

Appendix B- -Evolution of the CDC's Case Definition of AIDS

In 1981, the Centers for Disease Control (CDC) in the U.S. Department of Health and Human Services (DHHS) began surveillance for a newly recognized constellation of diseases, now termed acquired immunodeficiency syndrome (AIDS). As described below, CDC developed a surveillance case definition for this syndrome in 1982 and received case reports directly from health care providers and State and local health departments. Bear in mind that the CDC's case definition of AIDS was developed for surveillance purposes. According to the CDC, the goals of AIDS surveillance are to monitor trends in the number of AIDS cases and monitor the scope of severe morbidity due to infection with human immunodeficiency virus (HIV)(219). Since 1982, the CDC's case definition has been revised twice, once in 1985 and once in 1987. In November of 1991, the CDC proposed changing its definition once again.

The CDC's 1982 Case Definition of AIDS

From 1980 to 1981, the CDC received its first reports of five cases involving homosexual males diagnosed with *Pneumocystis carinii* pneumonia due to severe immunodeficiency.¹ From 1979 to 1981, CDC also received reports of 26 homosexual males diagnosed with Kaposi's sarcoma. Of these 26 men, 6 also had *Pneumocystis carinii* pneumonia (25 were white and 1 was African American) (200).

¹ *Pneumocystis carinii* pneumonia virtually always occurs in limited to severely immunocompromised patients (199).

The CDC published its first case definition of what is now called acquired immunodeficiency syndrome (AIDS) in September 1982 (201). The case definition was "a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease" (see table B-1).

The CDC received reports of 593 cases of what is now called AIDS between June 1, 1981 and September 15, 1982. Fifty-one percent of these 593 cases had *Pneumocystis carinii* pneumonia without Kaposi's sarcoma (with or without other opportunistic infections) , 30 percent had Kaposi's sarcoma without *Pneumocystis carinii* pneumonia (with or without other opportunistic infections) , 7 percent had both *Pneumocystis carinii* pneumonia and Kaposi's sarcoma (with or without opportunistic infections), and 12 percent had opportunistic infections with neither *Pneumocystis carinii* pneumonia nor Kaposi's sarcoma. Men who have sex with men made up 75 percent of 593 cases reported, while injection drug users made up 25.5 percent (201).

As of December 19, 1983, 3,000 cases that met the case definition of AIDS had been reported to the CDC (202).²The pattern of opportunistic illnesses remained fairly constant with 51 percent of cases reporting *Pneumocystis carinii* pneumonia without Kaposi's sarcoma, 26 percent reporting both Kaposi's sarcoma without *Pneumocystis carinii* pneumonia, 7 percent both *Pneumocystis carinii* pneumonia and Kaposi's sarcoma, and 16 percent reporting opportunistic infections without either Kaposi's sarcoma or *Pneumocystis carinii* pneumonia. Fifty-nine percent of the 3,000 AIDS cases reported occurred among whites, 26 percent among African Americans, and 14 percent

² This figure does not include 42 children under age 5 who met the surveillance definition for pediatric AIDS.

among Hispanics. Women accounted for only 7 percent of the cases reported at this time. The groups at highest risk for contracting AIDS were men who have sex with men (71 percent) and injection drug users (17 percent) (202).

Men who have sex with men and injection drug users with immunodeficiency represented the at-risk group for acquiring AIDS in 1982 when the syndrome was initially defined. The indicators of AIDS were limited to Kaposi's sarcoma and opportunistic infections diagnosed without known causes of immunodeficiency (87). Opportunistic illnesses that were most problematic for the high-risk groups, and therefore met the criteria for the CDC's 1982 definition of AIDS, are presented in table B-1. The CDC grouped symptoms into five etiologic categories: protozoal and helminthic, fungal, bacterial, viral, and neoplastic.

The CDC's 1985 Case Definition of AIDS

After the CDC's first case definition of what is now called AIDS was published in 1982, researchers identified human immunodeficiency virus (HIV) as the cause of AIDS.³ Furthermore, laboratory tests were developed to identify the presence of the HIV antibody. The HIV laboratory test could be used as a diagnostic indicator for severe manifestations of HIV disease that were not included in the 1982 case definition. Consequently, the CDC changed its AIDS surveillance definition in 1985 (see table B-2). Among other things, the 1985 definition specified that in patients with a positive HIV test, cases of disseminated histoplasmosis, isosporiasis causing chronic diarrhea,

³ At the time the virus was identified, HIV was termed human T-cell lymphotropic virus, type III (HTLV-III)/lymphadenopathy-associated virus (LAV).

bronchial or pulmonary candidiasis, non-Hodgkin's lymphoma, and Kaposi's sarcoma in persons 60 years of age or over were considered cases of AIDS (203).

