Council of State and Territorial Epidemiologists (CSTE)
Position Statement

Submission Date: March 30, 2005

05-ID-04

Committee: Infectious Disease

Title: Revision of Surveillance Case Definition for AIDS among adults and adolescents ≥ 13 years of age

Statement of problem:

Public health surveillance case definitions for Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) have changed over time to reflect increasing knowledge of the diseases under surveillance and advances in diagnostics and treatment. The existing case definition for AIDS in persons age ≥13 was last updated in 1993 (1), as an expansion of the 1987 case definition (2). The resulting definition allows a subset of adults and adolescents without evidence of laboratory-confirmed HIV infection to be reported as having a case of AIDS. This subset includes some patients with negative diagnostic antibody tests for HIV, and others with inconclusive or not performed HIV antibody tests. Specifically, a person can meet the existing case definition for AIDS if they have:

1) Inconclusive or not performed HIV antibody diagnostic tests *and*
    a) no other known cause of immunodeficiency *and*
    b) a definitive diagnosis for a subset of AIDS defining conditions

or

2) Negative HIV antibody diagnostic tests *and*
    a) exclusion of other known causes of immunodeficiency *and*
    b) a definitive diagnosis of *Pneumocystis carinii* pneumonia

or

3) Negative HIV antibody diagnostic tests *and*
    a) exclusion of other known causes of immunodeficiency *and*
    b) a definitive diagnosis for a subset of AIDS defining conditions *and*
    c) a CD4+ T lymphocyte count <400 cells/*u*L.

At the time of the 1993 AIDS case definition revision, the authors recognized that the case definition may be lacking in some specificity, stating "...the AIDS surveillance definition may rarely misclassify other patients as having serious HIV disease if they have no antibody test but have an AIDS-indicative disease with a background incidence unrelated to HIV infection" (1). Marked decreases in annual AIDS incidence since 1993 have made that statement even more applicable. Two other major changes have occurred since 1993. In 1993, the AIDS case definition change was specifically designed as an expansion of the

1987 AIDS case definition, and did not examine how technology could more readily and accurately identify HIV infection. In 1987, however, HIV antibody tests were relatively insensitive and could miss patients with advanced immunosuppression, and viral detection tests were not widely available; neither is true in 2005.

Advances in treatment and diagnostics and progressive knowledge about the spectrum of disease caused by HIV also warrant examination of the current AIDS case definition with respect to immunologic markers (CD4+ T lymphocytes) and AIDS defining opportunistic infections (OIs). Recent treatment recommendations for the use of antiretroviral agents in HIV infected persons identified asymptomatic persons with CD4+ T lymphocyte counts <350 cells/uL as having a short-term risk of developing an AIDS defining condition high enough to warrant offering antiretroviral therapy (3). Current AIDS surveillance identifies the portion of the HIV epidemic that comprises the severely immunocompromised. However, it is clear that those with higher CD4+ counts have significant risks that may be important to capture through surveillance as well. The World Health Organization is engaging in a similar examination of these issues in developing their recommendations for an AIDS case definition for worldwide public health surveillance.

Advances in diagnostics also warrant review of the current HIV case definition with respect to the role of confirmatory diagnostic algorithms using increasingly sensitive and specific assays. The current surveillance case definitions for HIV infection rely on diagnostic technologies that are rapidly advancing and changing. In particular, each of the recently approved rapid EIA tests for HIV antibodies use varying methods to detect specific subsets of antibodies. Therefore, algorithms are being investigated that use combinations of different diagnostic tests as a method for identifying and confirming HIV infection. Such algorithms may displace the use of Western Blots or IFAs for confirmation. WHO has outlined such algorithms for surveillance purposes in developing countries (4). Future HIV infection case definitions for surveillance will need to incorporate these testing technologies.

CDC needs to hold consultations with relevant partners in the surveillance, clinical care, and diagnostics arenas, to review the existing case definitions for public health HIV/AIDS surveillance for potential revisions related to clinical and laboratory criteria for AIDS diagnosis and to the role of diagnostic assay algorithms in HIV infection confirmation. These consultations will identify the options for case definition revisions and the effect on surveillance practices and data, and assess harmony with ongoing global case definition proposals.

Statement of desired action to be taken:

CSTE recommends that CDC adopt the new HIV/AIDS case definitions, as presented in the Attachment.

