

For Debate

AIDS surveillance in Africa: a reappraisal of case definitions

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Disease surveillance—the ongoing systematic collection, analysis, interpretation, and dissemination of data concerning particular diseases—is essential for setting public health priorities, for providing a rational basis for health policy, and for implementing and evaluating interventions.¹ In few epidemics has surveillance played such an important role as in the AIDS epidemic.

Although increasing emphasis is now placed on surveillance for infection with human immunodeficiency virus,^{2,3} which can precede AIDS by 10 years or more,^{4,6} the counting of AIDS cases remains important in all national efforts to monitor the epidemic. Surveillance for AIDS provides a measure of severe morbidity and mortality caused by HIV which would not be assessed by reporting of HIV infections. Reporting of HIV infections may be influenced by self selection of those tested, whereas reporting of AIDS cases includes only people with severe symptomatic illness, who come into contact more uniformly with the health care system. Estimates of AIDS cases and deaths allow evaluation of the social, economic, and human costs of this epidemic in terms understood by the public, the media, and decision makers.

AIDS reporting in the United States is relatively complete, capturing an estimated 70-90% of deaths related to HIV infection.⁷ In contrast, the World Health Organisation estimates that not more than 10% of AIDS cases in Africa are reported,⁸ although this region includes some of the most heavily affected countries in the world.

This paper reviews problems of surveillance for AIDS in Africa and suggests modifications to the provisional clinical case definition for AIDS in adults proposed by WHO in 1986.⁹ The proposed case definition is intended primarily for epidemiological surveillance and may not be adequate for clinical work. For the care of individual patients a simple staging system of HIV infection and disease¹⁰ will be more useful than a surveillance case definition.

Limitations of the WHO clinical case definition for AIDS in Africa

The surveillance case definition for AIDS that was introduced by the Centers for Disease Control¹¹ was generally inapplicable in Africa because of limited facilities for diagnosing HIV infection and associated indicator diseases. For this reason the WHO introduced a clinical case definition for AIDS (box).⁹ By combining symptoms and signs common in AIDS, this clinical case definition has been used for AIDS surveillance in many countries, without depending on laboratory tests. For diagnosing HIV infection in hospital patients in Kinshasa, Zaire, this definition had a sensitivity of 59%, a specificity of 90%, and positive

World Health Organisation clinical case definition of AIDS for use in Africa⁹

AIDS in an adult is defined by the existence of at least two major signs associated with at least one minor sign in the absence of known causes of immunosuppression such as cancer or severe malnutrition or other recognised aetiologies

Major signs

- Weight loss >10% body weight
- Chronic diarrhoea >1 month
- Prolonged fever >1 month (intermittent or constant)

Minor signs

- Persistent cough >1 month
- Generalised pruritic dermatitis
- Recurrent herpes zoster
- Oropharyngeal candidiasis
- Chronic progressive and disseminated herpes simplex infection
- Generalised lymphadenopathy

The presence of generalised Kaposi's sarcoma or cryptococcal meningitis are in themselves sufficient for the diagnosis of AIDS

and negative predictive values of 74% and 81% respectively.¹² Such evaluations of the case definition are not entirely satisfactory because not all people positive for HIV have AIDS; some seropositive inpatients may have early HIV infection without substantial immune deficiency, and some may have advanced disease associated with HIV infection but not meet the AIDS case definition.

Inadequacies of the WHO definition are its lack of sensitivity, that its positive predictive value is only moderate, and its failure to include certain symptoms and signs common in HIV infection, such as neurological disease. Use of the WHO clinical case definition for AIDS underestimates the frequency of serious disease related to HIV. For example, we have shown in Abidjan that death rates are higher in HIV positive patients who do not meet the case definition for AIDS than in HIV negative hospital patients; this suggests that some patients are dying of HIV associated disease not recognised as AIDS.¹³ In Nairobi an increased rate of life threatening bacterial infections, especially with *Streptococcus pneumoniae* and *Salmonella typhimurium*, was documented in HIV positive patients irrespective of whether they met the AIDS case definition.¹⁴

The fundamental problem with the clinical case definition is that laboratory test evidence of HIV

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HIV wasting syndrome

Centers for Disease Control

Findings of profound involuntary weight loss >10% of baseline body weight plus either chronic diarrhoea (at least two loose stools a day for 30 or more days) or chronic weakness and documented fever (for 30 or more days, intermittent or constant) in the absence of a concurrent illness or condition other than HIV infection that could explain the findings—for example, cancer, tuberculosis, cryptosporidiosis, or other specific enteritis

Modified definition used in Abidjan

Findings of profound involuntary weight loss >10% of baseline body weight or cachexia, plus either chronic diarrhoea (at least two loose stools a day for 30 or more days) or chronic fever (for 30 or more days, intermittent or constant) in the absence of a concurrent illness or condition unrelated to HIV infection that could explain the findings. It is not excluded by concurrent illnesses that may be related to HIV—for example, tuberculosis, cryptosporidiosis, isosporiasis, or lymphoma

infection is not included, although HIV infection plays a basic aetiological role in AIDS and associated conditions. We believe that AIDS case surveillance should make more use of HIV test results, and we outline our experience with different case definitions in the light of HIV test results.

