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1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults

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Summary

CDC has revised the classification system for HIV infection to emphasize the clinical importance of the CD4+ T-lymphocyte count in the categorization of HIV-related clinical conditions. This classification system replaces the system published by CDC in 1986 (1) and is primarily intended for use in public health practice. Consistent with the 1993 revised classification system, CDC has also expanded the AIDS surveillance case definition to include all HIV-infected persons who have less than 200 CD4+ T-lymphocytes/uL, or a CD4+ T-lymphocyte percentage of total lymphocytes of less than 14. This expansion includes the addition of three clinical conditions

- pulmonary tuberculosis, recurrent pneumonia, and invasive cervical cancer -- and retains the 23 clinical conditions in the AIDS surveillance case definition published in 1987 (2); it is to be used by all states for AIDS case reporting effective January 1, 1993.

REVISED HIV CLASSIFICATION SYSTEM FOR ADOLESCENTS AND ADULTS

The etiologic agent of acquired immunodeficiency syndrome (AIDS) is a retrovirus designated human immunodeficiency virus (HIV). The CD4+ T-lymphocyte is the primary target for HIV infection because of the affinity of the virus for the CD4 surface marker (3). The CD4+ T-lymphocyte coordinates a number of important immunologic functions, and a loss of these functions

results in progressive impairment of the immune response. Studies of the natural history of HIV infection have documented a wide spectrum of disease manifestations, ranging from asymptomatic infection to life-threatening conditions characterized by severe immunodeficiency, serious opportunistic infections, and cancers (4-13). Other studies have shown a strong association between the development of life-threatening opportunistic illnesses and the absolute number (per microliter o blood) or percentage of CD4+ T- lymphocytes (14-21). As the number of CD4+ T-lymphocytes decreases, the risk and severity of opportunistic illnesses increase.

Measures of CD4+ T-lymphocytes are used to guide clinical and therapeutic management of HIV-infected persons (22). Antimicrobial prophylaxis and antiretroviral therapies have been shown to be most effective within certain levels of immune dysfunction (23-28). As a result, antiretroviral therap should be considered for all persons with CD4+ T-lymphocyte counts of less than 500/uL, and prophylaxis against Pneumocystis carinii pneumonia (PCP), the most common serious opportunistic infection diagnosed in men and women with AIDS, is recommended for all persons with CD4+ T-lymphocyte counts of less than 200/uL and for persons who have had prior episodes of PCP. Because of these recommendations, CD4+ T- lymphocyte determinations are an integral part of medical management of HIV-infected persons in the United States.

The classification system for HIV infection among adolescents and adults has been revised to includ the CD4+ T-lymphocyte count as a marker for HIV-related immunosuppression. This revision establishes mutually exclusive subgroups for which the spectrum of clinical conditions is integrated with the CD4+ T-lymphocyte count. The objectives of these changes are to simplify the classificatio of HIV infection, to reflect current standards of medical care for HIV-infected persons, and to categorize more accurately HIV-related morbidity.

The revised CDC classification system for HIV-infected adolescents and adults * categorizes person on the basis of clinical conditions associated with HIV infection and CD4+ T- lymphocyte counts. The system is based on three ranges of CD4+ T- lymphocyte counts and three clinical categories and is represented by a matrix of nine mutually exclusive categories (Table 1). This system replaces the classification system published in 1986, which included only clinical disease criteria and which was developed before the widespread use of CD4+ T-cell testing (1).

- Criteria for HIV infection for persons ages greater than 13 years:

a. repeatedly reactive screening tests for HIV antibody (e.g., enzyme immunoassay) with specifi antibody identified by the use of supplemental tests (e.g., Western blot, immunofluorescence assay);

b. direct identification of virus in host tissues by virus isolation; c) HIV antigen detection; or d) a positive result on any other highly specific licensed test for HIV.

CD4+ T-Lymphocyte Categories

The three CD4+ T-lymphocyte categories are defined as follows:

- Category 1: greater than or equal to 500 cells/mL

- Category 2: 200-499 cells/uL

- Category 3: less than 200 cells/uL

These categories correspond to CD4+ T-lymphocyte counts per microliter of blood and guide clinical and therapeutic actions in the management of HIV-infected adolescents and adults (22-28). The revised HIV classification system also allows for the use of the percentage of CD4+ T-cells (Appendix A).