CSTE notes that there is an ongoing examination of the existing HIV and AIDS case definitions, in collaboration with partners in surveillance, clinical care, and diagnostic arenas, to address the consistency of the AIDS case definition with current clinical care recommendations and the consistency of the existing HIV case definition with advances in HIV testing technology. CSTE supports this process but recognized that it could take several years. Therefore this interim change in case definition is needed.

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Public health impact:

Implement revised HIV and AIDS case definitions as proposed in attachment.

- Simplifies case definition. Case reporting will be easier for clinicians and surveillance staff. When determining whether a patient meets AIDS diagnostic criteria, clinicians and surveillance staff will no longer need to evaluate patients reported with AIDS indicator conditions who do not have laboratory evidence of HIV infection.
- Increases the AIDS case definition's specificity by excluding patients without evidence of laboratory-confirmed HIV infection. Patients without immunodeficiency due to HIV infection will not be misclassified as having progressed to AIDS. This obviates erroneous diagnoses and partner notifications.
- Simplifies and clarifies the public health message that HIV is the etiology of AIDS.

Effects of proposed revision on AIDS surveillance data:

Under the existing HIV case definition, evidence of laboratory confirmation of HIV infection occurs when one or more of the following is present:

• Positive result on a screening test for HIV antibody (e.g., repeatedly reactive enzyme immunoassay) followed by a positive result on a confirmatory (sensitive and more specific) test for HIV antibody (e.g., a reactive Western blot or IFA test, *or*

• Positive result of a detectable quantity on any of the following HIV virologic (non-antibody) tests: HIV nucleic acid (DNA or RNA) detection (e.g., DNA polymerase chain reaction [PCR] or plasma HIV-1 RNA), HIV p24 antigen test, including neutralization assay, HIV isolation (viral culture), *or*

• Diagnosis of HIV infection, based on the laboratory criteria above, that is documented in a medical record by a physician.

Since AIDS reporting began through 1998, 115,932 (16.5%) cases lacked evidence of HIV infection. This includes those cases of AIDS early in the epidemic which were diagnosed before the availability of any HIV diagnostic tests. The contribution of cases without such evidence to all AIDS diagnosed among patients ≥ 13 years of age decreased 5-fold during the period 1999-2003. In 1999, 1,693 (4.2%) cases met AIDS diagnostic criteria in the absence of

laboratory evidence of HIV infection; in 2003, just 351 (0.8%) cases lacked such evidence. Therefore, the number of AIDS case reports that would have failed to meet the revision's diagnostic criteria comprised less than 1% all cases diagnosed in 2003. It is likely that many of these cases actually meet the laboratory criteria of the proposed AIDS case definition, but simply lack such documentation in the HIV/AIDS surveillance system. Given the observed trend of fewer cases without laboratory evidence over time, these data suggest that the impact of the proposed prospective revision on surveillance data will be minimal (Table), yet will greatly simplify data management and surveillance practices.

Table. Number* and percentage of AIDS patients ≥13 years of age by year of diagnosis and by evidence of laboratory-confirmed HIV infection status, United States—1983-2003

Evidence of laboratory-confirmed HIV infection	Year of AIDS Diagnosis					
	1983-1998	1999	2000	2001	2002	2003
Absent	115,932	1,693	1,675	1,000	670	351
	16.5%	*4.2%*	*4.1%*	*2.5%*	*1.7%*	*0.8%*
Present	588,398	39,013	39,043	39,263	40,033	42,203
	83.5%	*95.8%*	*95.9%*	*97.5%*	*98.4%*	*99.2%*
Total	704,330	40,706	40,718	40,263	40,703	42,554

* These numbers do not represent reported case counts. Rather, these numbers are point estimates, which result from adjustments of reported case counts. The reported case counts are adjusted for reporting delays.

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Attachment: Proposed Adult/Adolescent AIDS case definition.

References:

1) CDC. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. MMWR Recommendations and Reports, 1992. :41(RR-17).
2) CDC. Revision of the CDC Case Definition for Acquired Immunodeficiency Syndrome. MMWR. 1987; 36 (Suppl 1S).
3) HHS. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Oct 2004.
4) WHO. Guidelines for HIV diagnosis and monitoring of antiretroviral therapy. 2004. WHO Document : SEA-HLM-382, WHO Project No: ICP BCT 001.

