

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Joseph F. Fraumeni, Jr., M.D.
Chief, Environmental Epidemiology Branch, NCI

DATE: October 13, 1981

FROM : James J. Goedert, M.D.
Family Studies Section, EEB/NCI



SUBJECT: Studies of Immune Function, Viral Infections, and Drug Use in
Homosexual Men

Attached to this memorandum are copies of two memorandums summarizing the September 15 workshop on Kaposi's sarcoma and immunosuppression in homosexual men. Our ongoing research studies of this current epidemic are summarized as follows:

1. In vitro immune function studies, utilizing the fluorescence activated cell sorter (FACS), being conducted on 15 healthy male homosexual volunteers from the New York metropolitan area and on 2 homosexual men with Kaposi's sarcoma have shown a profound inversion of the normal helper/suppressor T-lymphocyte ratio in the patients with malignancy, and a similar (although less severe) inversion in 7 of the healthy homosexual men. These 17 homosexuals and an additional homosexual man with multiple opportunistic infections had serum antibodies performed for herpes group viruses at the same time that the FACS analysis was being performed. Virtually all of the patients had markedly elevated antibody titers to cytomegalovirus (CMV); but more remarkably, they showed a predominance of IgM-type antibody which probably indicates either repeated new infections or an immune defect in the ability to make the normal switch from IgM- to IgG-type antibodies. Dr. Bill Wallen of the NINCDS, our collaborating virologist, indicates that there is an animal model for this kind of immune defect.

Sequential studies of both immune function and virus antibody titers are planned for both the cases and healthy men. This should help elucidate the immunosuppressive capabilities of CMV, and perhaps sort out a broad range of high virus antibody titers and immune function abnormalities in these men.

2. Simultaneous with our follow-up studies in the healthy men described above, a "nitrite challenge test" has been designed to investigate the acute immunosuppressive capability of inhaled isobutyl nitrite in experienced nitrite users. FACS analysis will be performed before and after every half-hour nitrite inhalation in four regular nitrite users. Controls will include identical studies of a non-nitrite using homosexual and a heterosexual male, neither of whom have been acutely exposed to the drug. The subjects will be selected from the group described above.
3. Mutagenesis studies utilizing urine and perhaps blood will be performed on the entire group described above and before and after the nitrite challenge test. The specifics of these studies and the collaborators to be involved are being developed.

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4. Dr. Wallen is particularly interested in investigating the possibility that there is a neurologic deterioration syndrome with chronic CMV infection. A brief pilot interview of neurologic symptoms is being developed for the group described above.
5. A description of the current epidemic of Kaposi's sarcoma and immunosuppression in homosexual men was presented to the Capitol Area Physicians Association on Sunday evening, October 11. Several members of this Washington-based group of homosexual physicians has indicated an interest in contributing their patient resources and professional capabilities to our research studies. The most fruitful of these thus far has been the observation of diffuse undifferentiated or lymphoblastic lymphomas in four homosexual men. All four patients are currently alive, and we have been able to obtain serum and peripheral blood lymphocytes from one of these cases. We will probably obtain similar materials from two of the other homosexual lymphoma cases for immunologic and serologic studies similar to those described above.
6. The SEER system is currently tabulating the incidence rates for a wide variety of subtypes of non-Hodgkin's lymphomas by age group for never-married men compared to other marital categories. If it appears that the incidence of undifferentiated and lymphoblastic lymphomas in never-married men is increasing disproportionately with those in other marital categories, we will attempt to pursue a confirmatory investigation utilizing the U. S. Navy medical records system. Case-control studies of such patients are, of course, also contemplated.
7. Prospective evaluation during the course of the next 12 months of some 50 new renal transplant patients at the National Naval Medical Center utilizing FACS analysis and viral serology will commence shortly. This will better define the immune dysfunction induced by CMV in the setting of other immunosuppressive agents. This will be particularly useful since this group does not use inhaled nitrites.

The current epidemic of immunosuppression in homosexual men continues to evolve, but the essential questions appear to be as follows:

1. What is the scope of disease associated with immunosuppression in this group?
2. What is the immunosuppressive potential of inhaled nitrites?
3. What is the mutagenic potential of inhaled nitrites?
4. What is the immune defect induced by repeated or chronic CMV infection?

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5. Is there a profile of serologic and immunologic studies which can be used to describe the clinically immunosuppressed homosexual men?

We are making every effort to utilize the available resources of the Environmental Epidemiology Branch to answer these questions.

Attachments

cc: Dr. M. H. Greene
Dr. W. A. Blattner
Family #2000 file