

# Progress in Standardizing Neonatal Herpes Simplex Virus (nHSV) Surveillance in the United States

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## Abstract

Neonatal herpes simplex virus (nHSV) infection is a rare but potentially severe consequence of maternal genital herpes infection. Although nHSV is a reportable disease in some U.S. jurisdictions, no standardized national surveillance system exists for nHSV. In 2008, the Neonatal Herpes Simplex Virus Surveillance Working Group was formed. Since its inception, the Working Group has developed standards that can be used by public health agencies to establish or enhance existing nHSV surveillance. Use of these standards will improve understanding of the incidence of this disease and its risk factors, as well as identify opportunities for prevention, diagnosis and treatment.

## Background

Neonatal herpes simplex virus (nHSV) infection is typically acquired following exposure to HSV in the maternal genital tract during delivery. Infection can also occur *in utero* as well as postnatally, such as following exposure to an adult with an oral-labial infection. Both HSV-1 and -2 can cause these infections. Although in the past the majority of genital HSV infections were type 2, in younger women and certain populations the incidence of genital HSV-1 infections is increasing (1-3), and the proportion of nHSV infections from HSV-1 is estimated to be as high as 30 to 50% (4,5). The risk of vertical transmission is significantly higher among women who acquire genital HSV infection during pregnancy than among women with long-standing genital infections in whom the virus is reactivated at term (4).

In the literature, clinically recognized nHSV infections often are classified as follows: 1) localized infection of the skin, eyes, and/or mouth (SEM disease); 2) infection of the central nervous system (CNS disease), with or without SEM disease; or 3) disseminated disease involving multiple organs such as the liver and lungs, with or without SEM and/or CNS disease (4,6). Although the mortality rate among untreated infants with central nervous system (CNS) or disseminated disease is 50 to 85% (7), those who survive, even with antiviral treatment, often suffer neurologic impairment depending on the extent of disease. Estimates of morbidity are as high as 69% in survivors of CNS involvement, compared to 17% in those with disseminated disease, after treatment with high-dose acyclovir (8). Prompt diagnosis and treatment initiation are critical in limiting the extent of disease, but may be delayed because recognizable disease in the neonate may mimic other diseases (9,10) and because many maternal infections are subclinical (11,12).

Although nHSV infection is relatively rare, most incidence estimates in areas throughout the United States (US) range from 8.4 to 28.2 per 100,000 live births (13-15). nHSV incidence estimates having been derived using a variety of data sources, including population-based state and local inpatient administrative data coupled with birth registry information, managed care data, and facility-based chart reviews (16).

## Rationale

Because nHSV is not a nationally notifiable condition and no standard surveillance system exists to monitor this infection (17), accurate estimates of the incidence of this infection are lacking. Indeed, a number of experts in the field have recently called for nHSV infection to become a nationally notifiable condition, in part to address this gap as well as to monitor trends in disease rates, improve understanding of prevention and treatment efforts, and improve awareness of this disease among providers (18-21).

A study conducted in 2005 determined that 9 states included nHSV infection among their list of reportable diseases (17). However, this assessment noted a lack of a standard case definition for surveillance and under-reporting of cases in most jurisdictions.

In 2007, CSTE, in partnership with the Centers for Disease Control and Prevention (CDC) and the National Coalition of STD Directors (NCSD), convened an expert panel to discuss nHSV surveillance. The expert panel developed a case definition for surveillance purposes and recommended that nHSV be added to the CSTE list of nationally notifiable diseases. Although CSTE did not add this to the list of nationally notifiable diseases, CSTE and CDC developed a strategy whereby those jurisdictions where nHSV is a reportable disease would be contacted to assess their willingness to adopt the case definition and consider other options for improving surveillance efforts. Use of this strategy was seen as a means whereby jurisdictions could improve existing nHSV surveillance and data quality, and inform future efforts.

