SUMMARY OF PROJECTS PERTAINENT TO THE SYNDROME OF UNEXPLAINED ACQUIRED IMMUNODEFICIENCY

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Introduction

During the past two years more than 450 previously healthy American adults have been affected by a highly lethal syndrome characterized by profound cellular immune dysfunction, Kaposi's sarcoma, Pneumocystis carinii pneumonia, and other opportunistic infections. Although first recognized in homosexual men, it is now clear that the disease affects intravenous drug addicts, Haitian immigrants, and probably patients with Hemophilia A. The epidemic pattern, highly concentrated in groups with Hepatitis B, and reports of case clustering make the case for a new infectious agent plausible. Other reports have implicated recreational drugs as potentially immunosuppressive. Finally, antecedant host characteristics, such as chronic antigenic stimulation, may be important in the manifestation of the disease.

Studies of apparently healthy groups

1) In collaboration with Dr. Robert Biggar and a dozen other investigators we have recently completed the field work for a cross sectional immuno-epidemiology survey of 250 healthy homosexual men, 160 in Washington, D.C., and 90 in New York City. Data from questionnaires and physical examinations is being processed, and laboratory testing (helper/suppressor T-lymphocyte ratios, viral antibodies, etc.) will commence shortly on frozen specimens.

With multiple linear and logistic regression analyses we will focus on low helper/suppressor ratios and drug use, sexual practices and partners, and prior medical illnesses.

2) With investigators in Denmark, Dr. Biggar has done a cross sectional survey on Danish homosexuals with a questionnaire. Two hundred men participated in that survey, and 100 contributed semen specimens to evaluate the prevalence and correlates of active CMV excretion. Another 70 men contributed blood specimens for helper/suppressor ratios with an internal case-control design to evaluate the significance of drug use and/or sex with American men.

3) Three follow-up studies are in progress on the 15 healthy homosexual men that we reported in the Lancet. Their status was unchanged during six months of prospective evaluation, and we will examine them and repeat their immune studies in August 1982 to complete 12 months of intense scrutiny. With other investigators we will soon report that some of these men and more with Kaposi's sarcoma have a circulating lupus-like alpha interferon. Finally, an autoantibody panel is being evaluated as an investigatory tool.

4) Other groups that should be investigated with small pilot studies are as follows:

Lesbians--We have made preliminary inquiries with a group of New York lesbians as a negative control group. This would help to clean the slate regarding homosexual tendencies as risk factors.

Prostitutes--We consider this an extremely high-priority group to study because of the possibility for heterosexual transmission. Any study which hopes to focus on transmission must be done in the epidemic center, and we have an interested collaborator in the venereal disease section of the NYC Department of Health. Unfortunately, his superiors have stopped us from proceding. The reasons for this are unclear.

Promiscuous heterosexual men--The corollary to the prostitute study, with the same collaborator and the same problem.

Heroin addicts--Another high-priority group because of their established risk for immunodeficiency. Access will be a major stumbling block, since the best group to evaluate would probably be current IV drug users, perhaps at a police in-take center.

Caribbean Blacks--Haitians are being investigated in Miami, but laboratory studies have not been done on healthy Haitian immigrants or in Haiti. We have no contacts in Haiti, but would have ready access to and/or eager collaborators in Jamaica and the Virgin Islands. It is unclear how best to procede with these resources.

Hemophiliacs--Unlike with prostitutes, the vehicle of infection for these patients would be nationally distributed concentrated coagulation factors. Undoubtably others will study this group, but perhaps we could try a new tack like a prospective study of newly-diagnosed hemophiliacs with storage of part of every lot of factor concentrate that they use.

Hemodialysis patients and/or personnel--Two groups at theoretical risk. The data on uremic patients would be very difficult to evaluate, but a study of dialysis nurses might be readily feasible and very informative.

5) A sexual partners study (contacts of men with Kaposi's sarcoma or opportunistic infections) is proceding slowly because of the small number of local cases and the interests of other investigators. Thus far we have about six partners, and a perliminary immunologic evaluation is in progress.

Laboratory studies

1) A parasitology laboratory at CDC has evaluated eight semen specimens from our group of New York homosexuals for Pneumocystis carinii, but proteinaceous debris has limited this inquiry.

2) The laboratory of Drs. Ed Gelmann and Robert Gallo are evaluating peripheral blood lymphocytes from our two Kaposi's sarcoma patients and others from New York. Thus far none have been found.

3) We hope to address the issue of clonality of Kaposi's sarcoma by evaluating paired or triplicate tumor specimens from the same patient with cytogenetic or CMV-DNA molecular hybridization studies. The major limitation with these and a host of other potential NIH laboratory studies has been the unavailability of patients.

4) Drs. Bill Wallen, Paul Levine, and Bob Biggar have evaluated the potential immunosuppressive synergy of primary CMV infection and amyl nitrite exposure in Rhesus monkeys. The effects thus far are unclear.

Summary

The epidemiologic clues at this point to a transmissible agent, probably a virus. The critical needs at this point are the acquisition of adequate biologic materials for an intensive laboratory investigation and for the characterization and quantification of high risk groups. If there is a causitive agent, it will most likely reside in the lymphocytes, so specimen acquisition should not be as difficult as it has been. The other source might be coagulation factor concentrates, and perhaps a sample survey with retrovirus assays might prove useful. Every step would appear to require a coordinated, multidisciplinary epidemiologic and laboratory approach to sorting out this lethal syndrome.