

## SEXUALLY TRANSMITTED INFECTIONS IN HOMO-BISEXUAL MEN.

### A SEROEPIDEMIOLOGICAL STUDY

#### "Infezioni sessualmente trasmesse in maschi omo-bisessuali: studio sieroepidemiologico"

MOSCHEN M.E.\* - BRUSAFERRO S.\* - FARISANO G.\* -  
BONELLO C.\* - BALDO V.\* - MAJORI S.° - GASPARINI V.\*

\* Institute of Hygiene - University of Padua

\* Chair of Hygiene - University of Udine

\* Pathology Laboratory, General Hospital, Dolo (Venice)

° Institute of Hygiene - University of Verona

#### SUMMARY

A total of 197 healthy homo-bisexual men between ages of 18 and 60 years, from North East Italy, were studied for antibodies against Epstein Barr virus viral capsid antigen (EBV-VCA), Cytomegalovirus (CMV), Herpes simplex virus (HSV) type 1 and 2, Hepatitis Virus type B (HBV) and C (HCV), Human Immunodeficiency Virus (HIV) and *Treponema pallidum*. Healthy male volunteer blood donors (87 subjects) matched for age were used as controls. The percentage of seropositive individuals in the homosexual group was higher (5.6 - 91.9%) for all the viruses tested than in the control group (0 - 37.6%). An increase in age was also accompanied by significantly higher antibody prevalence to CMV, HBV and *T. pallidum*. Seropositivity to various infectious agents was evaluated in relation to main risk factors associated with life style and sexual behaviour of this population. Correlation was found between HIV ( $P < 0.05$ ;  $P < 0.001$ ), CMV ( $P < 0.05$ ;  $P < 0.05$ ) seropositivity and both sexual promiscuity and number of

#### RIASSUNTO

E' stata studiata la prevalenza degli anticorpi anti-EBV-VCA, anti-CMV, anti-HSV tipo 1 e tipo 2, anti-HBV, anti-HCV, anti-HIV e anti-*T. pallidum* in un campione di 197 omo-bisessuali del Nord-Est Italia (età: 18-60 anni) in relazione ai principali fattori di rischio relativi allo stile di vita ed ai comportamenti sessuali. L'indagine sierologica ha evidenziato un tasso di prevalenza per i vari virus compreso tra 5.6 e 91.9% (tasso di prevalenza negli 87 controlli: 0-37.6%). La sieropositività per CMV, HBV e *T. pallidum* è risultata statisticamente correlata all'età dei soggetti esaminati. E' stata pure osservata una correlazione fra sieropositività per HIV e CMV e promiscuità sessuale e numero di rapporti/mese; tra HIV e HSV tipo 1 e rapporto anogenitale passivo; tra sieropositività per HSV tipo 2 e lue progressiva.

intercourses per month and also with HIV (P<0.05), HSV type 1 (P<0.01) and anogenital intercourse. Anti-viral positivity was not correlated with TPHA positivity except for HSV type 2.

Key words:

Homosexuals, sexually transmitted diseases, seroepidemiology.

Parole chiave:

Omosessualità, infezioni sessualmente trasmesse, sieroepidemiologia.

---

## Introduction

Male homosexuality is an important risk factor for sexually transmitted infectious diseases. Particularly, viral infections are common in healthy and in HIV infected homosexuals, producing genital and even extragenital manifestations.

Active, recurrent, past infections with Herpes Simplex Virus (HSV), Cytomegalovirus (CMV), Epstein Barr Virus (EBV), Hepatitis B Virus (HBV) are frequent in this population (8, 10, 11, 28, 33, 35), more than in heterosexual control groups (5, 31).

Moreover, the natural history of human immunodeficiency virus (HIV) infection indicates that HIV replication and progression to AIDS are strictly related to the activation of T4 cells induced by other concomitant viral infections.

Therefore it might be interesting to verify the frequency of selected viral exposures in homosexual men capable of inducing T4 cell activation.

The present study was undertaken to examine the prevalence of antibodies to viruses of the Herpes group (HSV1, HSV2, CMV, EBV) and also against hepatitis viruses B and C (HBV, HCV), HIV and *Treponema pallidum* in a group of homo/bisexual men.

Association between our findings with age, life style and type of sexual promiscuity was carried out.

## Subjects and methods

### *Design of the study*

Between January 1989 and December 1991, homosexual and bisexual men without AIDS were voluntarily enrolled during consultation service offered to subjects attending gay associations in North-East Italy. Special attention was dedicated to sexually transmitted diseases.

At his first visit each participant completed a baseline questionnaire, identified by a code number, in order to ensure anonymity. A blood sample was collected and information on past clinical symptoms and sexual practices during the previous six months (number of partners, type and frequency of sexual intercourse), drug addiction, previous diseases or blood transfusions and trips to endemic areas were obtained.

Sera were kept frozen until tested. They were tested for anti-HIV, HBV markers (HBsAg, anti-HBs and anti-HBc), anti-HCV, anti-CMV, anti-HSV (type 1 and 2), anti-EBV-VCA and TPHA test for *Treponema pallidum*.