Definitions for AIDS and the HIV wasting syndrome in hospital patients in Abidjan

The commonest manifestations of AIDS in Africa are profound weight loss, chronic diarrhoea, and chronic fever, the symptoms of so called "slim disease."¹⁵ The 1987 revision of the Centers for Disease Control's surveillance case definition included these manifestations as indicators of AIDS, incorporating them in the HIV wasting syndrome (box), but only if they were not associated with other conditions that could cause them, such as cryptosporidiosis or tuberculosis.¹⁶ Because it is often impossible in Africa to exclude underlying diseases such as tuberculosis or cryptosporidiosis in patients infected with HIV we have modified this definition (box) and will use this version in all subsequent discussion of the HIV wasting syndrome. Criteria for this modified definition of the HIV wasting syndrome include not only a combination of the major criteria of the WHO clinical case definition but also laboratory evidence of HIV infection.

We compared the use of the WHO clinical case definition and the definition of the HIV wasting syndrome in 1715 patients admitted in 1988-9 to the medical wards of Abidjan's two largest hospitals (Table I).¹⁷ The overall prevalence of HIV infection in these patients was 40%. Ten per cent of seronegative patients (106) fulfilled the WHO clinical case definition. Using

TABLE I—Medical inpatients in Abidjan fulfilling clinical case definition for AIDS and definition of HIV wasting syndrome

	No (%) of HIV positive patients (n=684)	No (%) of HIV negative patients (n=1031)
Fulfil WHO clinical case definition for AIDS	240 (35)	106 (10)
Do not fulfil WHO clinical case definition for AIDS	444 (65)	925 (90)
Fulfil modified definition of HIV wasting syndrome used in Abidjan	299 (44)	
Do not fulfil modified definition of HIV wasting syndrome	385 (56)	1031 (100)

the HIV wasting syndrome as indicative of AIDS not only excluded all HIV negative patients (by definition) but also increased the sensitivity of the case definition from 35% to 44% for diagnosis of AIDS among HIV positive hospitalised patients.

In Côte d'Ivoire patients with AIDS reported to the WHO have all had positive HIV test results; those suspected to have AIDS but with negative results or without test results available have not been counted as cases of AIDS. Among a subset of 2196 HIV positive people reported to the WHO as cases of AIDS in 1988-9, 84% (1835) met the WHO clinical case definition.¹⁸ The other 16% (361) met only the criteria of the HIV wasting syndrome.

WHO clinical case definition for AIDS in patients with tuberculosis

Tuberculosis may be the most important opportunistic infection related to HIV infection in Africa. High rates of HIV infection have been reported among patients with tuberculosis in many countries,¹⁹ and the incidence of tuberculosis has been shown to be substantially increased in HIV positive people.^{20, 21} Conflicting opinions exist, however, about whether HIV positive people with pulmonary tuberculosis should be reported as AIDS cases. In the recently proposed WHO clinical staging system, pulmonary tuberculosis in HIV infection is considered indicative of intermediate or moderate disease.¹⁰

Many patients with tuberculosis, irrespective of HIV state, have weight loss, fever, and cough, and the WHO clinical case definition for AIDS therefore has a low specificity in this population.²²⁻²⁵ Excluding cough as a criterion increases specificity,²⁵ but performance of the definition remains poor. Unless the results of HIV tests are known many patients with tuberculosis who have no HIV infection might be reported as having AIDS. On the other hand, if tuberculosis is excluded from AIDS reporting then one of the diseases most often associated with HIV will go unreported as related to HIV. The way the WHO clinical case definition for AIDS was worded⁹ made it uncertain how patients with tuberculosis were to be considered.

Suggested case definition for AIDS in Africa

For epidemiological surveillance an adult (>12 years) is considered to have AIDS if:

The Centers for Disease Control surveillance case definition for AIDS is fulfilled*

OR

A test for HIV infection gives positive results

AND

One or more of the following are present:

- >10% body weight loss or cachexia, with diarrhoea or fever, or both, intermittent or constant, for at least one month, not known to be due to a condition unrelated to HIV infection
- Tuberculosis with the features given above, or tuberculosis that is disseminated (involving at least two different organs) or miliary, or extrapulmonary tuberculosis (which may be presumptively diagnosed)
- Kaposi's sarcoma
- Neurological impairment sufficient to prevent independent daily activities, not known to be due to a condition unrelated to HIV infection (for example, trauma)

*Certain diseases indicative of AIDS under the CDC surveillance case definition, such as Kaposi's sarcoma, may have a high background incidence or prevalence in Africa, independent of HIV infection. Such conditions should be considered to indicate AIDS only in the presence of a positive HIV test result.