## Objectives

Describe the development of the CSTE Neonatal Herpes Simplex Virus Surveillance Working Group and the progress made in developing standard surveillance methods.

## Methods

In 2008, representatives from those jurisdictions that had nHSV infection as a reportable condition were invited to participate in a conference call, and in April the first meeting of the Working Group, which also included representatives from CSTE and CDC, was held. In the two years since, the Working Group has continued to meet with the goal of developing standard methods to conduct nHSV surveillance. Additional jurisdictions have joined the Working Group, including those that are considering making nHSV infection a reportable disease. The sources of information used to inform these meetings included recommendations from the 2007 expert panel, policies and procedures jurisdictions have used to conduct surveillance, and lessons learned by those areas conducting surveillance activities.

## Results

### The Working Group has accomplished the following:

- Adopted a standard case definition for nHSV surveillance
- Developed a standard list of clinical, laboratory and epidemiological data elements
- Identified potential public health benefits of surveillance, including:
  - Determine the incidence of nHSV infection, including regional variations
  - Examine opportunities for prevention
  - Improve provider knowledge regarding disease recognition and management
  - Establish baseline data to monitor the impact of any future interventions, such as a HSV vaccine
  - Identify and respond to disease clusters
  - Improve the understanding of the natural history of nHSV infection

### Examples of other accomplishments of members of the Working Group:

Both **New York City** and **Connecticut** actively work with providers and laboratories to facilitate the identification and reporting of cases, and actively investigate all case reports to collect information on the full set of standard data elements.

In **New York City** (NYC), between April 2006 - December 2009, 60 cases of nHSV infection were reported and investigated; 11 (18.3%) were deceased. The incidence of nHSV infection in NYC is estimated to be 11.7/100,000 live births, based on these reports.

In **Connecticut**, during 2009, 2 cases of nHSV infection were reported and investigated, yielding a preliminary 2009 incidence estimate of 4.74/100,000 live births.

Ongoing discussions with State Health Officers and STD Controllers in **California** regarding making nHSV a reportable condition in that state.

Modifications to nHSV case definitions in **Washington** and **Massachusetts** to conform with the standard definition adopted by the Working Group.

Development of retrospective medical chart review activities to collect data on nHSV infections in select hospitals in **Chicago**.

## Conclusions

The Working Group has adopted a case definition and developed data collection standards that can be used at the state and local levels to establish, or enhance existing, surveillance for nHSV infection. Additionally, the Working Group has identified a number of potential public health benefits of nHSV infection surveillance that can be used to promote the establishment of surveillance in those jurisdictions currently without it, and to enhance the performance of existing nHSV surveillance activities.

## Implications for Programs, Policy, and/or Research

Established standards for nHSV surveillance will assist public health agencies, clinicians, and communities in efforts to improve timely identification of cases, assess the burden of disease, and identify opportunities for prevention and treatment of this potentially devastating disease.

## Working Group Members

Chicago – William Wong; Connecticut – Paul Gacek, Heidi Jenkins and Lynn Sosa; Florida – Karla Schmitt; Massachusetts – Thomas Bertrand and Katherine Hsu; New York – Perry Smith; New York City – Shoshanna Handel, Julia Schillinger and Kate Washburn; Ohio – Debbie Merz; San Francisco – Sally Stephens; Washington – Mark Stenger; Centers for Disease Control and Prevention - Stuart Berman, Elaine Flagg, Hillard Wienstock and Eileen Yee; and the Council of State and Territorial Epidemiologists – Edward Chao and Cort Lohff.

## Additional Information

For additional information about the CSTE Neonatal Herpes Simplex Virus Surveillance Working Group, including how to join, please contact Cort Lohff [312 746-6621/ email [lohff\\_cortland@cdph.org](mailto:lohff_cortland@cdph.org)] or Elaine Flagg [404 639-8348/ email [ewf2@cdc.gov](mailto:ewf2@cdc.gov)]

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