### *Study population*

One hundred and ninety seven subjects (18-60 years) were examined.

The study population was asymptomatic homo-bisexual men without lymphadenopathy or other evidence of disease on physical examination.

Intravenous drug users were excluded from this study.

Eighty seven serum samples obtained from random male heterosexual blood donors were collected in the same period and geographical area, matched for age, and used as controls for the serological analysis.

### *Laboratory tests*

Serum obtained from each volunteer was tested for antibodies to HIV by ELISA (Abbott) and confirmed by Western Blot (Du Pont).

Serum samples were tested for anti-HCV by means of a third

generation, commercially available ELISA (HCV 3.0 ELISA System, Ortho Diagnostics Inc., Raritan, NJ). In addition all sera were also tested for the presence of serum antibodies by means of another enzyme immunoassay, using three synthesized peptides as antigens, as previously described by one of the Authors (34). Anti-HCV reactive samples were considered positive only if both determinations resulted reactive. All ELISA positive specimens were confirmed by RIBA (Chiron Riba HCV 3.0 strip Immunoblot Assay).

Serum samples from HCV-positive subjects at the double screening test were suitable for HCV RNA determination, which was carried out by PCR amplification, as described by the same above mentioned Author (34).

Various HBV markers (HBsAg, ant-HBs and anti-HBc) were examined by ELISA tests (Abbott).

Antibodies (IgG) against CMV, HSV (type 1 and type 2), EBV (VCA-IgG) were assayed by ELISA (Wellcome; Du Pont). We investigated the presence of virus specific IgG since it acts as an indicator of past infection and also because it has been commonly used to assess the prevalence of these infectious agents in a study population.

A VDRL test and a TPHA test for *Treponema pallidum* antibodies was also performed (Wellcome).

### *Statistical analysis*

Standard statistical methods were used for data analysis: chi-square test, with Yate's continuous correction if necessary, Fisher's exact test, Mantel Haenszel test.

In particular, possible association between viral seropositivity and various aspects of the homosexual's personal life style (number of partners, frequency and type of sex) were estimated by a Mantel Haenszel odds ratio (OR). The 95% confidence intervals (CI) were determined by Cornfield method.

All variables were available from all men except condom use which was referred only by a minority of the study group and therefore rejected.

Chi-square test for trend was used to check increasing risk of

viral infection with increasing age and number of sexual partners.

Statistical analyses were carried out using EpiInfo (ver. 5.01) computer software package supplied by the Centers for Disease Control, Atlanta, Georgia (USA).

## Results

The mean age of subjects at enrollment was 36.1. Table I summarizes the results of antiviral and anti-*T. pallidum* antibodies in both homosexual and control blood donor groups. The highest antibody prevalence was observed for HSV type 1 in the homosexual group and for EBV-VCA in the control group.

TAB. I - Association between sexual orientation and viral and treponemal seropositivity.

| Sexual preference     | % seropositive to |               |               |                 |                |               |       |        |            |
|-----------------------|-------------------|---------------|---------------|-----------------|----------------|---------------|-------|--------|------------|
|                       | HIV               | EBV           | CMV           | HSV1            | HSV2           | HBV           | HBsAg | HCV    | T.pallidum |
| homosexual            | 5.6               | 81.2          | 66.0          | 91.9            | 79.7           | 46.7          | 9.1   | 30.9   | 17.7       |
| heterosexual          | --                | 37.6          | 22.4          | 7.1             | 12.9           | 8.2           | --    | --     | --         |
| Odds Ratio            | *                 | 7.16          | 6.74          | 148.95          | 26.40          | 9.76          | *     | *      | *          |
| 95% C.I. <sup>a</sup> | *                 | 3.92<br>13.15 | 3.60<br>12.71 | 52.04<br>452.32 | 12.22<br>38.33 | 4.09<br>24.40 | *     | *      | *          |
| P <sup>b</sup>        | 0.059             | <0.001        | <0.001        | <0.001          | <0.001         | <0.001        | <0.01 | <0.001 | <0.001     |

\* Not calculable

<sup>a</sup> C.I. confidence interval

<sup>b</sup> Chi-square test with Yate's continuous correction

Differences with high statistical significance ( $p < 0.001$ ) in viral seroprevalence were observed for all, but HIV the examined viruses and also for *T. pallidum*.

By serological criteria, 61 out of 197 (30.9%) subjects had antibody to HCV. RIBA confirmed 41 samples (67.2%) as positive, while 15 (24.5%) were indeterminate, and 5 (8.2%) were negative.

HCV RNA was detected by PCR in 12 of the 61 homo-bisexual men with serological evidence of HCV infection.

In Table II the distribution of antibody prevalences in homo/bisexual men was investigated according to age. An increase in age was accompanied by significantly higher antibody prevalence levels to both viruses, CMV ( $P<0.01$ ) and HBV ( $P<0.001$ ) and also to *T. pallidum* ( $P<0.001$ ), while the highest prevalence rates in the various age groups were associated with HSV type 1 (91.9%), type 2 (79.7%) and EBV (81.2%).