HIV-infected persons should be classified based on existing guidelines for the medical management of HIV-infected persons (22). Thus, the lowest accurate, but not necessarily the most recent, CD4+ T-lymphocyte count should be used for classification purposes.

Clinical Categories

The clinical categories of HIV infection are defined as follows: Category A

Category A consists of one or more of the conditions listed below in an adolescent or adult (greater than or equal to 13 years) with documented HIV infection. Conditions listed in Categories B and C must not have occurred.

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute (primary) HIV infection with accompanying illness or history of acute HIV infection (29,30) Category B

Category B consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical Category C and that meet at least one of the following criteria: a) the conditions are attributed to HIV infection or are indicative of a defect in cell-mediatec immunity; or b) the conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection. Examples of conditions in clinical Category B include, but are not limited to:

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting greater than 1 month
- Hairy leukoplakia, oral
- Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome
- Idiopathic thrombocytopenic purpura

- Listeriosis
- Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess
- Peripheral neuropathy

For classification purposes, Category B conditions take precedence over those in Category A. For example, someone previously treated for oral or persistent vaginal candidiasis (and who has not developed a Category C disease) but who is now asymptomatic should be classified in clinical Category B.

Category C

Category C includes the clinical conditions listed in the AIDS surveillance case definition (Appendix B). For classification purposes, once a Category C condition has occurred, the person will remain in Category C.

EXPANSION OF THE CDC SURVEILLANCE CASE DEFINITION FOR AIDS

In 1991, CDC, in collaboration with the Council of State and Territorial Epidemiologists (CSTE), proposed an expansion of the AIDS surveillance case definition. This proposal was made available for public comment in November 1991 and was discussed at an open meeting on September 2, 1992 Based on information presented and reviewed during the public comment period and at the open meeting, CDC, in collaboration with CSTE, has expanded the AIDS surveillance case definition to include all HIV-infected persons with CD4+ T- lymphocyte counts of less than 200 cells/uL or a CD4+ percentage of less than 14. In addition to retaining the 23 clinical conditions in the previous AIDS surveillance definition, the expanded definition includes pulmonary tuberculosis (TB), recurrent pneumonia, and invasive cervical cancer. * This expanded definition requires laboratory confirmation of HIV infection in persons with a CD4+ T-lymphocyte count of less than 200 cells/uL or with one of the added clinical conditions. This expanded definition for reporting cases to CDC becomes effective January 1, 1993.

- Diagnostic criteria for AIDS-defining conditions included in the expanded surveillance case definition are presented in Appendix C and Appendix D.

In the revised HIV classification system, persons in subcategories A3, B3, and C3 meet the immunologic criteria of the surveillance case definition, and those persons with conditions in subcategories C1, C2, and C3 meet the clinical criteria for surveillance purposes (Table 1).

COMMENTARY Revised Classification System

The revised classification system for HIV infection is based on the recommended clinical standard of monitoring CD4+ T- lymphocyte counts, since this parameter consistently correlates with HIV-related immune dysfunction and disease progression and provides information needed to guide medical management of persons infected with HIV (14-18, 22-28). The classification system also allows for use of the percentage of CD4+ T-cells instead of absolute CD4+ T-lymphocyte counts (Appendix A). Other markers of immune status -- such as serum neopterin, beta-2 microglobulin, HIV p24 antigen, soluble interleukin-2 receptors, immunoglobulin A, and delayed-type

hypersensitivity (DTH) skin-test reactions -- may be useful in the evaluation of individual patients bu are not as strongly predictive of disease progression or as specific for HIV-related immunosuppression as measures of CD4+ T-lymphocytes (14-21, 31). DTH skin-test reactions are often used in conjunction with the Mantoux tuberculin skin test to evaluate HIV-infected patients for TB infection and anergy (31-33).

Other systems have been proposed for classification and staging of HIV infection (1, 31, 34-39). In 1990, the World Health Organization (WHO) published an interim proposal for a staging system for HIV infection and diseases that was based primarily on clinical criteria and included the use of CD4+ T-lymphocyte determinations (34). The WHO system incorporates a performance scale and total lymphocyte counts to be used in lieu of CD4+ T-lymphocyte determinations in countries where CD4+ T-lymphocyte testing is not available.