From June 1981 to September 8, 1986, health departments and physicians in the United States reported 24,576 cases of AIDS to the CDC. Of the reported cases, 25 percent (6,192) occurred among African Americans and 14 percent (3,488) occurred among Hispanics, although African Americans and Hispanics only make up 12 percent and 6 percent respectively of the U.S. population. African American and Hispanic women accounted for 51 percent and 21 percent respectively of women with AIDS, while African American and Hispanic men accounted for 23 percent and 14 percent respectively of men with AIDS (205). The CDC estimated that approximately 750,000 people in the United States were infected with the AIDS virus at the beginning of 1986 (215).

The CDC's 1987 Case Definition of AIDS

In August of 1987, the CDC's case definition of AIDS was once again modified to reflect increases in the understanding of HIV infection, and the 1987 case definition is the definition currently in use (see table B-3). The CDC's goals in making the 1987 revision were: 1) to simplify AIDS reporting; 2) to make the definition consistent with standards of medical care for HIV-infected persons; and 3) to more accurately record the number of persons with severe HIV-related immunosuppression (208).

The CDC expanded the case definition of AIDS to include 23 AIDS-defining conditions, including bronchial, tracheal, or pulmonary candidiasis; esophageal candidiasis; HIV encephalopathy; HIV wasting syndrome; and a broader range of malignancies (208).

The 1987 case definition of AIDS is arranged in three sections according to laboratory evidence of HIV infection: unknown or inconclusive HIV test, positive HIV test, and negative HIV test (see table B-3). With laboratory evidence of HIV infection, the 1987 definition allows some opportunistic illnesses to be presumptively (rather than definitively) diagnosed. In other words, these conditions (e.g. , *Pneumocystis carinii* pneumonia and Kaposi's sarcoma) in HIV-positive persons can be diagnosed on the basis of clinical signs and symptoms, without confirmation by a laboratory test.

Twenty-nine percent of the 40,836 AIDS cases reported between September 1987 and December 1988 met the criteria of the CDC's 1987 case definition only and would not have been reported as AIDS cases under earlier definitions. The use of the 1987 case definition of AIDS increased the proportions of AIDS cases in women, injection drug users, and minorities. Of the cases meeting only the criteria of the 1987 definition, 15 percent were women, as compared with 9 percent of cases meeting the pre-1987 definition. Thirty-five percent of the cases meeting only the 1987 definition were heterosexual injection drug users, as compared with 18 percent meeting the pre-1987 definition. Of cases meeting the 1987 definition only, 34 percent were African Americans, as compared with 26 percent meeting the pre-1987 definition; and 21 percent were Hispanic, as compared with 14 percent meeting the pre-1987 definition (211).

The CDC's Proposed 1992 Case Definition of AIDS

In November of 1991, the CDC has proposed changing its case definition of AIDS (219). The proposed case definition would count as AIDS cases persons with the clinical conditions listed in the 1987 case definition (see table B-3). In addition, the proposed case definition would include as AIDS cases all HIV-infected adolescents and adults who have laboratory evidence of severe

HIV-related immunosuppression--defined as a CD4⁺ lymphocyte count of below 200 cells per cubic millimeter (mm^3) of blood (or a CD4⁺ percent of total lymphocytes below 14 if the absolute count is not available). The proposed expanded AIDS case definition also includes persons with clinical conditions listed in the 1987 case definition (table B-3). The case definition of AIDS is expected to become effective in the summer of 1992 (219).

Table B-1--CDC's 1982 Case Definition of AIDS

In 1982, the Centers for Disease Control's (CDC) case definition of what is now referred to as acquired immunodeficiency syndrome (AIDS) was "a disease at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that **disease**" (U.S. DHHS, PHS, CDC, MMWR, September 1982). Examples of opportunistic illnesses associated with the syndrome are listed below.

A. Protozoal and helminthic infections

1. Cryptosporidiosis, intestinal, causing diarrhea for over one month (on histology or stool microscopy).
2. Pneumocystis *carinii* pneumonia (on histology or on microscopy of a "touch" preparation or bronchial washings).
3. Strongyloidosis, causing pneumonia, central nervous system (CNS) infection, or disseminated infection (on histology) .
4. Toxoplasmosis, causing pneumonia or CNS infection (on histology or microscopy of a "touch" preparation).

