the **use of fetal scalp electrodes and other instrumentation during pregnancy**, and the **type of HSV**. Maternal HSV-1 genital infection is associated with a higher risk of neonatal HSV than HSV-2. To **lower the risk** of transmission to the neonate, **cesarean delivery** is recommended. However, cesarean delivery in the case of prolonged rupture of membranes in a mother who is shedding the virus might not lower the risk of virus transmission to the neonate.

Clinical Presentation of Neonatal HSV Infections

Neonatal HSV infections can be classified into:

1. Disseminated disease
2. Central nervous system disease
3. Skin, eye or mouth (SEM) disease

The manifestations, involvement sites, development, treatment, and mortality depend on the type of disease.

Intrauterine HSV Infection

The **least common type** of HSV infection in the pediatric population is **intrauterine HSV infection**. The estimated incidence of intrauterine HSV infection is 1 in 300,000 live births.

The main manifestations of intrauterine HSV infection are:

- Skin scarring
- Rash
- Aplasia cutis
- Hyperpigmentation
- Hypopigmentation
- Microphthalmia
- Chorioretinitis
- Optic atrophy
- Intracranial calcifications
- Microcephaly
- Encephalomalacia

Because of its severe manifestations, the **diagnosis is rarely missed** at the time of birth.

Disseminated Neonatal HSV Infection

The disseminated form of neonatal HSV infection is reported in **one-quarter of cases**.

The disease involves the:

- Central nervous system
- Liver
- Lungs
- Adrenal glands
- Skin
- Eyes
- Mucous membranes

Patients might present with:

- Encephalitis
- Hepatic failure
- Respiratory failure
- Skin rash
- Disseminated intravascular coagulation

Despite the severity of the presentation, up to 83% of infected neonates recover and develop normally. The mortality rate is around 29%.

Central Nervous System (CNS) Neonatal HSV Infection

One-third of the cases of neonatal HSV infection present with CNS disease. Unfortunately, CNS neonatal HSV disease has a **grim prognosis**; only one-third of the survivors develop normally one year after adequate antiviral treatment. Mortality from CNS disease is estimated to be around 4%.

The main presentations of CNS neonatal HSV disease are:

- Seizures
- Poor feeding
- Temperature instability
- Lethargy
- Skin rash

SEM Neonatal HSV Infection

This is the most common form of neonatal HSV infection. Up to 45% of the cases belong to the SEM disease type. Involvement is **limited to the skin, eyes, and mucus membranes**. Patients typically present with a **vesicular rash**. All neonates with SEM disease **recover and develop normally** after one year of adequate antiviral therapy.

Diagnostic Workup for Neonatal HSV Infections

Initial Diagnosis

The definitive method of diagnosing neonatal HSV infection is the **isolation of HSV by culture**. HSV can be cultured from the conjunctivae, nasopharynx, mouth, or anus of the neonate. In severe cases, a culture of the cerebrospinal fluid or blood might be prepared. However, the diagnostic yield of skin and eye cultures is excellent and superior to any other site.

Neonates with central nervous system HSV infections should **undergo a polymerase chain reaction (PCR) test** to confirm the diagnosis. PCR is superior to HSV cultures because it can provide results much faster. The PCR's sensitivity and specificity for CNS HSV infections is around 100%.

Negative PCR, HSV cultures, and other rapid tests do not exclude neonatal HSV.

Serologic testing for diagnosing neonatal HSV infections is **not recommended**.

Workup to detect complications

1. Brain imaging, by CT & MRI, is recommended to detect the severity and extent of brain involvement. **HSV infection usually affects the temporoparietal region (High Yield USMLE question).**
2. A chest radiograph may detect bilateral diffuse pneumonitis in patients with disseminated disease.
3. Abdominal U/S may detect an enlarged liver or evidence of ascites in infants with acute liver failure.

Management of Neonatal HSV Infections

Once the diagnosis of neonatal HSV infection is confirmed, **antiviral therapy** should be started. Intravenous acyclovir at the dose of 20 mg/kg three times a day is the standard treatment for neonatal HSV infections regardless of the form of the disease.

The duration of the acute stage of treatment depends on the form of the disease.

1. **SEM disease** is typically treated with **14 days of intravenous acyclovir**.
2. **Disseminated disease** is treated for **21 days**.
3. **CNS disease** is treated for **21 days**, then a repeat cerebrospinal fluid PCR is indicated. If the PCR is still positive, then intravenous acyclovir should be continued until the PCR is negative.

After this initial treatment, the infant should be put on **maintenance antiviral suppressive therapy**. The standard treatment for all forms of the disease is oral acyclovir at the dose of 300 mg/m²/dose three times a day for 6 months. Acyclovir might cause neutropenia. Therefore, the absolute neutrophil count should be monitored while the infant is receiving treatment.

References

Pinninti, Swetha G. "[Neonatal Herpes Simplex Virus Infections.](#)" *Pediatrics Clinic of North America*. 2013;60(2): 351-365. <http://dx.doi.org/10.1016/j.pcl.2012.12.005>. Available at: <http://www.sciencedirect.com/science/article/pii/S0031395512002076?via%3Dihub>

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