The accuracy of CD4+ T-lymphocyte counts is important for medical care of individual patients. To assure reliability, laboratories conducting CD4+ T-lymphocyte measurements should be experienced with test procedures, have established quality assurance methods, and participate in proficiency testing programs conducted by CDC or other organizations (22, 40). CDC has published guidelines for the performance of CD4+ T-cell determinations for HIV-infected persons (41). To assure that test results are indicative of a patient's medical condition, the health-care provider should evaluate the results with those of earlier tests and with the patient's clinical condition. In clinical practice, repeat CD4+ testing may be judged necessary in guiding thera- peutic decisions for individual patients. For surveillance purposes, however, a requirement for repeat CD4+ determinations is impractical for population-based monitoring.

The revised classification system of the clinical and immunologic manifestations of HIV infection provides a framework for categorizing HIV-related morbidity and immunosuppression and will assis efforts to evaluate the overall impact of the HIV epidemic. Knowledge of the spectrum of clinical conditions and the extent of immunosuppression that may occur during the course of HIV infection is important for prompt evaluation and for provision of appropriate health services. Clinicians should be aware of the clinical conditions suggestive of HIV infection and the need for prophylactic and therapeutic interventions.

This revised HIV classification system should be used by state and territorial health departments that conduct HIV infection surveillance. Because AIDS surveillance data will continue to represent only portion of the total morbidity caused by HIV, surveillance for HIV infection may be particularly useful in depicting the total impact of HIV on health-care and social services (42). More accurate reporting and analysis of CD4+ T-lymphocyte counts, together with HIV-related clinical conditions, should facilitate efforts to evaluate health-care and referral needs for persons with HIV infection and to project future needs for these services.

Expanded AIDS Surveillance Case Definition

The population of HIV-infected persons with CD4+ T-lymphocyte counts of less than 200/uL is substantially larger than the population of persons with AIDS-defining clinical conditions (43). The inclusion in the AIDS surveillance definition of persons with a CD4+ T-lymphocyte count of less than 200 cells/uL or a CD4+ percentage less than 14 will enable AIDS surveillance to reflect more accurately the number of persons with severe HIV-related immunosuppression and those at highest risk for severe HIV-related morbidity. Since the AIDS surveillance case definition was last revised in 1987, the increasing use of prophylaxis against PCP and antiretroviral therapy for persons infected

with HIV has slowed the rate at which HIV-infected persons develop AIDS-defining clinical conditions (2,22-25). For example, among homosexual/bisexual men with AIDS reported to CDC, the proportion with PCP decreased from 62% in 1988 to 46% in 1990 (44). This trend is expected to continue.

The ability of clinicians to report HIV-infected persons on the basis of CD4+ T-lymphocyte counts may also simplify the case-reporting process. A simplified AIDS surveillance case definition will be particularly important for outpatient clinics in which the availability of staff to conduct surveillance limited and from which an increasing proportion of AIDS cases are being reported. For example, from pre-1985 to 1988, the proportion of AIDS cases reported from outpatient sites in the state of Washington increased from 6% (9/155) to 25% (55/219) (45). A similar increase occurred in Oregon (25% {44/171} before 1987 to 38% {40/105} in the first half of 1989) (46).

Pulmonary Tuberculosis

Throughout the world, pulmonary TB is the most common type of TB in persons with HIV infection (47). The addition of pulmonary TB to the list of AIDS-indicator diseases is based on the strong epidemiologic link between HIV infection and the development of TB (48-50). Persons co-infected with HIV and TB have a substantially increased risk of developing active TB compared with persons without HIV infection (48, 49). In a prospective evaluation of injecting-drug users (IDUs) with positive tuberculin skin tests, the estimated annual incidence of active TB among 49 HIV-infected IDUs was 7.9 cases/100 person-years; however, no cases of active TB occurred among 62 tuberculin-positive but HIV-seronegative IDUs followed for as long as 30 months (48).

