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Editorial points out the different purposes for Center For Disease Control (CDC) case definition and the Walter Reed (WR) staging classification of HIV infection. CDC classification having a primarily epidemiological and public health bias while WR classification a prognostic and severity of illness indicator for a specific patient. Authors agree with Dr. Justice who wants a classification system for patients with end stage disease, but believe her system falls short in four areas, 1) use of CDC definition as starting place, 2) possibility of biased patient population as basis, 3) use of broad measures of physiologic deficits, 4) inability of system to predict survivability of end stage patients.

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A staging system for infection with the human immunodeficiency virus (HIV) must meet similar objectives. However, HIV infection results in multisystem disease, and individual subspecialties have developed their own classification schemes to help them understand the involvement of a particular organ system. But such schemes cannot stand alone. Eventually, the clinical classification of HIV infection must be consolidated in one common, comprehensive system that is based on pathogenesis, so as to encompass diagnosis, prognosis, and treatment.

In 1982 the Centers for Disease Control (CDC) formulated a case definition for the surveillance of a new and mysterious condition, the acquired immunodeficiency syndrome (AIDS).¹ This arbitrary classification was designed to speed the discovery of the cause of this clinical enigma. Within three years, the AIDS case definition fulfilled its purpose by helping researchers identify the causative agent and thus define HIV disease, thereby making the concept of the syndrome "AIDS" an anachronism.

In 1985 the Walter Reed Staging Classification of HIV infection was introduced,^{2,3} dividing HIV infection into a hierarchy of stages of clinical immunologic dysfunction in order to provide a prognostic framework for patient care that was based on pathogenesis and to hasten the evaluation of new therapeutic interventions. This system has been used extensively to evaluate more than 3000 personnel of the U.S. armed forces, and it continues to fulfill both of its original goals.⁴

In 1986 the CDC introduced an alternative classification system,^{5,6} intended for "disease reporting and surveillance, epidemiological studies, prevention and control activities, and public health policy and planning." According to the new system, "classification in a particular group [was] not explicitly intended to have prognostic significance, nor to designate severity of illness."⁵

Both these HIV classification systems encompass the full range of manifestations of HIV infection — a perspective whose importance was emphasized in the executive summary of the report issued by the Presidential Commission on the Human Immunodeficiency Virus Epidemic.⁷ But the report goes further:

The term AIDS is obsolete. HIV infection more correctly defines the problem. The medical, public health, political, and community leadership must focus on the full course of HIV infection rather than concentrating on the later stages of disease (ARC and AIDS). Continual focus on AIDS rather than the entire spectrum of HIV infection has left our nation unable to deal adequately with the epidemic.⁷

Why, then, on the anniversary of the Presidential commission's report, is the *Journal* publishing a description of a classification system that is entirely restricted to patients with AIDS?⁸ Dr. Justice and her colleagues maintain in this issue that improved clinical staging is needed for patients with end-stage disease, and they propose that a new scheme is required for the potential evaluation of new AIDS therapy and

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TOWARD A BETTER CLASSIFICATION SYSTEM FOR HIV INFECTION

HAVING a useful classification system is critical to understanding and treating any complex disease process. Some classification systems help with diagnosis, such as the Jones criteria for acute rheumatic fever. Some describe the natural history of a disease, such as the primary, secondary, and tertiary stages of syphilis. Others emphasize prognosis, such as the Dukes classification of adenocarcinoma of the colon or the staging classification for Hodgkin's disease. But all time-honored classification systems provide a basis for treatment, and all have conceptual value.

to assist physicians, patients, and families in planning. We agree. None of the classification systems currently employed addresses these needs adequately.

Although HIV infection causes a predictable, progressive, and ultimately fatal immunologic disease, the infection itself is treatable, though not currently curable. Our therapeutic arsenal for use against HIV infection and its complications is expanding rapidly. Just a few years ago, survival after the first episode of *Pneumocystis carinii* pneumonia was approximately 10 months, but with early diagnosis, antiretroviral therapy (zidovudine), and prophylaxis against pneumocystis, the average survival now approaches two years. Furthermore, the distinctions in HIV infection between clinical research and the standard of care have become blurred. Because of the relentlessness of end-stage infection, advances in research have quickly become standard treatments. However, there is often substantial variation in care from one center to the next. In the evaluation of patients in the end stage, any useful prognostic classification will require an accurate assessment of the progression of disease at that stage in order to guarantee comparability for randomization, identification of therapeutic end points, and help clinicians formulate optimal care plans. The last requirement is essential when physicians, patients, and their families attempt to predict entry into the preterminal stage of infection.

Despite our wholehearted concurrence on the need for a classification that will meet these objectives, we fear that the system developed by Justice et al.,⁹ although it is a start, may ultimately fall short. Our pessimism is based on four serious areas of concern: the use of the CDC definition of AIDS as a starting point in the development of the classification scheme; the possibility that the population sample used to develop the system may have been biased in its selection or unrepresentative of the current population of patients with AIDS; the use of extremely broad measures of physiologic deficits; and the system's inability to identify end-stage patients who, though acutely ill, may survive for a long time nonetheless.

As noted above, the CDC diagnosis of AIDS was not intended for clinical prognostic use. It has become clear, for example, that the prognosis of AIDS when Kaposi's sarcoma is present differs markedly from that observed when opportunistic infection (Walter Reed stage 6) is involved.¹⁰ Any prognostic classification must reflect some degree of immunologic parity among the patients to whom it is applied. The overall median survival of five months in the present study was rather poor.¹¹ The patients with Kaposi's sarcoma in the study survived a median of 5.3 months, and patients with isolated candida esophagitis only 5.5 months. The most likely explanation is that these patients represented a highly selected tertiary-referral population.

Major limitations in the system of Justice et al. also result from the broad definition of deficits and the lack

of temporal continuity in the definition criteria. Each defect may arise from multiple causes, potentially under markedly differing clinical circumstances with widely varying outcomes. For example, a patient with a first episode of pneumocystis pneumonia and a partial pressure of arterial oxygen of 48 mm Hg, confusion due to hypoxia, and transient leukopenia would be classified Stage III. Yet all these conditions may be readily reversed with standard medical intervention. It is also suggested that HIV-infected persons with Kaposi's sarcoma and thrombocytopenia have an extremely poor prognosis. Yet this contrasts with the clinical experience in which prolonged survival in these subpopulations has been documented.¹² A review of the life-table curves suggests that "distinctive prognostic gradients" were unique to the first four months of survival. After that period, all three groups appear to have parallel linear regression curves, suggesting comparable survival. However, the emphasis this system places on the vital function of the bone marrow is valuable, since the natural history of progressive HIV infection is strongly associated with progressive bone marrow failure.

All physicians who care for patients infected with HIV have experienced the frustration expressed by the authors.⁹ The challenge to develop a practical, systematic classification system for end-stage disease (Walter Reed stage 6) is clearly evident. Already, the survival of such patients has more than doubled, heightening the need for a discriminator of end-stage survival. In patients with end-stage HIV infection, such predictors will depend on the function of vital organs, particularly bone marrow, and not on overall immunologic function.

But awareness of the repeating nature of the process of defeating disease may be helpful: first description and empiricism, then understanding of pathogenesis with consequent improvement in therapies, and finally a cure. Ultimately, to promote early diagnosis, accurate clinical staging, and timely treatment, we must focus on HIV infection within its pathogenic framework. In this way we optimize both the science and the art of the practice of medicine.

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