

# Neonatal CNS Herpes Is a Diagnostic Challenge

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ASPEN, COLO. — A negative cerebrospinal fluid polymerase chain reaction test for herpes simplex virus does not rule out neonatal herpes with CNS involvement, Dr. April Palmer said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver, and the University of Colorado.

That's just one of several reasons why

early diagnosis of neonatal herpes simplex virus (HSV) CNS disease can be so difficult. Another is that 30%-40% of affected babies don't have skin lesions, added Dr. Palmer of the University of Mississippi, Jackson.

Herpes encephalitis in neonates often involves both temporal and extratemporal areas of the brain. It can look in certain respects like bacterial or enteroviral meningitis, cytomegalovirus infection, syphilis, or toxoplasmosis, all of which are in the differential diagnosis.

The sensitivity of cerebrospinal fluid (CSF) polymerase chain reaction (PCR) for HSV in neonates is 75%-100%. The test is most likely to be negative early in the disease course, but it can remain falsely negative on repeat spinal taps as well. Still, PCR is a big improvement over CSF viral culture, which is positive in only about 40% of cases, she continued.

Blood PCR for HSV is useful in ruling in neonatal disseminated HSV infection, which includes CNS disease in 60%-75% of

cases. However, blood PCR can't be used to rule out disseminated HSV because the test is sometimes falsely negative in this setting.

As in neonatal CNS herpes, up to 40% of neonates with disseminated HSV don't have skin lesions. They present with a septic picture that may be marked by liver failure, disseminated intravascular coagulation, and respiratory failure. One of the key points in making the diagnosis of neonatal disseminated HSV is the associated extreme elevation of liver enzymes; bacterial sepsis seldom entails such high liver transaminase levels, she said.

For skin lesions the diagnostic test of choice remains viral culture, which is typically positive within several days if the lesions are fresh and the patient hasn't been



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treated with acyclovir. If the culture is still negative on day 5, it can be considered a negative result.

Symptoms of neonatal CNS HSV include seizures, lethargy, fever, tremors, irritability, temperature instability, poor feeding, and a bulging fontanelle. Affected babies most often present on days 16-19 of life; however, they can present anytime in the first 3 months. In contrast, neonatal disseminated HSV involving visceral organs almost always presents within the first 2 weeks of life, and disease limited to the skin, eyes, or mucous membranes typically appears on days 10-11.

In the pre-antiviral therapy era, about 33% of neonates with HSV presented with CNS disease, compared with 17% today. Similarly, the proportion of neonates presenting with disseminated disease has been cut in half, compared with the 48% prevalence in the pre-antiviral therapy era.

The treatment recommended by the American Academy of Pediatrics for CNS or disseminated neonatal HSV is intravenous acyclovir at 60 mg/kg per day for 21 days.

It's a less than ideal therapy. In the landmark randomized trial that established high-dose acyclovir as the treatment of choice in neonatal CNS and disseminated herpes, only 31% of treated patients with CNS HSV were developing normally at age 12 months (Pediatrics 2001;108:230-8).

Acyclovir is far more effective in older children and adults with CNS disease. The drug is a potent suppressor of viral replication. So the current thinking is that achieving improved developmental outcomes in affected neonates is likely to require adjunctive therapy that addresses apoptosis or the increased cytokine response to HSV that characterizes neonatal CNS infection, according to Dr. Palmer.

An effective vaccine is thought to be a decade or more away, she added. ■



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**References:** 1. Arvola T, Laiho K, Torkkeli S, et al. Prophylactic Lactobacillus GG reduces antibiotic-associated diarrhea in children with respiratory infections: a randomized study. *Pediatrics*. 1999;104:e64. 2. Vanderhoof JA, Whitney DB, Antonson DL, et al. Lactobacillus GG in the prevention of antibiotic-associated diarrhea in children. *J Pediatrics*. 1999;135:564-568.

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