TAB. II - Prevalence of antiviral and treponemal antibodies in homo/bisexual men by age.

| Age Group (years) | Subjects N° | % seropositive to |       |       |       |       |        |       |      |            |
|-------------------|-------------|-------------------|-------|-------|-------|-------|--------|-------|------|------------|
|                   |             | HIV               | EBV   | CMV   | HSV1  | HSV2  | HBV    | HBsAg | HCV  | T.pallidum |
| < 20              | 5           | --                | 100.0 | 40.0  | 100.0 | 100.0 | 20.0   | 20.0  | 20.0 | 20.0       |
| 20-29             | 92          | 8.7               | 81.5  | 58.7  | 90.2  | 77.1  | 39.1   | 7.6   | 31.5 | 8.7        |
| 30-39             | 61          | 1.6               | 77.0  | 68.8  | 90.1  | 75.4  | 44.2   | 8.1   | 34.4 | 21.3       |
| 40-49             | 28          | 7.1               | 89.2  | 82.1  | 96.4  | 89.2  | 71.4   | 10.7  | 28.6 | 32.1       |
| ≥ 50              | 11          | --                | 72.7  | 81.8  | 100.0 | 90.9  | 72.7   | 18.2  | 18.2 | 36.3       |
| Total             | 197         | 5.6               | 81.2  | 66.0  | 91.9  | 79.7  | 46.7   | 9.1   | 31.0 | 17.7       |
| P*                |             | 0.27              | 0.98  | <0.01 | 0.27  | 0.23  | <0.001 | 0.43  | 0.68 | <0.001     |

\*Chi-square test for linear trend

Of the entire homosexual study group, 106 subjects (53.8%) had a history of relationship with occasional partners (Table III), whereas 53 men (26.9%) had sexual contacts only with a steady partner in the previous six months before enrollment. Moreover 38 subjects (19.2%) referred both steady and non-steady partners. Sexual behaviour was significantly associated with both HIV and CMV. The type of relationship (steady and occasional partners or both) were each significantly associated ( $P<0.05$ ) with both HIV and CMV infection.

TAB. III - Prevalence of antiviral antibodies in homo/bisexual men by type of relationship.

| Partner           | Subjects N° | % seropositive to |      |       |      |      |      |      |
|-------------------|-------------|-------------------|------|-------|------|------|------|------|
|                   |             | HIV               | EBV  | CMV   | HSV1 | HSV2 | HBV  | HCV  |
| steady            | 53          | --                | 75.5 | 62.2  | 96.2 | 84.9 | 37.7 | 28.3 |
| occasional        | 106         | 5.6               | 85.8 | 60.3  | 90.5 | 77.3 | 49.0 | 27.4 |
| steady/occasional | 38          | 13.1              | 78.9 | 86.8  | 94.7 | 81.5 | 52.6 | 44.7 |
| P*                |             | <0.05             | 0.3  | <0.05 | 0.37 | 0.52 | 0.28 | 0.12 |

\* Chi-square test

In the homo/bisexual group with occasional partners the frequency of sexual encounters per month showed a wide variety (Table IV). Rates of viral seropositivity increased with the number of sexual intercourses, and differed significantly only for HIV and CMV: the number of partners/month was strongly associated ( $P < 0.001$ ) with anti-HIV prevalence. There was some, but less significant ( $P < 0.05$ ) difference in the CMV rates of seropositivity.

TAB. IV - Prevalence of antiviral antibodies in homo/bisexual men by number of partners/month.

| Partners/month | N° | % seropositive to |      |       |       |       |      |       |      |
|----------------|----|-------------------|------|-------|-------|-------|------|-------|------|
|                |    | HIV               | EBV  | CMV   | HSV1  | HSV2  | HBV  | HBsAg | HCV  |
| <2             | 45 | 4.4               | 84.4 | 53.3  | 93.3  | 71.1  | 51.1 | 11.1  | 22.2 |
| 3-5            | 42 | --                | 85.7 | 61.9  | 88.0  | 80.9  | 47.6 | 16.6  | 28.6 |
| 6-10           | 10 | --                | 80.0 | 70.0  | 90.0  | 80.0  | 40.0 | --    | 40.0 |
| ≥ 50           | 9  | 55.5              | 88.8 | 88.8  | 100.0 | 100.0 | 33.3 | 11.1  | 33.3 |
| P*             |    | <0.001            | 0.89 | <0.05 | 0.83  | 0.06  | 0.29 | 0.19  | 0.30 |

\* Chi-square test for linear trend

There was a wide variety of sexual practices in the study group. Measures of sexual behaviour has been classified into four specific groups which are presented in Table V.

