Immunological abnormalities in South African homosexual men

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Summary

Immunological tests of cell-mediated immunity (CMI), serological tests for antibodies to sexually transmitted and possibly immunosuppressive viruses, determination of serum immunoglobulin levels, full blood counts and serotyping for the HLA-DRw5 antigen were performed in 10 homosexual men with a mean age of 35 years (range 21-59 years). Five of these were associates of a patient who had died of confirmed acquired immunodeficiency syndrome (AIDS). At the time of investigation 9 of the men were apparently healthy and 1 had active pulmonary tuberculosis.

Only in 2 subjects were no abnormalities of CMI found; they were 23 and 28 years of age and, interestingly, were also the only 2 whose sera were negative for antibodies to cytomegalovirus (CMV) and for the other viruses investigated. Of the remainder, 1 was lymphopenic, 6 had increased numbers of circulating suppressor T lymphocytes, 4 had reduced delayed-type hypersensitivity skin responses to recall antigens, and in 6 mitogen-induced lymphocyte transformation was decreased. Of these 8 subjects, 4 and 2 had antibodies to hepatitis B surface and core antigens respectively and 1 was positive for hepatitis B surface antigen and HBe antigen.

The most severe abnormalities were observed in individuals who were seropositive for both CMV and hepatitis B virus. These findings indicate the existence of acquired immunosuppression in some members of the South African homosexual community. On the basis of these findings an immunological classification of potential sufferers of AIDS in the male homosexual community is proposed.

Since the medical community was alerted to the existence of the acquired immunodeficiency syndrome (AIDS) by the Centers for Disease Control in Atlanta, USA there has been an alarming increase in the number of cases documented. AIDS is associated with severe opportunistic infections and/or Kaposi’s sarcoma. The condition has been documented primarily in homosexual and bisexual men, with some cases reported in heterosexual drug abusers, haemophiliacs and Haitian immigrants to the USA.

The common denominator in cases of AIDS is the presence of serious immunosuppression. A severe acquired deficiency of cell-mediated immunity (CMI), as measured by delayed skin tests and in vitro tests of T-lymphocyte function, has been demonstrated. This anergic condition is associated with a selective reduction in the numbers of circulating helper T cells which promote CMI, with a consequent reversal of the ratio of the helper subset to the suppressor subset (the T4 : T8 ratio) resulting in a selective predominance of suppression. Humoral immune responses remain intact. The types of opportunistic infections which these patients develop reflect the selective impairment of CMI. Of particular note were infections with Pneumocystis carinii, Cryptococcus neoformans, Candida albicans, Mycobacterium tuberculosis, Myco. avium (intracellular) and Toxoplasma gondii. Cytomegalovirus (CMV), herpesvirus infections were strikingly predominant as regards both documented infections and serum antibody titres indicating recent exposure.

However, the primary cause of AIDS remains unknown. It may be a novel sexually transmitted immunosuppressive agent (possibly a virus) or alternatively a promiscuity-related phenomenon due to repeated infection with sexually transmitted agents which cause transient immunosuppression and which may be cumulative over a prolonged period.

Recent reports have documented the existence of partial immunosuppression in apparently healthy homosexual men. The extent of the immunosuppression was related to the degree of promiscuity. In this study we have investigated the immunological status of 10 South African homosexual men, 5 of whom were associates of a man who died from confirmed AIDS. Our suggested test protocol for immunological investigation in suspected cases of AIDS is shown in Table 1.

Subjects and methods

All the men in this study were self-confessed homosexuals. The average age was 35 years (range 21-59 years). One patient was recovering from hepatitis B infection and 1 had active pulmonary tuberculosis at the time of investigation and was receiving treatment with antituberculosis drugs. All were South African and 9 had not been overseas within the last 5 years. The patient recovering from hepatitis B infection had recently returned from the USA. Seven requested investigation and 3 were referred by consultant physicians as possible AIDS cases. Five were associates of a patient who had recently died of AIDS, which had been diagnosed in Pretoria. Only 1 subject confessed to the occasional use of 'recreational' drugs, in this case amyl nitrite.

