

07-ID-10

Committee: Infectious Disease

Title: Revision of CSTE 06-ID-01: Surveillance Case Definition for HIV Infection among Children age < 18 months

Statement of Problem:

CSTE Position Statement 06-ID-01 approved in 2006 entitled, "Revision of the Surveillance Case Definition for HIV Infection among Children age < 18 months" needs to be changed to account for more recent data. A minor change is being made to 06-ID-01 due to review of additional data sources and further discussion with pediatric experts at the American Academy of Pediatrics after publication of 06-ID-01. The only change is to the presumptive uninfected category. This Position Statement is an amendment to 06-ID-01.

Statement of desired action to be taken:

CSTE recommends that CDC adopt the revised presumptive uninfected category which will be incorporated into the new HIV surveillance case definition for children age <18 months, as presented below.

Goals of Surveillance:

The goal is to be sufficiently accurate to presumptively classify perinatally exposed infants as HIV negative for surveillance purposes.

Methods for Surveillance

Data are obtained from HIV surveillance programs at the state, city and territorial levels as a part of their active HIV/AIDS surveillance systems. Areas obtain the information in a variety of ways: laboratory and clinician reporting are the most prominent.

Case Definition narrative:

For the presumptive uninfected category, CSTE proposes the inclusion of the following change:

- Two negative RNA or DNA virologic tests, for which both specimens were obtained ≥ 2 weeks of age and for which one specimen was obtained ≥ 4 weeks of age.¹

¹ When both specimens are obtained at greater than or equal to 4 weeks of age the specimens should be obtained on separate days.

DRAFT: 2007 REVISION OF THE SURVEILLANCE CASE DEFINITION FOR HIV INFECTION AMONG CHILDREN AGED <18 MONTHS

This revised definition of HIV infection supersedes the definition published in 1999 (1), applies to any variant of HIV (e.g., HIV-1, HIV-2), and is intended for public health surveillance only. This definition is not presented as a guide for clinical diagnosis or for other uses.

This revised definition takes into account more recent data related to the use of newer testing technologies. Laboratory criteria for children aged <18 months at the time of diagnosis include revisions to the category *presumptive uninfected*. However, no substantial changes are made to the categories *definitive and presumptive infected* or *definitive uninfected*, and no changes are made to exclude conditions that meet criteria in the 1987 pediatric surveillance case definition for AIDS for children aged <18 months (1,2). Perinatally exposed children aged <18 months of age whose illness meets the AIDS case definition on the basis of existing clinical criteria will still be considered HIV-infected because of the greater uncertainty associated with diagnostic testing for HIV in this population and because of a positive HIV test result for the

mother. The result of these changes is to reduce the number of HIV-exposed infants who have a very low probability of infection but whose infection status is classified for surveillance purposes as indeterminate according to the prior surveillance diagnostic criteria (1). The definitive or presumptive exclusion of HIV infection for surveillance purposes does not mean that one can rule out HIV infection clinically. For the purposes of calculating the exact timing of tests (e.g. when a specimen was obtained for laboratory testing) based on the surveillance case definition, 1 month corresponds to 30 days.

A. HIV Infected (Definitive, Presumptive)

A child aged <18 months born to an HIV-infected mother will be categorized for surveillance purposes as "HIV infected" if at least one of the following criteria is met.

Definitive

Laboratory Criteria

Positive results on two separate specimens (excluding cord blood) by the use of one or more of the following HIV virologic (non-antibody) tests:

- HIV nucleic acid (DNA or RNA) detection*
- HIV p24 antigen test, including neutralization assay, for a child ≥ 1 month of age
- HIV isolation (viral culture)

Presumptive

A child will be categorized as presumptive HIV-infected if the criteria for definitively HIV-infected are not met, but the following criteria are met:

Laboratory Criteria

Positive results on only one specimen (excluding cord blood) by the use of the HIV virologic tests listed above (Definitive—Laboratory Criteria) and no subsequent negative results from HIV virologic or HIV antibody tests*

OR

Clinical or Other Criteria (if the above laboratory criteria for definitively or presumptively HIV-infected are not met, but the child is born to an HIV-infected mother)

- Diagnosis of HIV infection, based on the laboratory criteria above, that is documented in a medical record by a physician
- or**
- When diagnostic testing for HIV infection or the results of such testing are not available, conditions that meet the criteria in the 1987 pediatric surveillance case definition for AIDS (2, *Appendix*)

B. Uninfected with HIV (Definitive, Presumptive)

A child aged <18 months born to an HIV-infected mother will be categorized for surveillance purposes as "uninfected with HIV" if the criteria for "definitive or presumptive HIV-infected" are not met, but the following criteria are met.