Case definition for AIDS in patients with tuberculosis in Abidjan

In Abidjan the overall prevalence of HIV infection in adult outpatients with tuberculosis is currently 43% (Projet RETRO-CI, unpublished data). The Centers for Disease Control's 1987 revised surveillance case definition for AIDS includes extrapulmonary tuberculosis in HIV positive people but not pulmonary tuberculosis as an indicator for AIDS. In developing countries the facilities to diagnose extrapulmonary tuberculosis are often limited, so that this diagnosis is often based solely on clinical grounds without laboratory confirmation.

Among 4219 consecutive adult patients with tuberculosis diagnosed in Abidjan over a recent 18 month period, only 18% (751)—and 25% (454) of 1833 HIV positive patients—were considered to have extrapulmonary tuberculosis. Patients found to have pulmonary tuberculosis on sputum smear testing accounted for 80% of all cases of tuberculosis (3384 cases) and for 73% of cases among HIV positive people (1331 cases), the rest being cases of suspected pulmonary tuberculosis based on findings on chest radiography and negative results on sputum microscopy. Clearly, pulmonary tuberculosis is the predominant type of tuberculosis in people infected with HIV. The attributable fraction²⁶ of cases of tuberculosis among HIV positive patients (the proportion of HIV positive patients in whom tuberculosis is attributable to HIV infection) in Abidjan is 84%.²⁷ This is sufficiently high to assume for surveillance purposes that pulmonary tuberculosis in an HIV positive person is attributable to HIV infection.

Being attributable to HIV infection is not enough by itself to justify tuberculosis in HIV positive people being considered an indicator of moderate to severe HIV disease. Evidence that tuberculosis (predominantly pulmonary) in HIV positive people represents severe HIV associated disease is provided by the important clinical differences between HIV positive and HIV negative patients with tuberculosis (table II). Among 4219 consecutive adult patients with tuberculosis, 62% (1130) of HIV positive patients met the WHO clinical case definition for AIDS compared with 49% (1160) of HIV negative patients (rate ratio 1.3, 95% confidence interval 1.2 to 1.3). Forty nine per cent (892) of HIV positive patients and 23% (550) of HIV negative patients met a modified case definition that excludes cough as a minor criterion (rate ratio 2.1, 95% confidence interval 1.9 to 2.3). Although tuberculosis responds well to standard treatment in most HIV positive patients, a significantly higher mortality on follow up has been found in HIV positive people.^{28, 29} In Abidjan, patients with pulmonary tuberculosis positive for HIV-I have a 17-fold risk of death compared with HIV negative patients (unpublished data). HIV infection clearly has an adverse effect on the clinical course of tuberculosis.

To provide a high specificity for moderate to severe HIV disease in a new case definition for AIDS for use in Africa we propose that not all HIV positive patients with pulmonary tuberculosis be reported as cases of AIDS but only those in whom tuberculosis is accom-

panied by features of the wasting syndrome, such as severe weight loss and chronic fever. In Abidjan, therefore, 62% of HIV positive patients with tuberculosis would be reported as cases of AIDS (table II).

The fact that tuberculosis is itself a serious communicable disease provides an additional reason for reporting it as an indicator of AIDS when it is associated with HIV. It is important for AIDS surveillance systems to document what proportion of patients with AIDS have tuberculosis. In addition, tuberculosis surveillance should take account of what proportion of patients with tuberculosis are HIV positive.

HIV infection and case definitions for AIDS in patients with neurological disease and Kaposi's sarcoma

Neurological manifestations of AIDS have received relatively little attention in Africa, and their incidence is probably underestimated. A study of 200 patients with AIDS from Tanzania showed that 72% had some abnormal neurological finding and documented prevalences of 11% for focal neurological abnormalities and 54% for AIDS dementia complex.³⁰ Cryptococcal meningitis is included under the WHO clinical case definition for AIDS, but other neurological manifestations are not. Scarcity of diagnostic facilities precludes inclusion in a surveillance case definition of any complex criteria requiring brain imaging or biopsy, such as those for diagnosing toxoplasmosis or lymphoma of the brain. The prevalence of even more easily diagnosed conditions such as cryptococcal meningitis is uncertain among African patients with AIDS. As a result the causes of AIDS associated neurological abnormalities are not always easily categorised. Therefore we propose the inclusion within the surveillance case definition of any severe neurological impairment interfering with independent daily life and not due to any known cause unrelated to HIV infection (for example, trauma or hypertension). This would probably cover most neurological presentations of AIDS without undue lack of specificity. Cases of HIV encephalopathy as defined under the revised Centers for Disease Control surveillance case definition for AIDS¹⁶ would clearly be included when such criteria were used, as would infections or cancers affecting the central nervous system.