There is also a substantial immunologic association between HIV-infected persons and pulmonary TB when compared with HIV-infected persons with extrapulmonary TB (a condition included in the 1987 surveillance definition). In a recent review, median CD4+ T-lymphocyte counts in HIV-infected patients with pulmonary TB ranged from 250 to 500 cells/uL (51). In comparison, the median CD4+ lymphocyte count was 242 cells/uL in one study of persons with localized extrapulmonary TB and ranged from 70 to 79 cells/uL in two studies of patients with disseminated or miliary TB (51-53). In CDC's Adult and Adolescent Spectrum of HIV Disease (ASD) Project, 69% of HIV-infected persons with pulmonary TB had CD4+ T-lymphocyte counts of less than 200/uL, compared with 77% of persons with extrapulmonary TB (CDC, unpublished observations).

The addition of pulmonary TB to AIDS surveillance criteria will require continued collaboration between state and local TB and HIV/AIDS programs. Knowledge of a patient's HIV status is important for the proper medical management of TB because longer courses of therapy and prophylaxis are recommended for HIV-infected patients with TB (54). Furthermore, HIV-infected TB patients should be a priority for epidemiologic investigation because these persons are more likely to have HIV-infected contacts than are seronegative TB patients. TB contact follow-up among HIV-infected persons will help to ensure delivery of a full course of preventive therapy to these contacts, who are at greatly increased risk of developing active TB themselves.

Recurrent Pneumonia

With the exception of conditions included in the 1987 AIDS surveillance case definition, pneumonia, with or without a bacteriologic diagnosis, is the leading cause of HIV-related morbidity and death (55, 56). In addition, several studies have shown that persons with HIV-related immunosuppression are at an increased risk of bacterial pneumonia (57-59). For example, one study found that the yearly

incidence rate of bacterial pneumonia among HIV-infected IDUs without AIDS was five times that found in non-HIV-infected IDUs (58). Recurrent episodes of pneumonia (two or more episodes within a 1-year period) are required for AIDS case reporting because pneumonia is a relatively common diagnosis and multiple episodes of pneumonia are more strongly associated with immunosuppression than are single episodes. For example, data from the ASD Project indicate that the risk of an HIV-infected person having had one episode of pneumonia in a 12-month period is approximately five times higher among infected persons with CD4+ T-lymphocyte counts of less than 200/uL (320/2,411) than among those with higher CD4+ T-lymphocyte counts (90/2,792). In contrast, data from the same study indicate that the risk for multiple episodes of pneumonia in a 12-month period is approximately 20 times higher among HIV-infected persons with CD4+ T-lymphocyte counts of less than 200/uL (67/2,411) than among those with higher CD4+ T-cell counts (4/2,792) (CDC, unpublished observations).

Invasive Cervical Cancer

Several studies have found an increased prevalence of cervical dysplasia, a precursor lesion for cervical cancer, among HIV-infected women (60, 61). In a study of 310 HIV-infected women attending methadone maintenance and sexually transmitted disease clinics in New York City and Newark, New Jersey, cervical dysplasia was confirmed by biopsy and/or colposcopy in approximately 22%, a prevalence rate 10 times greater than that found among women attending family planning clinics in the United States (Wright TC, personal communication; 62). Several studies have documented that a higher prevalence of cervical dysplasia among HIV-infected women is associated with greater immunosuppression (Wright TC, personal communication; 61,63). In addition, HIV infection may adversely affect the clinical course and treatment of cervical dysplasia and cancer (64-69).

Invasive cervical cancer is a more appropriate AIDS-indicator disease than is either cervical dysplasi or carcinoma in situ because these latter cervical lesions are common and frequently do not progress to invasive disease (70). Also, cervical dysplasia or carcinoma in situ among women with severe cervicovaginal infections, which are common in HIV-infected women, can be difficult to diagnose. I contrast, the diagnosis of invasive cervical cancer is generally unequivocal.

Invasive cervical cancer is preventable by the proper recognition and treatment of cervical dysplasia. Thus, the occurrence of invasive cervical cancer among all women -- including those who are HIV-infected -- represents missed opportunities for disease prevention. The addition of invasive cervical cancer to the list of AIDS-indicator diseases emphasizes the importance of integrating gynecologic care into medical services for HIV-infected women.