Definitive

Laboratory Criteria

- Virologic testing: At least two negative HIV virologic tests* from separate specimens, both of which were obtained at ≥ 1 month of age and one of which was obtained at ≥ 4 months of age
- or**
- Serologic testing: At least two negative HIV antibody tests from separate specimens obtained at ≥ 6 months of age
- AND**

No other laboratory or clinical evidence of HIV infection (i.e., no positive results from virologic tests* if tests were performed and no current or previous AIDS-defining condition – Appendix)

Presumptive

Laboratory Criteria

A child aged <18 months will be categorized as presumptive uninfected with HIV if the criteria for definitive uninfected with HIV are not met, but the following criteria are met:

- Two negative RNA or DNA virologic tests* of which both specimens were obtained ≥ 2 weeks of age and one of which was obtained ≥ 4 weeks of age²
or
- One negative RNA or DNA virologic test* of a specimen from a child ≥ 8 weeks of age
or
- One negative enzyme immunoassay (EIA) HIV antibody test of a specimen from a child ≥ 6 months of age
or
- One positive result from an HIV virologic test* followed by at least two negative tests, one of which is from a virologic test of a specimen from a child ≥ 8 weeks of age or from an HIV antibody test of a specimen from a child ≥ 6 months of age

AND

No other laboratory or clinical evidence of HIV infection (i.e., no AIDS-defining condition for which there is no other underlying condition indicative of immunosuppression and no subsequent positive results from virologic tests if tests were performed)

OR

Clinical or Other Criteria (if the above criteria for definitive or presumptive uninfected with HIV are not met)

- Determination of “uninfected with HIV” made by a physician and a physician has noted the HIV diagnostic tests results in the medical record
and
- No other laboratory or clinical evidence of HIV infection (i.e., no positive results from virologic tests if tests were performed, and no AIDS-defining condition for which there is an underlying condition indicative of immunosuppression – listed below)

C. Indeterminate HIV infection

A child aged <18 months born to an HIV-infected mother will be categorized as having perinatal exposure with an “indeterminate HIV infection” status if the criteria for “HIV-infected” or the criteria for “uninfected with HIV” are not met (see Sections A and B).

² When both specimens are obtained at greater than or equal to 4 weeks of age the specimens should be obtained on separate days.

*HIV nucleic acid (DNA or RNA) detection tests are the virologic methods of choice for the diagnosis or exclusion of infection in children aged <18 months. Although HIV culture can be used for this purpose, it is more complex, less standardized, and less sensitive than nucleic acid detection tests. The use of p24 antigen testing to exclude infection in children aged <18 months is not recommended because of poor sensitivity, especially in the presence of HIV antibody. During the past decade, commercial tests for RNA and DNA detection have become widely available. Quantitative RNA tests have been approved by the Food and Drug Administration (FDA) for monitoring HIV infection and qualitative RNA tests have been approved as an aid to diagnosis. The quantitative and qualitative RNA tests meet FDA standards for high analytic and clinical sensitivity and specificity (3, 4, 5). Currently, all the commercial virologic tests detect the major (M) subtypes of HIV-1 as well as most O-subtypes. HIV-2 can be diagnosed with HIV-2 DNA PCR. Because of the possibility of mutation or recombination in the sequences detected by a particular test, an occasional specimen in an HIV-2 individual may not be detected. If suspicion for HIV-2 infection is high and results are negative, it may be prudent to test with another test.

AIDS-defining Conditions

- Bacterial infections, multiple or recurrent (including *Salmonella* septicemia)[†]
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal*
- Cervical cancer, invasive[§]
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at >1 month of age
- Cytomegalovirus retinitis (with loss of vision)*
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonitis, or esophagitis, onset at >1 month of age
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi's sarcoma*
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex^{*.†}
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- *Mycobacterium avium* complex or *M. kansasii*, disseminated or extrapulmonary*
- *Mycobacterium tuberculosis*, any site (pulmonary^{*.§}, disseminated*, or extrapulmonary*)
- *Mycobacterium*, other species or unidentified species, disseminated* or extrapulmonary*
- *Pneumocystis* pneumonia*
- Pneumonia, recurrent^{*.§}
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain, onset at >1 month of age*
- Wasting syndrome due to HIV

* Conditions that may be diagnosed presumptively.