TAB. V - Prevalence of antiviral antibodies in homo/bisexual men by sexual practices.

| Sexual intercourse            | Subjects N° | % seropositive to |       |      |       |      |      |      |
|-------------------------------|-------------|-------------------|-------|------|-------|------|------|------|
|                               |             | HIV               | EBV   | CMV  | HSV1  | HSV2 | HBV  | HCV  |
| anogenital receptive          | 5           | 20.0              | 100.0 | 80.0 | 100.0 | 80.0 | 60.0 | 20.0 |
| anogenital receptive + others | 91          | 9.9               | 83.5  | 75.8 | 92.3  | 82.4 | 53.8 | 30.8 |
| anogenital insertive          | 47          | --                | 80.8  | 63.8 | 74.4  | 87.2 | 42.5 | 36.2 |
| non-anogenital                | 54          | 1.8               | 81.5  | 62.9 | 92.5  | 74.0 | 37.0 | 27.8 |
| P*                            |             | <0.05             | 0.73  | 0.3  | <0.01 | 0.39 | 0.20 | 0.77 |

\* Chi-square test

Viral seropositivity reached the highest levels among participants with a history of only anogenital receptive sexual practices or combination of anogenital receptive and other types of sexual intercourses.

All measures of sexual behaviour were significantly related to seropositivity only for HIV ( $P < 0.05$ ) and for HSV type 1 ( $P < 0.01$ ).

Among the HIV-positive subjects higher levels of seropositivity, although not attaining statistical significance, were detected even for other sexually transmitted viruses and also for *T. pallidum* than among HIV-seronegative subjects (Table VI). OR were somewhat smaller for HSV type 1, type 2 and HCV positivity and the CI were narrower for HCV.

TAB. VI - Correlation between anti-HIV positivity and other sexually transmitted infections.

|                         | Subjects<br>N° | % seropositive to |       |       |      |       |      |            |
|-------------------------|----------------|-------------------|-------|-------|------|-------|------|------------|
|                         |                | EBV               | CMV   | HSV1  | HSV2 | HBV   | HCV  | T.pallidum |
| HIV +                   | 11             | 90.9              | 81.8  | 90.9  | 81.8 | 63.6  | 45.5 | 36.3       |
| HIV -                   | 186            | 81.7              | 64.5  | 90.8  | 79.0 | 45.7  | 30.1 | 15.6       |
| Odds Ratio <sup>■</sup> |                | 2.24              | 2.47  | 1.01  | 1.19 | 2.08  | 1.93 | 3.09       |
| 95% C.I. <sup>♦</sup>   |                | 0.28              | 0.48  | 0.12  | 0.23 | 0.52  | 0.45 | 0.71       |
|                         |                | 48.25             | 17.12 | 22.25 | 8.56 | 8.79  | 7.93 | 12.85      |
| P <sup>*</sup>          |                | 0.39              | 0.20  | 0.73  | 0.58 | 0.39* | 0.22 | 0.09       |

■ C.I. confidence interval

♦ Fischer's exact test

\* Chi-square test with Yate's continuous correction

Thirty-three sera (16.7%) from the study group were reactive in TPHA test (Table VII) and non-reactive in non-treponemal test. Since only the results of serological tests were available, no distinction could be made between treated and untreated syphilis. All of them had syphilis previously.

TAB. VII - Correlation between TPHA positivity and other sexually transmitted infections.

|                       | Subjects<br>N° | % seropositive to |      |      |       |        |      |       |      |
|-----------------------|----------------|-------------------|------|------|-------|--------|------|-------|------|
|                       |                | HIV               | EBV  | CMV  | HSV1  | HSV2   | HBV  | HBsAg | HCV  |
| TPHA +                | 33             | 12.1              | 81.8 | 78.7 | 100.0 | 96.9   | 63.3 | 6.0   | 33.3 |
| TPHA -                | 164            | 4.2               | 82.9 | 62.1 | 91.4  | 78.6   | 43.2 | 9.7   | 30.5 |
| Odds Ratio            |                | 3.09              | 0.93 | 2.26 | *     | 8.68   | 2.29 | 0.60  | 1.14 |
| 95% C.I. <sup>■</sup> |                | 0.71              | 0.32 | 0.87 | *     | 1.20   | 0.99 | 0.09  | 0.48 |
|                       |                | 12.85             | 2.77 | 6.10 |       | 176.64 | 5.34 | 2.93  | 2.70 |
| P <sup>*</sup>        |                | 0.87*             | 0.92 | 0.10 | 0.07* | <0.05  | 0.05 | 0.38* | 0.90 |

\* Not calculable

■ C.I. confidence interval

\* Chi-square test with Yate's continuous correction

♦ Fischer's exact test



No significant associations were observed between antiviral antibody prevalences and TPHA positivity, except for HSV type 2 ( $p < 0.05$ ; 95% CI=1.20-176.64), although lower levels of viral seropositivity were detected in subjects without reactive treponemal test. OR for EBV and HBsAg were  $\sim 1$  and had CI with lower limit values.

## Discussion

Various viral infections, especially those of the Herpesvirus group are observed frequently, and generally are persistent, in subjects at risk or already suffering from AIDS, in particular in homosexual men.

