THE DIAGNOSIS AND DEFINITION OF THE ACQUIRED IMMUNODEFICIENCY SYNDROME*

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INTRODUCTION

Since June 1981, the acquired immunodeficiency syndrome (AIDS) has been reported in over 10,000 individuals in the United States and in over 500 individuals from other countries. Epidemiologic evidence has suggested that a new transmissible agent is, at least in part, responsible. The Center for Disease Control (CDC) has defined this syndrome as the occurrence of opportunistic infections or Kaposi's sarcoma in previously healthy individuals less than 60 years of age with no other underlying medical condition or therapy associated with immunodeficiency. This surveillance definition has been easily applied by clinicians from a variety of backgrounds and has been useful in monitoring the evolution of this epidemic at the national level. It has helped to define major risk groups in the population with approximately 95% of cases continuing to be restricted to homosexual or bisexual males, intravenous drug users, hemophiliacs. However, the full extent of this problem is undoubtedly underestimated by this definition. In areas where AIDS is endemic, a syndrome which includes unexplained persisting generalized lymphadenopathy or a chronic wasting syndrome has also been increasingly recognized, principally in the major risk groups noted\(^1-3\). One prospective study has demonstrated that as high as 15% of such individuals will either develop AIDS as defined by the CDC or lymphomas, and raises the concern that a poorly defined AIDS-related disorder currently exists affecting a larger population\(^1\). The scope of this problem is further complicated by case reports suggesting possible carrier states in asymptomatic individuals capable of transmitting the disease\(^4-6\) and by the recognition of a related syndrome in infants born principally to mothers who are Haitian or intravenous drug users\(^7,8\).

*Editor's note: The Chapter represents the state of knowledge of AIDS in 1983. A brief addendum follows the text.
Delineating the full spectrum of AIDS will ultimately require a broadened definition which relates complex immunologic, virologic, and clinical abnormalities to the natural history of AIDS and related disorders. Common to all affected individuals with the fully developed syndrome has been a severe and thus far irreversible depression of the host immune system. The complexity of these abnormalities likely relates to the combined effects of the etiologic agent in AIDS and the immunosuppressive effects of secondary de novo or reactivated viral infections. This report will review the characteristic immunologic abnormalities seen in CDC-defined AIDS and summarize the clinical and laboratory characteristics of these other AIDS-related disorders.

Early descriptions of AIDS occurring with opportunistic infections recognized profound deficits in cellular immunity. Patients were anergic to a variety of recall antigens and in vitro their T cells demonstrated hyporesponsiveness to mitogens soluble antigens, and to alloantigens. Lymphopenia was seen frequently and analysis with monoclonal antibodies to T cell subsets demonstrated a marked reduction in the relative and absolute number of helper/inducer T cells reactive with the antibodies OKT4 or Leu-3a. In the setting of normal absolute numbers and a relative increased percentage of suppressor/cytotoxic T cells reactive with OKT8 or Leu-2a, severe reductions in the "helper to suppressor cell ratio" or T4/T8 ratio were seen. Normally, about 2.0, T4/T8 ratios less than 0.1 were often present in patients whose primary disease manifestation was opportunistic infection. Less severe but significant reductions were seen in patients presenting with Kaposi's sarcoma alone without opportunistic infections. Limited reports of functional studies have indicated that T4 cells are not only reduced in number but are qualitatively defective in their ability to provide help to B cells in immunoglobulin production. T8 cells, on the other hand, were shown to have normal suppressor function in this assay. Less severe but significant alterations in T lymphocyte subsets and proliferative capacity have been reported in homosexual men from endemic areas with a syndrome characterized by chronic (>3-6 months), unexplained generalized lymphadenopathy. Others have noted mild but significant reductions in the helper/suppressor ratio in asymptomatic homosexual men from endemic but not nonendemic areas. Although the progressive decline in T4/T8 ratios seen in these groups suggest a related disorder differing only in severity, the nonspecificity of this alteration, which can be seen particularly in viral infections common among homosexual men, has complicated the interpretation of these results. Fahey has drawn attention to the absolute numbers of T cell subsets rather than percentages and has suggested that a low helper/suppressor cell ratio in asymptomatic