[†] Restricted to only children aged <13 years.

[§] Restricted to only adults and adolescents (persons ≥13 years).

Period of Surveillance:

From the present time forward.

Data sharing/release and print criteria:

Data are shared with CDC in the same manner as all other HIV/AIDS surveillance data: individual cases are sent without names to CDC monthly.

Background and Justification:

In order to further evaluate the accuracy of the proposed test interval periods in the revised case definition, we used data from the Women and Infants Transmission Study (WITS) combined with data from the Pediatric Spectrum of Disease (PSD) Project. Requiring two negative RNA or DNA virologic tests, both of which were obtained at ≥ 2 weeks of age and one of which was obtained at ≥ 4 weeks of age, would have resulted in the correct diagnosis of over 99% of the cases as being negative, with a negative likelihood ratio of 15. These data and analyses will be published in a future manuscript.

Table 1 indicates all definitive and presumptive infected (diagnosed HIV, not AIDS), definitive and presumptive uninfected, and indeterminate cases of HIV infection among children <18 months of age from 1996-2005 by birth year reported to the National HIV/AIDS Reporting System. The table's "Current (before)" rows satisfy the current case definition based on infant HIV infection status and birth year. The "After Proposed Change" rows take into account the recommended change to the presumptive uninfected category among children aged <18 months based on infant HIV infection status and birth year. The highlighted rows indicate the impact of the proposed case definition change in the number of cases by year. These data indicate that from 1996-2005, the percent of indeterminate cases would decrease from 32% to 25% with a corresponding increase in the number of presumptive uninfected cases (from 8% to 15%) when taking into account the case definition change (e.g. the proposed change in testing interval). This suggests that a moderate reduction of children aged <18 months classified as indeterminate in the National HIV/AIDS Reporting System can be attained with implementation of the proposed revision of the perinatal HIV surveillance case definition. No changes to the definitive infected, presumptive infected or definitive uninfected criteria are proposed to the case definition.

**Table 1. Number and percentage of infants <18 months of age
by infant birth year and HIV infection status before and after proposed case definition change reported to the CDC HIV/AIDS Reporting
System
1996-2005
Revised data are highlighted**

	Infection Status	Year of Birth														Total	
		1996-1999		2000		2001		2002		2003		2004		2005		N	%
		N	%	N	%	N	%	N	%	N	%	N	%				
Current (before proposed change)	Definitive +	955	9.53	155	4.97	128	4.44	91	3.51	73	3.19	57	2.90	37	2.21	1496	6.09
	Presumptive +	122	1.22	29	0.93	32	1.11	20	0.77	23	1.01	17	0.87	18	1.07	261	1.06
	Definitive -	5544	55.30	1860	59.65	1670	57.89	1462	56.36	1147	50.13	898	45.75	413	24.61	12994	52.93
	Presumptive-	972	9.70	227	7.28	214	7.42	212	8.17	180	7.87	168	8.56	92	5.48	2065	8.41
	Indeterminate	2431	24.25	847	27.16	841	29.15	809	31.19	865	37.81	823	41.93	1118	66.63	7734	31.50
After Proposed Change	Definitive +	955	9.53	155	4.97	128	4.44	91	3.51	73	3.19	57	2.90	37	2.21	1496	6.09
	Presumptive +	122	1.22	29	0.93	32	1.11	20	0.77	23	1.01	17	0.87	18	1.07	261	1.06
	Definitive -	5544	55.30	1860	59.65	1670	57.89	1462	56.36	1147	50.13	898	45.75	413	24.61	12994	52.93
	Presumptive-	1523	15.19	400	12.83	405	14.04	350	13.49	344	15.03	342	17.42	289	17.22	3653	14.88
	Indeterminate	1880	18.75	674	21.62	650	22.53	671	25.87	701	30.64	649	33.06	921	54.89	6146	25.03

References

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5. Gallarda JL, Dragon E. Blood screening by nucleic acid amplification technology: current issues, future challenges. Molecular Diagnosis 2000; 5:11-22.

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