Serological markers of virus infection

Antibodies to CMV were determined by a standard complement fixation test, antibodies to herpesvirus and Epstein-Barr virus by indirect immunofluorescence and hepatitis virus markers by radio-immunoassay (Abbott Laboratories, Abbott Park, North Chicago, Illinois).
Suggested screening programme

TABLE I. PROTOCOL OF PROPOSED IMMUNOLOGICAL INVESTIGATION OF INDIVIDUALS WITH SUSPECTED AIDS


*Only if low platelet counts are observed.

TABLE II. TOTAL LEUCOCYTE AND LYMPHOCYTE COUNTS AND SERUM IMMUNOGLOBULIN LEVELS IN THE 10 HOMOSEXUAL MALES

<table>
<thead>
<tr>
<th></th>
<th>Heterosexual males</th>
<th>Homosexual males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total leucocyte count (x 10^9/lt)</td>
<td>6.4 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Absolute lymphocyte count (x 10^9/lit)</td>
<td>2.4 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>Serum immunoglobulin levels (g/lit)</td>
<td>11.8 ± 1.4</td>
<td>11.8 ± 1.4</td>
</tr>
<tr>
<td>IgG</td>
<td>2.9 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>IgA</td>
<td>1.4 ± 0.2</td>
<td></td>
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</tbody>
</table>

Results

Virus serology

Of the 10 subjects investigated, elevated titres for antibodies to CMV were found in 8, to herpesvirus in 6, to Epstein-Barr virus in 5, to hepatitis A virus in 3, and to hepatitis B virus surface and core antigens in 4 and 2 respectively. Circulating hepatitis B surface antigen and HBc antigen were detected in 1 subject.

Leucocyte counts and serum immunoglobulin levels

These are listed in Table II. An abnormal leucocyte count (< 4 x 10^9/l) with lymphopenia (< 1.5 x 10^9/l) was consistently observed in 1 subject who was tested on three different occasions. Increased serum IgG and IgA levels were observed in the patient with pulmonary tuberculosis.

CMI

Numbers and ratios of T and B lymphocytes were normal in all. However, when compared with a group of 6 healthy heterosexual male controls the mitogen-induced lymphocyte transformation and T4:T8 ratios were noted to be altered in the homosexuals. Decreased lymphocyte transformation and altered T4:T8 ratios were associated with reduced delayed-type hypersensitivity skin responses to recall antigens (Table III).

Only 2 of the homosexual men showed no abnormality of CMI as measured by lymphocyte transformation, assessment of T4:T8 ratios and skin testing. Interestingly, neither of these individuals was seropositive for CMV or hepatitis B virus. The 8 subjects with abnormalities in respect of one or more of the following—lymphocyte transformation, T4:T8 ratios and skin-test respon-

HLA-DRW5 typing

This was performed on purified B lymphocytes using HLA-DR typing trays supplied by the National Institutes for Health, Bethesda, Maryland, and eosin-exclusion antibody/complement cytotoxicity test.

TABLE III. CMI IN 10 HOMOSEXUAL MALES AND 6 HETEROSEXUAL MALE CONTROLS

<table>
<thead>
<tr>
<th></th>
<th>Delayed-type hypersensitivity to PHA (5 µg/ml)</th>
<th>Lymphocyte transformation to PHA (5 µg/ml)</th>
<th>T4 : T8 ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterosexual males</td>
<td>4.7 ± 1.5</td>
<td>39 362 ± 8 856</td>
<td>2.0 : 1</td>
</tr>
<tr>
<td>Homosexual males</td>
<td>2.5 ± 0.4</td>
<td>32 006 ± 8 856</td>
<td>1.7 : 1</td>
</tr>
<tr>
<td>No. with abnormal responses</td>
<td>4</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

*Results expressed as the mean number of positive skin tests ± standard error.
†Results expressed as the mean value ± standard error in radioactive counts per minute.
‡An abnormal response is taken as being less than the mean control value minus 1 standard deviation.
PHA = phytohaemagglutinin.
TABLE IV. TESTS OF CMI IN HOMOSEXUAL MALES SEROPOSITIVE FOR CMV ONLY AND IN THOSE SEROPOSITIVE FOR BOTH CMV AND HEPATITIS B VIRUS