Studies of HSVs infections in homosexual subjects might be considered important for several reasons. First of all because HSVs infections have been recognized in these subjects as causes of very common diseases, with serious infections when affecting homosexual AIDS patients. Second because there is a reported association of CMV infection with Kaposi's sarcoma (4, 14, 15) and of EBV with primary CNS lymphoma in homosexuals (17). Moreover several immunologic abnormalities, primarily depression of cell mediated immunity, are also potentially associated with HSVs infections (especially CMV and EBV) (37).

Therefore CMV and/or EBV might be related to the pathogenesis of the acquired immunodeficiency syndrome.

The prevalence rates of HSVs infections among homo/bisexual men were, as expected, much more significantly ( $P < 0.0001$ ) higher than those among heterosexual controls of the same age range and geographical area.

The higher proportion of homosexual (94%) compared to heterosexual men (54%) showing CMV-specific antibodies (31) and the isolation of CMV and EBV through throat gargling (13, 35) and semen or urethral discharge (2, 5, 18, 21) of homosexual and also heterosexual men suggests sexual transmission of such viruses in both homosexual and heterosexual population (6), but with higher propensity in homosexual males. In fact, boosted immune response

following repeated exposures to herpes viruses from multiple partners or reactivation of latent infections or superimposed infections by different strains of the same virus have been reported in homosexuals with significantly higher titre levels compared to the normal blood donors (8, 31).

All together our results are quite in agreement with the findings of most seroepidemiological surveys, even though reaching lower seroprevalence rates (1, 5, 6, 11, 12, 22, 28, 31, 38).

The comparison between different data is particularly difficult due to such different kinds of serological tests employed, to variable serologic patterns of HSVs infections in different countries and also to distinct time of sera examination. Moreover different sexual behaviour in various homosexual groups or alternatively the use of "safe sex" measures during AIDS epidemic may have led to an effective decrease in the incidence of HSVs infections towards the end of the '80s, as seen in our results.

Influence of different risk factors on the herpesvirus humoral immunity of these men was evaluated. In our experience there was no statistically significant correlation, except for CMV and HSV type 1, between age or particular form of unsafe sexual habits (e.g.: relationship with occasional partners, higher number of partners, anogenital intercourse) and anti-HSVs antibody prevalence.

The CMV antibody prevalence among homosexual males in this report showed correlation with age as a result either of reactivation of latent virus or of reinfection by new different strains, since homosexual life style could expose a man to multiple CMV strains (41).

There are several reports indicating prevalence of CMV antibodies increasing significantly with age in homosexual men and at a faster rate than shown in heterosexual controls (2, 11, 16, 25, 28).

Moreover the seropositive homosexual men appear more likely to excrete CMV, although intermittently, compared to heterosexual men, showing an inverse relationship between age and CMV excretion (6). Although both homosexual and heterosexual men may be exposed to infected saliva of their sexual partners, homosexuals have an additional risk of exposure due to infected semen.

Since homosexual men appear to excrete CMV in semen at a higher titre and for a longer duration than in saliva and in urine (20)

and since anorectal mucosa is more susceptible to penetration by CMV than is mucosa of the oral cavity or upper gastrointestinal tract, it is understandable that CMV is an important pathogen in homosexual men who, due to their life style, may be exposed to recurrent infections by this virus, mainly from multiple partners as seen in our study group.

In our report the prevalence of HSV type 1 antibodies correlated with type of sexual practices with a higher IgG seroprevalence among those practising receptive anal intercourse compared to those practising anogenital insertive or non-anogenital practices, whereas no correlation was seen between HSV type 1 and number of sexual partners in the last six months of relationship.

In our study the higher number of sexual partners and sexual encounters with occasional partners did not allow increasing frequency of exposure inducing a specific antibody response to HSV-type 1, as was seen for CMV. This probably suggests a higher propensity of CMV to be sexually transmitted in homosexual men by frequent reinfections.

EBV has been discussed as a possible cofactor in the pathogenesis and clinical outcome of HIV infection, since EBV and HIV may coinfect B-lymphocytes (29). In our experience serologic evidence suggests that EBV infection is more common in homosexual than in heterosexual men, particularly in association with HIV infection. These results are in accordance with those of other serological and virological reports (23, 36, 40).

The immunosuppression caused by HIV infection may induce reactivation of EBV with various consequences which are still not well understood. It could be possible that EBV may be a "stimulus" for producing tumors or may have some important function in further evolution of AIDS, because of increased immunosuppression produced by a reactivated EBV infection.

Sexual promiscuity, the number of sexual intercourses/month and the unprotected ano-genital sex were the main recognized risk factors for HIV infection in our study group.

The present study examined sexual behaviour at the end of the '80s, a decade in which high-risk sexual behaviour, which favour the spreading of the virus was dramatically high in various urban settings

in developed countries. Although recently two main types of behaviour change have been recommended in USA gay clubs (i.e.: reduce the number of different sexual partners and eliminate the exchanging of body fluids during sexual encounters), the persistence of high-risk sexual activity continues among gay-bisexual men particularly in smaller cities, where very often the changes are not maintained over a length of time.