Impact on AIDS Case Reporting

The expanded AIDS surveillance case definition is expected to have a substantial impact on the number of reported cases. The immediate increase in case reporting will be largely attributable to the addition of severe immunosuppression to the definition; a smaller impact is expected from the addition of pulmonary TB, recurrent pneumonia, and invasive cervical cancer, since many persons with these diseases will also have CD4+ T-lymphocyte counts of less than 200 cells/uL. If all of the approximately 1,000,000 persons in the United States with HIV infection were diagnosed and their immune status were known, it is estimated that 120,000- 190,000 persons who do not have AIDS-indicator diseases would be found to have CD4+ T-lymphocyte counts of less than 200 cells/uL (71) However, not all of these persons are aware of their HIV infection and of those who know their HIV

infection status, not all have had an immunologic evaluation; thus, the immediate impact on the number of AIDS cases will be considerably less than 120,000- 190,000. If AIDS surveillance criteria were unchanged, approximately 50,000-60,000 reported AIDS cases would be expected in 1993. Based on current levels of HIV and CD4+ testing, CDC estimates that the expanded definition could increase cases reported in 1993 by approximately 75%. Early effects of expanded surveillance will b greater than long-term effects because prevalent as well as incident cases of immunosuppression will be reported following implementation of the expanded surveillance case definition. In subsequent years, the effect on the number of reported cases is expected to be much smaller.

Uses of the HIV Classification System or AIDS Surveillance Case Definition

The revised HIV classification system and the AIDS surveillance case definition are intended for use in conducting public health surveillance. The CDC's AIDS surveillance case definition was not developed to determine whether statutory or other legal requirements for entitlement to Federal disability or other benefits are met. Consequently, this revised surveillance case definition does not alter the criteria used by the Social Security Administration in evaluating claims based on HIV infection under the Social Security disability insurance and Supplemental Security Income programs. Other organizations and agencies providing medical and social services should develop eligibility criteria appropriate to the services provided and local needs.

Confidentiality

The confidentiality of AIDS case reports -- including laboratory reports of HIV test results, CD4+ T-lymphocyte test results, and medical records under review by health department staff -- is of critical importance to maintaining effective HIV/AIDS surveillance. CDC and state health departments have implemented procedures and policies to maintain confidentiality and security of HIV/AIDS surveillance data (72). CDC's efforts include a federal assurance of confidentiality, the removal of names before encrypted records are transmitted to CDC, strict guidelines for the release of aggregate data, and the inclusion of confidentiality and security safeguards as evaluation criteria for federal funding of state HIV/AIDS surveillance activities (73). These strict criteria will continue to apply to cases reported under the expanded definition. CDC funding of surveillance cooperative agreements is dependent on the recipient's ability to ensure the physical security of case reports and on state policies or laws to protect the confidentiality of persons reported with AIDS. Failure to ensure the security and confidentiality of personal identifying information collected as part of AIDS or HIV surveillance activities will jeopardize federal surveillance funding.

CD4+ T-lymphocyte test results reported by laboratories will be an important adjunct to medical record review and provider-initiated reporting in order to increase completeness, timeliness, and efficiency of AIDS surveillance. Information from a laboratory-initiated report of a CD4+ T-lymphocyte count is insufficient for reporting a case of AIDS. Confirmation of HIV infection status and receipt of other surveillance information from the health-care provider or from medical or public health records will remain necessary.

Every effort should be made by health-care providers, laboratories, and public health agencies to protect the confidentiality of CD4+ T-lymphocyte test results, including the review of record-keeping practices in laboratories and health-care settings. Some states have considered additional means to assure the confidentiality of CD4+ T-lymphocyte test results. For example, a proposal in Oregon would allow health-care providers to send specimens to laboratories for CD4+ T-lymphocyte testing with a unique code for each person being tested. If the test result indicates a

CD4+ T-lymphocyte count of less than 200 cells/uL, the health department would notify the health-care provider that an AIDS case report is required if the person is HIV infected, the CD4+ T-lymphocyte count is valid, and the case has not been previously reported. Informed consent for CD4+ T-lymphocyte testing should be obtained in accordance with local laws or regulations. CD4+ T-lymphocyte test results alone should not be used as a surrogate marker for HIV or AIDS. A low CD4+ T-lymphocyte count without a positive HIV test result will not be reportable since other conditions may result in a low CD4+ T-lymphocyte count. Health-care providers must ensure that persons who have a CD4+ T-lymphocyte count of less than 200/uL are HIV infected before initiating treatment for HIV disease or reporting those persons as cases of AIDS.