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Delayed-type hypersensitivity skin tests</th>
<th>PHA (5 μg/ml)</th>
<th>T4:T8 ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All 10 homosexual males</td>
<td>2.5 ± 0.4</td>
<td>320.6 ± 8.56</td>
<td>1.7:1</td>
</tr>
<tr>
<td>8 homosexual males with serum antibodies to CMV only</td>
<td>2.0 ± 0.4</td>
<td>21.81 ± 1.757</td>
<td>1.6:1</td>
</tr>
<tr>
<td>4 homosexual males with serum antibodies to both CMV and hepatitis B virus</td>
<td>2.0 ± 1.4</td>
<td>21.53 ± 5.649</td>
<td>1:1</td>
</tr>
</tbody>
</table>

*Results expressed as the mean number of positive skin tests ± standard error.
†Results expressed as the mean value ± standard error in radioactive counts per minute. PHA = phytohaemagglutinin.

siveness to recall antigens — were all seropositive for antibodies to CMV. Of these 8, 4 also had one or more serological markers for hepatitis B infection. These 4 subjects (seropositive for both CMV and hepatitis B infection) had the most striking changes in T4:T8 ratios (Table IV).

HLA-DRw5 typing

Of 9 subjects tested, 4 were positive for HLA-DRw5 antigen.

Discussion

In this study of the CMI status of 10 South African homosexual men we have documented the existence of immunological abnormalities in 8 of the 10 subjects investigated. Only 2 individuals showed a completely normal profile of responses. They were 23 and 28 years of age (less than the average age of the group) and stated that they were not promiscuous. This was indirectly confirmed by negative serological tests for antibodies to sexually transmitted viruses. The remaining 8 homosexual men showed abnormalities of one or more of the following: T4:T8 ratio, mitogen-induced lymphocyte transformation and delayed-type hypersensitivity skin testing.

The most severe abnormalities were noted in 3 of a subgroup of 4 individuals who had serological markers for both CMV and hepatitis B virus infection. One, aged 21 years, had active pulmonary tuberculosis at the time of investigation and a T4:T8 ratio of 1:1. In this case it is not yet known whether the underlying disease is the cause or the consequence of abnormal CMI. Another, a 42-year-old who had recently returned from a vacation in the USA, was convalescing after a bout of serum hepatitis infection and was a contact of one of the AIDS patients identified in Pretoria. He had markedly depressed lymphocyte transformation, total anergy to all 7 skin-test antigens, and a T4:T8 ratio of 1:1. The third was a 59-year-old with persistent lymphopenia, depressed lymphocyte transformation and an inverted T4:T8 ratio (1:1,5) but no history of opportunistic infections.

It has previously been reported that apparently healthy male members of the American homosexual community are partially immunosuppressed.6,7 The severity of the immunological abnormalities is related to the degree of promiscuity.6 These findings have been confirmed in the present study. It is unlikely that in this study the results were influenced by the use of 'recreational' drugs, such as marijuana, cocaine and amyl or butyl nitrite, commonly used by homosexuals.8 Some of these agents may be immunosuppressive.10 Active virus infections are also unlikely to have affected the results since 9 of the subjects were in good health according to clinical and laboratory investigations. CMV infection, infectious mononucleosis (Epstein-Barr virus),11 influenza, acute and chronic hepatitis B virus infection and primary biliary cirrhosis12,13 may cause alterations of the circulating