Seroprevalence of anti-HCV in homosexual men has been found significantly higher than that observed in heterosexuals, but lower than positivity to HBV.

No clear-cut correlation was found between hepatitis C virus and HIV positivity or sexual behaviour variables, in agreement with other surveys on homosexual men (7, 9, 26).

Sexual transmission of HCV in these subjects seems to be less important than that demonstrated for HBV.

However in our experience HIV infection appears to account for most cases of HCV infection, as reported also by Mortimer (30), even though without statistical significance, possibly due to the high serum globulin levels reached in HIV infected subjects, or depending on HIV immunodepression.

The seroprevalence of HBV among unvaccinated homosexual men is strikingly different from that of HCV and is comparable with the findings of Schreeder et al (39), but lower than that of other Authors (3, 19, 27, 32). The higher seroprevalence rate of HBV markers was related to sexual practices with occasional partners, although without statistical significance.

The immunological abnormalities caused by HIV infection probably permit reactivation or reinfection in particular with Herpesvirus group often with severe consequences.

Thus in AIDS epidemic time it seems very important to identify the factors that permit exposure to these agents among homosexuals. This was of particular importance in our study in the case of CMV, EBV, HSV type 1 and 2 for their high frequent infection rate for adverse effects on cell-mediated immune functions and because they have been suggested as cofactors in the progression of HIV infection to AIDS.

## REFERENCES

- 1) BERRY N.J., MACDONALD BURNS D., WANNAMETHEE G., GRUNDY J.E., LUIS F., PRENTICE H.G., GRIFFITHS P.D.: "Seroepidemiologic studies on the acquisition of antibodies to cytomegalovirus, herpes simplex virus, and human immunodeficiency virus among general hospital patients and those attending a clinic for sexually transmitted diseases". *J. Med. Virol.*, 24: 385-393 (1988).
- 2) BIGGAR R.J., ANDERSEN H.K., EBBESEN P., MELBYE M., GOEDERT J.J., MANN D.L., STRONG D.M.: "Seminal fluid excretion of cytomegalovirus related to immunosuppression in homosexual men". *Brit. Med. J.*, 286: 2010-2012 (1983).
- 3) BLEEKER A., COUTINHO R.A., BAKKER-KOK J., TIO D., DE KONING G.: "Prevalence of syphilis and hepatitis B among homosexual men in two saunas in Amsterdam". *Br. J. Vener. Dis.*, 57: 196-199 (1981).
- 4) BOLDOGH I., BETH E., HUANG E.S., KYALWAZI S.K., GIRALDO G.: "Kaposi's sarcoma. IV Detection of CMV DNA, CMV RNA and CMNA in tumor biopsies". *Int. J. Cancer.*, 28: 469-474 (1981).
- 5) BUIMOVICI-KLEIN E., LANGE M., ONG K.R., GRIECO M.H., COOPER L.Z.: "Virus isolation and immune studies in a cohort of homosexual men". *J. Med. Virol.*, 25: 371-385 (1988).
- 6) COLLIER A.C., MEYERS J.D., COREY L., MURPHY V.L., ROBERTS P.L., HANDSFIELD H.H.: "Cytomegalovirus infection in homosexual men. Relationship to sexual practices, antibody to human immunodeficiency virus, and cell-mediated immunity". *Am. J. Med.*, 82: 593-601 (1987).
- 7) CORONA R., PRIGNANO G., MELE A., GENTILI G., CAPRILLI F., FRANCO E., FERRIGNO L., GIGLIO A., TITTI F., BRUNO C., VERANI P., PASQUINI P.: "Heterosexual and homosexual transmission of hepatitis C virus: relation with hepatitis B virus and human immunodeficiency virus type 1". *Epidemiol. Infect.*, 107: 667-672 (1991).
- 8) DETELS R., VISSCHER B.R., FAHEY J.C., SCHWARTZ K., GREENE R.S., MADDEN D.L., SEVER J.L., GOTTLIEB M.S.: "The relation of cytomegalovirus and Epstein-Barr virus antibodies to T-cell subsets in homosexually active men". *JAMA*, 251: 1719-1722 (1984).
- 9) DONAHUE J.G., NELSON K.E., MUNOZ A., VLAHOV D., RENNIE L.L., TAYLOR E.L., SAAH A.J., COHN S., ODAKA N.J., FARZADEGAN H.: "Antibody to hepatitis C virus among cardiac surgery patients, homosexual men, and intravenous drug users in Baltimore, Maryland". *Am. J. Epidemiol.*, 134: 1206-1211 (1991).
- 10) DREW W.L., MILLS J., LEVY J., DYLEWSKI J., CASAVANT C., AMMAN A., BRODIE H., MERIGANT T.: "Cytomegalovirus infection and abnormal T-lymphocyte subset ratios in homosexual men". *Ann. Intern. Med.*, 103: 61-63 (1985).