B. Fungal infections

1. Candidiasis, causing esophagitis (on histology, microscopy of a "wet" preparation from the esophagus, or endoscopic findings of white plaques on an erythematous mucosal base).
2. Cryptococcosis, causing pulmonary, CNS, or disseminated infection (on culture, antigen detection, histology, or India ink preparation of CSF) .

C. Bacterial infection

1. "Atypical" mycobacteriosis (species other than tuberculosis or lepra), causing disseminated infection (on culture).

D. Viral infections

1. Cytomegalovirus, causing pulmonary, gastrointestinal tract, or CNS infection (on histology).
2. Herpes simplex virus, causing chronic mucocutaneous infection with ulcers persisting more than 1 month or pulmonary, gastrointestinal tract, or disseminated infection (on culture, histology, or cytology).
3. Progressive multifocal leukoencephalopathy (presumed to be caused by papovavirus) (on histology).

E. Cancer

1. Kaposi's sarcoma in persons less than 60 years of age (on histologic study).
2. Lymphoma, limited to the brain.

SOURCE: Selik, R.M., Haverkos, H.W., Curran, J.W., "Acquired Immune Deficiency Syndrome (AIDS) Trends in the United States, 1978-1982, " American Journal of Medicine 76(3):493-500, 1984.

Table B-2--The CDC's 1985 Case Definition of AIDS

[The Centers for Disease Control agreed] that the following refinements be adopted in the case definition of AIDS used for national reporting:

- A. In the absence of the opportunistic diseases required by the current [1982] case definition, any of the following diseases will be considered indicative of AIDS if the patient has a positive serologic or virologic test for HTLV-III/LAV [human T-cell lymphotropic virus, type III/lymphadenopathy-associated virus, presently termed human immunodeficiency virus (HIV)]:
1. Disseminated histoplasmosis (not confined to lungs or lymph nodes), diagnosed by culture, histology, or antigen detection;
 2. Isosporiasis, causing chronic diarrhea (over 1 month), diagnosed by histology or stool microscopy;
 3. Bronchial or pulmonary candidiasis, diagnosed by microscopy or by presence of characteristic white plaques grossly on the bronchial mucosa (not by culture alone);
 4. Non-Hodgkin's lymphoma of high-grade pathologic type (diffuse, undifferentiated) and of B-cell or unknown immunologic phenotype, diagnosed by biopsy;
 5. Histologically confirmed Kaposi's sarcoma in patients who are 60 years old or older when diagnosed. .
- B. In the absence of the opportunistic diseases required by the current case definition, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis in a child (under 13 years of age) will be considered indicative of AIDS unless test(s) for HTLV-III/LAV are negative.
- C. Patients who have a lymphoreticular malignancy diagnosed more than 3 months after the diagnosis of an opportunistic disease used as a marker for AIDS will no longer be excluded as AIDS cases.
- D. To increase the specificity of the case definition, patients will be excluded as AIDS cases if they have a negative result on testing for serum antibody to HTLV-III/LAV, have no other type of HTLV-III/LAV test with a positive result, and do not have a low number of T-helper lymphocytes or a low ratio of T-helper to T-suppressor lymphocytes. In the absence of test results, patients satisfying all other criteria in the definition will continue to be included.
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SOURCE: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Morbidity and Mortality Weekly Report, "Revision of the Case Definition of Acquired Immunodeficiency Syndrome for National Reporting--United States," 34(25):373-374, 1985.

Table B-3--The CDC's 1987 Case Definition of AIDS

I. Without Laboratory Evidence Regarding HIV Infection

If laboratory tests for HIV were not performed or gave inconclusive results . . . and the patient had no other cause of immunodeficiency listed in Section I.A below, then any disease listed in Section I.B indicates AIDS if it was diagnosed by a definitive method:

- A. Causes of immunodeficiency that disqualify diseases as indicators of AIDS in the absence of laboratory evidence for HIV infection.
 - 1. High-dose or long-term systemic corticosteroid therapy or other immunosuppressive/cytotoxic therapy < 3 months before the onset of the indicator disease.
 - 2. Any of the following diseases diagnosed < 3 months after diagnosis of the indicator disease: Hodgkin's disease, non-Hodgkin's lymphoma (other than primary brain lymphoma), lymphocytic leukemia, multiple myeloma, any other cancer of lymphoreticular or histiocytic tissue, or angioimmunoblastic lymphadenopathy.
 - 3. A genetic (congenital) immunodeficiency syndrome or an acquired immunodeficiency syndrome atypical of HIV infection, such as one involving hypogammaglobulinemia.