The WHO clinical case definition for AIDS specifies disseminated Kaposi's sarcoma as indicative of AIDS. However, HIV associated Kaposi's sarcoma may be localised and sometimes resembles the classic, endemic variety. In contrast, aggressive Kaposi's sarcoma sometimes occurs in the absence of HIV infection. We propose that all cases of Kaposi's sarcoma in a person with HIV infection, whatever the clinical pattern, should be considered indicative of AIDS.

Recommendations for future action

Surveillance for severe HIV associated disease should be based on clinical presentation combined with HIV test results. For surveillance, any test used in current practice for diagnosing HIV-I or HIV-II infections would be acceptable. Supplemental testing should not be an issue for surveillance as the predictive value of positive screening test results in patients with symptoms is high. For AIDS surveillance in Africa we propose the case definition shown in the box. Use of this case definition would improve sensitivity of case finding among HIV positive people, encompass neurological presentations of AIDS as well as HIV associated tuberculosis, but exclude HIV negative patients from being reported as cases of AIDS. This proposed case definition is simpler than that suggested by the Pan

TABLE II — Patients with tuberculosis in Abidjan fulfilling different AIDS case definitions

	No (%) of HIV positive patients (n = 1833)	No (%) of HIV negative patients (n = 2386)
Fulfil WHO clinical case definition for AIDS	1130 (62)	1160 (49)
Do not fulfil WHO clinical case definition for AIDS	703 (38)	1226 (51)
Fulfil modified WHO clinical case definition (cough excluded as criterion)	892 (49)	550 (23)
Do not fulfil modified WHO clinical case definition	941 (51)	1836 (77)
Fulfil modified definition of HIV wasting syndrome used in Abidjan	1141 (62)	
Do not fulfil modified definition of HIV wasting syndrome	692 (38)	2386 (100)

American Health Organisation,³¹ which also incorporates HIV test results but depends on a points scoring system which makes it cumbersome to use; there has been little published evaluation of its use. The definition we propose could be used in countries outside Africa, where the Centers for Disease Control surveillance case definition is inapplicable, but it would need to be evaluated.

Because the Centers for Disease Control surveillance case definition remains the international standard, patients fulfilling its criteria should be reported as cases of AIDS irrespective of whether the features of the proposed new definition are present. Nevertheless, diseases that have a high background incidence in Africa independent of HIV infection, such as endemic Kaposi's sarcoma in certain areas, should be considered indicative of AIDS only in the presence of a positive HIV test result.

Against this proposal it may be argued that resources in some areas will be inadequate to perform widespread HIV testing and that scarce tests should be used for prevention rather than clinical purposes or surveillance. We agree that priorities must be set in the use of resources, but we believe that much more use of HIV testing is needed in sub-Saharan Africa for clinical activities as well as public health activities. Discussion should focus on how reliable HIV testing can be made available on a large scale, how supplemental ("confirmatory") testing can be undertaken in a valid and cost effective manner, and how ethical standards can be guaranteed in all work entailing HIV testing. The epidemic of AIDS in Africa deserves more resources than have been allocated to it to date.

Some would argue that it is unrealistic to expect AIDS surveillance in Africa to provide data of sufficient quality to be useful for public health planning. By use of relatively simple mathematical models that take account of seroprevalence, duration of the HIV epidemic, and known rates of disease progression, current and future AIDS cases can be estimated.³² The results provided by such models require validation, and even if case surveillance is imperfect, if done at all it should be done in the best possible fashion, with the best possible case definition. Specific studies to examine the incidence of AIDS³³ or mortality related to AIDS³³ can also provide useful information but still require an appropriate case definition.

Changes in the performance of surveillance systems or in the sensitivity and specificity of case definitions may make it difficult to analyse and project trends and to distinguish between increasing incidence and increasing completeness of diagnosis or reporting. Because surveillance for AIDS in Africa is currently very incomplete we believe this to be a minor disadvantage. More serious is the loss of sensitivity that may result from failure to report cases of AIDS because of lack of HIV testing. If lack of sensitivity of the system is suspected because of the requirement for positive results on HIV testing then investigations should be undertaken to assess this and define needed resources. In the immediate future, reporting of AIDS where HIV testing is not possible could continue using the WHO clinical case definition for AIDS until the proposed new definition could be introduced, but reports should clearly specify that HIV testing was not performed. Such data would be of increasingly limited value.

The WHO clinical case definition has served its purpose well, but experience has highlighted difficulties with its use. We hope that this paper will stimulate broad discussion about surveillance for AIDS in Africa. Although a simple and reliable case definition is required, this alone cannot satisfy the need for strong political and medical commitment

to complete and timely reporting of AIDS or for determined interventions to control the spread of HIV infection.

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