Revised Surveillance Case Definition for HIV/AIDS Among Adults and Adolescents ≥ 13 years of age

These revised definitions of HIV infection and of AIDS are intended for public health surveillance only. The revised AIDS case definition for adults and adolescents ≥ 13 years of age now requires evidence of laboratory-confirmed HIV infection to accompany evidence of low CD4+ T lymphocyte counts or AIDS indicator conditions. The revised HIV definition, which applies to any variant of HIV (e.g., HIV-1 and HIV-2), excludes confirmation of HIV infection through diagnosis of AIDS defining conditions alone. These definitions are not presented as a guide to clinical diagnosis or for other uses (1).

I. **In adults and adolescents aged greater than or equal to 13 years, a reportable case of HIV infection must meet at least one of the following criteria:**

Laboratory Criteria

- Positive result on a screening test for HIV antibody (e.g., repeatedly reactive enzyme immunoassay) followed by a positive result on a confirmatory (sensitive and more specific) test for HIV antibody (e.g., a reactive Western blot or immunofluorescence antibody test)

or

- Positive result of a detectable quantity on any of the following HIV virologic (non-antibody) tests:
  - HIV nucleic acid (DNA or RNA) detection (e.g., DNA polymerase chain reaction [PCR] or plasma HIV-1 RNA)*
  - HIV p24 antigen test, including neutralization assay
  - HIV isolation (viral culture)

OR

Other Criterion, if the above laboratory criteria are not met

- Diagnosis of HIV infection, based on the laboratory criteria above, that is documented in a medical record by a physician

* In patients infected by other than perinatal exposure, negative or undetectable plasma viral nucleic acid tests do not rule out the diagnosis of HIV infection.

II. **In adults and adolescents aged greater than or equal to 13 years, a reportable case of AIDS must meet criteria for a case of HIV infection (above at *I*) *plus* at least one of the following criteria:**

Criterion 1. Depressed CD4+ T Lymphocytes defined as:

- Either of the following:
    - a CD4+ T-lymphocytes count of less than 200 cells/uL
    - a CD4+ T-lymphocyte percentage of total lymphocytes of less than 14%

Criterion 2. Diagnosis of an AIDS Indicator Condition:

The expanded definition retains the 26 clinical conditions in the AIDS surveillance case definitions published in 1987 (2) and 1993 (1). Definitive diagnostic methods for these conditions are detailed in the 1987 and 1993 MMWR case definition supplement and recommendations (2), (1). Because all AIDS diagnoses now require evidence of laboratory confirmed HIV infection, the additional presence of any disease listed below indicates a diagnosis of AIDS. Guidance on diagnosis of these diseases in the context of all nationally notifiable diseases is available at http://www.cdc.gov/epo/dphsi/casedef/case_definitions.htm .

- Any of the following diagnoses (asterisk indicates conditions that may be diagnosed presumptively)
    - Candidiasis of bronchi, trachea, or lungs
    - Candidiasis, esophageal*
    - Cervical cancer, invasive
    - Coccidioidomycosis, disseminated or extrapulmonary
    - Cryptococcosis, extrapulmonary
    - Cryptosporidiosis, chronic intestinal (greater than 1 month's duration)
    - Cytomegalovirus disease (other than liver, spleen, or nodes)
    - Cytomegalovirus retinitis (with loss of vision)*
    - Encephalopathy, HIV-related
    - Herpes simplex: chronic ulcer(s) (greater than 1 month's duration); or bronchitis, pneumonitis, or esophagitis
    - Histoplasmosis, disseminated or extrapulmonary
    - Isosporiasis, chronic intestinal (greater than 1 month's duration)
    - Kaposi's sarcoma*
    - 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* or extrapulmonary*)
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary*
- *Pneumocystis carinii* pneumonia*
- Pneumonia, recurrent*
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain*
- Wasting syndrome due to HIV

References
(1) Centers for Disease Control and Prevention. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. MMWR 1992;41 (RR-17).
(2) Centers for Disease Control and Prevention. Revision of the CDC Surveillance Case Definition for Acquired Immunodeficiency Syndrome. MMWR 1987:36(suppl no. 1S):4S-6S.