- B. Indicator diseases diagnosed definitively:
 - 1. Candidiasis of the esophagus, trachea, bronchi, or lungs.
 - 2. Cryptococcosis, extrapulmonary.
 - 3. Cryptosporidiosis with diarrhea persisting > 1 month.
 - 4. Cytomegalovirus disease of an organ other than liver, spleen, or lymph nodes in a patient "> 1 month of age.
 - 5. Herpes simplex virus infection causing a mucocutaneous ulcer that persists longer than 1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a patient > 1 month of age.
 - 6. Kaposi's sarcoma affecting a patient < 60 years of age.
 - 7. Lymphoma of the brain (primary) affecting a patient < 60 years of age.
 - 8. Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia (LIP/PHL complex) affecting a child < 13 years of age.
 - 9. Mycobacterium avium complex or *M. kansasii* disease, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes).
 - 10. *Pneumocystis carinii* pneumonia.
 - 11. Progressive multifocal leukoencephalopathy.
 - 12. Toxoplasmosis of the brain affecting a patient > 1 month of age.

II. With Laboratory Evidence of HIV Infection

Regardless of the presence of other causes of immunodeficiency (I.A.), in the presence of laboratory evidence for HIV infection . . . any disease listed above (I.B) or below (II.A or II.B) indicates a diagnosis of AIDS.

- A. Indicator diseases diagnosed definitively:
 - 1. Bacterial infections, multiple or recurrent (any combination of at least two within a 2-year period), or the following types affecting a child < 13 years of age:

septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media or superficial skin or mucosal abscesses), caused by *Haemophilus*, *Streptococcus* (including pneumococcus), or other pyogenic bacteria;

2. Coccidioidomycosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes);
3. HIV encephalopathy (also called "HIV dementia," "AIDS dementia," or "subacute encephalitis due to HIV") ...;
4. Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes);
5. Isosporiasis with diarrhea persisting > 1 month;
6. Kaposi's sarcoma at any age;
7. Lymphoma of the brain (primary) at any age.
8. Other non-Hodgkin's lymphoma of B-cell or unknown immunologic phenotype and the following histologic types:
 - a. small noncleaved lymphoma (either Burkitt or non-Burkitt type);
 - b. immunoblastic sarcoma (equivalent to any of the following, although not necessarily all in combination: immunoblastic lymphoma, large-cell lymphoma, diffuse histiocytic lymphoma, diffuse undifferentiated lymphoma, or high-grade lymphoma)
Note: Lymphomas are not included here if they are of T-cell immunologic phenotype or their histologic type is not described or is described as "lymphocytic," "lymphoblastic," "small cleaved," or "plasmacytoid lymphocytic";
9. Any mycobacterial disease caused by mycobacteria other than *M. tuberculosis*, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes),
10. Disease caused by *M. tuberculosis*, extrapulmonary (involving at least one site outside the lungs, regardless of whether there is concurrent pulmonary involvement) ;
11. *Salmonella* (nontyphoid) septicemia, recurrent;
12. HIV wasting syndrome (emaciation, "slim disease").

B. Indicator diseases diagnosed presumptively:

Note: Given the seriousness of diseases indicative of AIDS, it is generally important to diagnose them definitively, especially when therapy that would be used may have serious side effects or when definitive diagnosis is needed for eligibility for antiretroviral therapy. Nonetheless, in some situations, a Patient's condition will not permit the performance of definitive tests. In other situations, accepted clinical practice may be to presumptively based on the presence of characteristic clinical and laboratory abnormalities.

1. Candidiasis of the esophagus;
2. Cytomegalovirus retinitis with loss of vision;
3. Kaposi's sarcoma;
4. Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia (LIP/PHL complex) affecting a child < 13 years of age;
5. Mycobacterial disease (acid-fast bacilli with species not identified by culture), disseminated (involving at least one site other than or in addition to lungs, skin, or cervical or hilar lymph nodes);
6. Pneumocystis *carinii* pneumonia;
7. Toxoplasmosis of the brain affecting a patient > 1 month of age.

III. With Laboratory Evidence Against HIV Infection

With laboratory test results negative for HIV Infection . . . a diagnosis of AIDS for surveillance purposes is ruled out unless:

- A. all the other causes of immunodeficiency listed above in Section I.A are excluded; AND
- B. the patient has had either;
 - 1. *Pneuznocystis carinii* pneumonia diagnosed by a definitive method . . . ; or
 - 2. a. any of the other diseases indicative of AIDS listed above in Section I.B diagnosed by a definitive method . . . ; and
 - b. a T-helper/inducer (CD4⁺) lymphocyte count <400/mm³.

SOURCE: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, "1987 Revision of Case Definition for AIDS for Surveillance Purposes," Morbidity and Mortality Weekly Report 36(1S):4s-14s, 1987.