CONCLUSION

The revised HIV classification system provides uniform and simple criteria for categorizing conditions among adolescents and adults with HIV infection and should facilitate efforts to evaluate current and future health-care and referral needs for persons with HIV infection. The addition of a measure of severe immunosuppression, as defined by a CD4+ T-lymphocyte count of less than 200 cells/uL or a CD4+ percentage of less than 14, reflects the standard of immunologic monitoring for HIV-infected persons and will enable AIDS surveillance data to more accurately represent those who are recognized as being immunosuppressed, who are in greatest need of close medical follow-up, and who are at greatest risk for the full spectrum of severe HIV-related morbidity. The addition of three clinical conditions -- pulmonary TB, recurrent pneumonia, and invasive cervical cancer -- to AIDS surveillance criteria reflects the documented or potential importance of these diseases in the HIV epidemic. Two of these conditions (pulmonary TB and cervical cancer) are preventable if appropriate screening tests are linked with proper follow-up. The third, recurrent pneumonia, reflects the importance of pulmonary infections not included in the 1987 definition as leading causes of HIV-related morbidity and mortality. Successful implementation of expanded surveillance criteria will require the extension of existing safeguards to protect the security and confidentiality of AIDS surveillance information.

APPENDIX A. Equivalences for CD4+ T-lymphocyte count and percentage of total lymphocytes

Compared with the absolute CD4+ T-lymphocyte count, the percentage of CD4+ T-cells of total lymphocytes (or CD4+ percentage) is less subject to variation on repeated measurements (18,74). However, data correlating natural history of HIV infection with the CD4+ percentage have not been as consistently available as data on absolute CD4+ T-lymphocyte counts (14-16,18,19,21,31). Therefore, the revised classification system emphasizes the use of CD4+ T-lymphocyte counts but allows for the use of CD4+ percentages.

Equivalences (Table A1) were derived from analyses of more than 15,500 lymphocyte subset determinations from seven different sources: one multistate study of diseases in HIV-infected adolescents and adults (59) and six laboratories (two commercial, one research, and three university-based). The six laboratories are involved in proficiency testing programs for lymphocyte subset determinations. In the analyses, concordance was defined as the proportion of patients classified as having CD4+ T-lymphocyte counts in a particular range among patients with a given CD4+ percentage. A threshold value of the CD4+ percentage was calculated to obtain optimal concordance with each stratifying value of the CD4+ T-lymphocyte counts (i.e., less than 200/uL and greater than or equal to 500/uL). The thresholds for the CD4+ percentages that best correlated with a CD4+ T-lymphocyte count of less than 200/uL varied minimally among the seven data sources (range, 13%-14%; median, 13%; mean, 13.4%). The average concordance for a CD4+ percentage of less than 14

and a CD4+ T-lymphocyte count of less than 200/uL was 90.2%. The threshold for the CD4+ percentages most concordant with CD4+ T-lymphocyte counts of greater than or equal to 500/uL varied more widely among the seven data sources (range, 22.5%-35%; median, 29%; mean, 29.1%). This wide range of percentages optimally concordant with greater than or equal to 500/uL CD4+ T-lymphocytes makes the concordance at this stratifying value less certain. The average concordance for a CD4+ percentage of greater than or equal to 29 and a CD4+ T-lymphocyte count of greater than or equal to 500/uL was 85% (CDC, unpublished data). Clinicians and other practitioners must recognize that these suggested equivalences may not always correspond with values observed in individual patients.

APPENDIX B. Conditions included in the 1993 AIDS surveillance case definition

- 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
- Added in the 1993 expansion of the AIDS surveillance case definition.

APPENDIX C. Definitive diagnostic methods for diseases indicative of AIDS

Cryptosporidiosis, Isosporiasis, Kaposi's sarcoma, Lymphoma, Pneumocystis carinii pneumonia, Progressive multifocal leukoencephalopathy, Toxoplasmosis, Cervical cancer Microscopy (histology or cytology)

Candidiasis Gross inspection by endoscopy or autopsy or by microscopy (histology or cytology) on a specimen obtained directly from the tissues affected (including scrapings from the mucosal surface), not from a culture

Coccidioidomycosis, Cryptococcosis, Cytomegalovirus, Herpes simplex virus, Histoplasmosis Microscopy (histology or cytology), culture, or detection of antigen in a specimen obtained directly from the tissues affected or a fluid from those tissues

Tuberculosis, Other mycobacteriosis, Salmonellosis Culture

HIV encephalopathy (dementia) Clinical findings of disabling cognitive or motor dysfunction interfering with occupation or activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings. Methods to rule out such concurrent illness and conditions must include cerebrospinal fluid examination and either brain imaging (computed tomography or magnetic resonance) or autopsy.