- 11) DREW W.L., MINTZ L., MINER R.C., SANDS M., KETTERER B.: "Prevalence of cytomegalovirus infection in homosexual men". *J. Infect. Dis.*, 144: 188-192 (1981).
- 12) DYLEWSKI J.S., RASMUSSEN L., MILLS J., MERIGAN T.C.: "Large-scale serological screening for cytomegalovirus antibodies in homosexual males by enzyme-linked immunosorbent assay". *J. Clin. Microbiol.*, 19: 200-203 (1984).
- 13) FAUCIA S., MACHER A.M., LONGO D.L., LANE H.C., ROOK A.H., MASUR H., GELMANN E.P.: "Acquired immunodeficiency syndrome: Epidemiologic, clinical, immunologic and therapeutic considerations". *Ann. Intern. Med.*, 100: 92-106 (1984).
- 14) FENOGLIO C.M., OSTER M.W., LAGERFO P.: "Kaposi's sarcoma following chemotherapy for testicular cancer in homosexual man: Demonstration of cytomegalovirus RNA in sarcoma cells". *Hum. Pathol.*, 13: 955-959 (1982).
- 15) GIRALDO G., BETHE., HENLE W., HENLE G., MIKE V., SAFAI B., HURAUX J.M., MCHARDY J., DE-THÈ G.: "Antibody patterns to Herpesviruses in Kaposi's sarcoma. II. Serological association of American Kaposi's sarcoma with cytomegalovirus". *Int. J. Cancer.*, 22: 126-131 (1978).
- 16) GOEDERT J.J., BIGGAR R.J.: "Cytomegalovirus transmission among homosexual men". *Ann. Intern. Med.*, 100: 156 (1984).
- 17) HOCHBERG F.H., MILLER G., SCHOOLEY R.T., HIRSCH M.S., FEORINO P., HENLE W.: "Central nervous system lymphoma related to Epstein-Barr virus". *N. Engl. J. Med.*, 309: 745-748 (1983).
- 18) ISRAEL V., SHIRLEY P., SIXBEY J.W.: "Excretion of Epstein-Barr virus from the genital tract of men". *J. Infect. Dis.*, 163: 1341-1343 (1991).
- 19) KRYGER P., PEDERSEN N.S., MATHIESEN L., NIELSEN J.O.: "Increased risk of infection with hepatitis A and B viruses in men with a history of syphilis: relation to sexual contacts". *J. Infect. Dis.*, 145: 23-26 (1982).
- 20) LANG D.J., KUMMER J.F.: "Demonstration of cytomegalovirus in semen". *N. Engl. J. Med.*, 287: 756-758 (1972).
- 21) LANG D.J., KUMMER J.F., HARTLEY D.P.: "Cytomegalovirus in semen: persistence and demonstration in extracellular fluids". *N. Engl. J. Med.*, 291: 121-123 (1974).
- 22) LEVY E., MARGALITH M., SAROV B., SAROV I., RINALDO C.R., DETELS R., PHAIR J., KASLOW R., GINZBURG H., SAAH A.J.: "Cytomegalovirus IgG and IgA serum antibodies in a study of HIV infection and HIV related diseases in homosexual men". *J. Med. Virol.*, 35: 174-179 (1991).
- 23) MARGALITH M., SAROV B., SAROV I., RINALDO C., DETELS R., PHAIR J., KASLOW R., GINSBERG H., SAAH A.: "Serum IgG and IgA antibodies specific to Epstein-Barr virus capsid antigen in a longitudinal study of human immunodeficiency virus infection and disease progression in homosexual men". *AIDS Research and Human Retroviruses*, 6: 607-616 (1990).
- 24) MARTIN J.L., MARC A., GARCIA M.A., BEATRICE S.T.: "Sexual

*behavior changes and HIV antibody in a cohort of New York city gay men*". Am. J. Public. Health., 79: 501-503 (1989).

25) MELBYE M., BIGGAR R.J., EBBESEN P., ANDERSEN H.K., VESTERGAARD B.F.: "*Lifestyle and antiviral antibody studies among homosexual men in Denmark*". Acta Pathologica, Microbiologica et Immunologica Scandinavica [Section B Microbiology], 91: 357-364 (1983).

26) MELBYE M., BIGGAR R.J., WANTZIN P., KROGSGAARD K., EBBESEN P., BECKER N.G.: "*Sexual transmission of hepatitis C virus: cohort study (1981-9) among European homosexual men*". Br. Med. J., 301: 210-212 (1990).

27) MELE A., FRANCO E., CAPRILLI F., GENTILI G., STAZI M.A., ZARATTI L., CAPITANIO B., CRESCIMBENI E., CORONA R., PANÀ A., PASQUINI P.: "*Hepatitis B and Delta virus infection among heterosexuals, homosexual and bisexual men*". Eur. J. Epidemiol., 4: 488-491 (1988).

28) MINTZL., DREW W.L., MINER R.C., BRAFFE H.: "*Cytomegalovirus infections in homosexual men: an epidemiological study*". Ann. Intern. Med., 99: 326-329 (1983).