TABLE V. PROPOSED CLASSIFICATION OF HOMOSEXUAL MEN AT RISK OF DEVELOPING AIDS

<table>
<thead>
<tr>
<th>Class</th>
<th>Characteristics</th>
<th>Abnormalities according to protocol in Table I</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not promiscuous, age &lt; 30 years</td>
<td>Antibodies to CMV, partial skin-test anergy, slightly altered T4:T8 ratios, decreased lymphocyte transformation ± lymphopenia, total or partial skin-test anergy, reversed T4:T8 ratios, markedly depressed lymphocyte transformation, antibodies to CMV and hepatitis B virus</td>
</tr>
<tr>
<td>2</td>
<td>Promiscuous</td>
<td>As for class 3, but quantitatively more abnormal</td>
</tr>
<tr>
<td>3</td>
<td>Highly promiscuous, lymphadenopathy, weight loss, user of stimulant or other drugs</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Highly promiscuous, lymphadenopathy, weight loss, user of stimulant or other drugs, frequent attender of 'gay' bars, opportunistic infections with or without Kaposi's sarcoma present</td>
<td></td>
</tr>
</tbody>
</table>
T4:T8 lymphocyte ratios. The most likely interpretation of our findings is that the depressed CMI found in some South African homosexual men is a consequence of repeated infection with immunosuppressive sexually transmitted agents. Homosexual men are known to have an increased incidence of several sexually transmitted diseases, including infections with CMV, hepatitis A and B virus, Treponema pallidum, Neisseria gonorrhoeae, Giardia lamblia and Entamoeba histolytica. The immunosuppression observed may therefore be cumulative and promiscuity-related, arising over a number of years. In some individuals a threshold may be reached at which the immunosuppression is severe and irreversible, with development of opportunistic infections and AIDS. A classification of homosexual men at risk of developing AIDS is given in Table V.

Four of 9 individuals tested were positive for the HLA phenotype HLA-DRw5 which is found with increased frequency in homosexual men, especially those who develop Kaposi's sarcoma. The significance of our findings is difficult to assess because the study group is small.

Assuming that this group is representative, South African homosexual men are therefore similar to their counterparts in the USA in that many are likely to be partially immunosuppressed. If this partial immunosuppression is an intermediate state in a progressive deterioration of CMI terminating in fully developed AIDS, we are likely to see more cases of AIDS in South Africa.

The medical management of persons at risk of or already suffering from AIDS poses many problems. A high index of suspicion, based on the characteristics in Table V, should be maintained; the screening programme of tests (Table I) is well within the ambit of the general practitioner. If the skin tests indicate compromised cell-mediated reactions and more than two of the viral antibody tests are positive, we think that referral of the patient to an immunology centre for further assessment is justified.

All persons at risk should be warned about the consequences of promiscuity and the possible effects of drug abuse. Those failing in classes 3 and 4 (Table V) should, in addition, be advised to seek medical care as soon as any symptoms or signs of infection appear or if there is noticeable further weight loss, lymphadenopathy or signs of any tumour.

REFERENCES


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**Nuus en Kommentaar/News and Comment**

**Uterine rupture in Black patients**

Rupture of the uterus is not uncommon in Africa south of the Sahara, this being a measure of the low standard of obstetric care available. Vavdin and his colleagues analyse a series of 87 cases collected over a 5-year period at a hospital in Northern Ruanda (Med Trop 1983; 43: 37) during which 9994 births and 511 caesarean sections were recorded. The uterine rupture incidence of 0.9% of hospital confinements is similar to other figures quoted from Central Africa. There were 18 maternal and 79 fetal deaths, and 27 of the women had had two pregnancies or less before the uterus ruptured. All but 2 ruptures occurred during labour, and only 8 were due to an obstetric intervention.

The usual factors were found to favour uterine ruptures: (i) grand multiparity; (ii) previous caesarean sections (17%); (iii) pelvic contraction; (iv) abnormal presentations (20%); and (v) a large or hydrocephalic fetus. Yet in 22 cases none of these features were present and the labour appeared to be proceeding normally in a woman in good general condition. The authors suggest that in some of these cases a powerful oxytocic herbal preparation may have been given before admission to hospital.

**Sweaty palms and armpits**

'Make your armpits your charmpits' wrote an enthusiastic advertising copy writer in a pithy commercial on deodorants which was (possibly unfairly) rejected, but it serves to introduce a topic which causes considerable embarrassment to many people. Axillary hyperhidrosis, to revert to a more formal tone, can be treated surgically by excising a small area of skin containing most of the active sweat glands, and gives good results (Br Med J 1983; 286: 580). It can also be treated medically with topical aluminum chloride hexahydrate in alcoholic solution, as the aqueous solution is intolerably irritant. Sweaty palms are not quite so easy to deal with, although topical methenamine and alcoholic aluminium hydrate hexachloride have been tried. As neither of these were well absorbed into the palm, iontophoresis was used to improve passage through the skin, and a surprise finding was that tap-water iontophoresis worked as well as the other solution, and was devoid of side-effects. Surgery in these cases should not be undertaken lightly as supraclavicular sympathectomy carries a high risk of producing Horner's syndrome.