HIV wasting syndrome Findings of profound involuntary weight loss of greater than 10% of baseline body weight plus either chronic diarrhea (at least two loose stools per day for greater than or equal to 30 days), or chronic weakness and documented fever (for greater than or equal to 30 days, intermittent or constant) in the absence of a concurrent illness or condition other than HIV infection that could explain the findings (e.g., cancer, tuberculosis, cryptosporidiosis, or other specific enteritis).

Pneumonia, recurrent Recurrent (more than one episode in a 1-year period), acute (new x-ray evidence not present earlier) pneumonia diagnosed by both: a) culture (or other organism-specific diagnostic method) obtained from a clinically reliable specimen of a pathogen that typically causes

pneumonia (other than Pneumocystis carinii or Mycobacterium tuberculosis), and b) radiologic evidence of pneumonia; cases that do not have laboratory confirmation of a causative organism for one of the episodes of pneumonia will be considered to be presumptively diagnosed.

APPENDIX D. Suggested guidelines for presumptive diagnosis of diseases indicative of AIDS

Candidiasis of esophagus

a. Recent onset of retrosternal pain on swallowing; AND

b. Oral candidiasis diagnosed by the gross appearance of white patches or plaques on an erythematous base or by the microscopic appearance of fungal mycelial filaments from a noncultured specimen scraped from the oral mucosa.

Cytomegalovirus retinitis A characteristic appearance on serial ophthalmo-scopic examinations (e.g., discrete patches of retinal whitening with distinct borders, spreading in a centrifugal manner along the paths of blood vessels, progressing over several months, and frequently associated with retinal vasculitis, hemorrhage, and necrosis). Resolution of active disease leaves retinal scarring and atrophy with retinal pigment epithelial mottling.

Mycobacteriosis Microscopy of a specimen from stool or normally sterile body fluids or tissue from a site other than lungs, skin, or cervical or hilar lymph nodes that shows acid-fast bacilli of a species not identified by culture.

Kaposi's sarcoma A characteristic gross appearance of an erythematous or violaceous plaque-like lesion on skin or mucous membrane. (Note: Presumptive diagnosis of Kaposi's sarcoma should not be made by clinicians who have seen few cases of it.)

Pneumocystis carinii pneumonia

a. A history of dyspnea on exertion or nonproductive cough of recent onset (within the past 3 months); AND

b. Chest x-ray evidence of diffuse bilateral interstitial infiltrates or evidence by gallium scan of diffuse bilateral pulmonary disease; AND

c. Arterial blood gas analysis showing an arterial pO((2)) of less than 70 mm Hg or a low respiratory diffusing capacity (less than 80% of predicted values) or an increase in the alveolar-arterial oxygen tension gradient; AND

d. No evidence of a bacterial pneumonia.

Pneumonia, recurrent Recurrent (more than one episode in a 1-year period), acute (new symptoms, signs, or x-ray evidence not present earlier) pneumonia diagnosed on clinical or radiologic grounds by the patient's physician.

Toxoplasmosis of brain

a. Recent onset of a focal neurologic abnormality consistent with intracranial disease or a

reduced level of consciousness; AND

b. Evidence by brain imaging (computed tomography or nuclear magnetic resonance) of a lesion having a mass effect or the radiographic appearance of which is enhanced by injection of contrast medium; AND

c. Serum antibody to toxoplasmosis or successful response to therapy for toxoplasmosis.

Tuberculosis, pulmonary When bacteriologic confirmation is not available, other reports may be considered to be verified cases of pulmonary tuberculosis if the criteria of the Division of Tuberculosis Elimination, National Center for Prevention Services, CDC, are used. The criteria in use as of January 1, 1993, are available in MMWR 1990;39(No. RR-13):39- 40.

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