29) MONTAGNIER L., GRUEST S., CHAMARET C., DAUGUET C., AXLER D., GUETARD D., NUGEYRE M.T., BARRE-SINOUSSE F., CHERMANN J.C., KLATZMANN D., GLUCKMAN J.C.: "*Adaptation of lymphadenopathy associated virus (LAV) to replication in EBV-transformed B lymphoblastoid cell lines*". Science, 226: 63-66 (1984).

30) MORTIMER P.P., COHEN B.J., LITTON P.A., VANDERVELDE E.M., BASSENDINE M.F., BRIND A.M., HAMBLING M.H.: "*Hepatitis C virus antibody [letter]*". Lancet, 2: 798 (1989).

31) NERURKAR L.S., BIGGAR R.J., GOEDERT J.J., BECKER W.W.P., WEST F., TZAN N., TRAUB R., LEE Y.J., BOTELAR W., FUCCILLO D., MADDEND L., SEVER J.L.: "*Antiviral antibodies in the sera of homosexual men: correlation with their lifestyle and drug usage*". J. Med. Virol., 21: 123-135 (1987).

32) OSMOND D.H., CHARLEBOIS E., SHEPPARD H.W., PAGE K., WINKELSTEIN W., MOSS A.R., REINGOLD A.: "*Comparison of risk factors for hepatitis C and hepatitis B virus infection in homosexual men*". J. Infect. Dis., 167: 66-71 (1993).

33) PERRILO R.P., CAMPBELL R.C., SANDERS G.E., REGENSTEIN F.G., BODICKY C.J.: "*Spontaneous clearance and reactivation of hepatitis B virus infection among male homosexuals with chronic type B hepatitis*". Ann. Intern. Med., 100: 43-46 (1984).

34) PIRISI M., FABRIS C., TONIUTTO P., VITULLI D., SOARDO G., FALLETI E., GONANO F., FERRONI P., GASPARINI V., BARTOLI E.: "*Reactivity to B Cell Epitopes within hepatitis C virus core protein and hepatocellular carcinoma*". Canc. Res., 55: 111-114 (1993).

35) QUINNAN G.V. JR, MASUR H., ROOK A.H., ARMSTONG G., FREDERIK W.R., EPSTEIN J., MANISCHEWITZ J.F., MACHER A., JACKSON

L., AMES J., SMITH H., PARKER M., PEARSON G.R., PARILLO J., MITCHELL C., STRAUSS S.E.: "Herpes virus infection in the acquired immune deficiency syndrome". *JAMA*, 252: 72-77 (1984).

36) RAHMAN M.A., KINGSLEY L.A., BREINIG M.K., HO M., ARMSTRONG J.A., ATCHINSON R.W., LYTER D.W., RINALDO C.R. Jr.: "Enhanced antibody responses to Epstein-Barr virus in HIV-infected homosexual men". *J. Infect. Dis.*, 159: 472-479 (1989).

37) RINALDO C.R., CARNEY W.P., RICHTER B.S., BLACK P.H., HIRSCH M.S.: "Mechanisms of immunosuppression in cytomegaloviral mononucleosis". *J. Infect. Dis.*, 141: 488-495 (1980).

38) RINALDO C.R., KINGSLEY L.A., LYTER D.W., BODNER A.Y., WEISS S.H., SAXINGER W.C.: "Excretion of cytomegalovirus in semen associated with HTLV-III seropositivity in asymptomatic homosexual men". *J. Med. Virol.*, 20: 17-22 (1986).

39) SCHREEDER M.T., THOMPSON S.E., HADLER S.C., BERQUIST K.R., ZAIDI A., MAYNARD J.E., OSTROW D., JUDSON F.N., BRAFF E.H., NYLUND T., MOORE J.N., GARDNER P., DOTO I.L., REYNOLDS G.: "Hepatitis B in homosexual men: prevalence of infection and factors related to transmission". *J. Infect. Dis.*, 146: 7-15 (1982).

40) SCULLEY T.B., CROSS S.M., BORROW P., COOPER D.A.: "Prevalence of antibodies to Epstein-Barr virus nuclear antigen 2B in persons infected with the human immunodeficiency virus". *J. Infect. Dis.*, 158: 186-192 (1988).

41) SPECTOR S.A., HIRATA K.K., NEUMAN T.R.: "Identification of multiple cytomegalovirus strains in homosexual men with acquired immune deficiency syndrome". *J. Infect. Dis.*, 150: 953-955 (1984).

#### ACKNOWLEDGEMENTS

The Authors wish to thank Prof. Mario Bolzan (Federico II University of Naples) for critical overview of statistical evaluation.

We are grateful for technical help provided by Monica Riondato.

ACCETTATO PER LA PUBBLICAZIONE: DICEMBRE 1994

#### Indirizzo per la corrispondenza:

Prof. Maria Elisa MOSCHEN  
Istituto di Igiene  
Università degli Studi  
Via Loredan, 18  
35131 PADOVA