# Seroconversion to Human Immunodeficiency Virus (HIV) in Persons Attending an STD Clinic in Copenhagen

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1182 males and 155 females attending an STD clinic from June 1984 to October 1985 were investigated for the presence of antibodies to human immunodeficiency virus (HIV). 348 (29.5%) of the males and 5 (3.2%) of the females were antibody positive (ab+). 237 of the males were initially antibody negative (ab-) and were tested more than once, and during a 16-month period 40 of these seroconverted from ab- to antibody positive. The mean follow-up period of these 40 patients was 7.1 months, and thus the seroconversion rate is estimated to be 2.4% per month. Samples from 37 of these were available for HIV antigen testing. 19 of the patients were antigen positive in the latest ab- sample and accordingly, 18 patients were antigen negative in the latest ab- sample. No difference was found between the mean follow-up periods of those with and those without HIV antigen in the latest ab- serum and the presence of HIV antigen in serum was not associated with symptoms of acute HIV infection. After 20 months of follow-up, none (0.0-8.8%, 97.5% confidence limits) of the 40 patients have developed AIDS or AIDS-related complex. (Received June 6, 1987.)

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The etiological agent of the acquired immunodeficiency syndrome (AIDS) is the retrovirus human immunodeficiency virus (HIV) (1). Highly specific and sensitive tests for determination of antibodies against HIV have made it possible to identify a number of risk groups, among which the foremost are homosexual/bisexual males and intravenous drug abusers (2). Since the start of the AIDS epidemic in 1981, rising prevalences of seropositivity have been observed in both groups (3, 4), in which, likewise, high prevalences of other STD's are found (5, 6).

We have therefore conducted the present study at a public health STD clinic in Copenhagen in order to determine 1) the prevalence of HIV antibodies among the clientele, 2) the rate of seroconversions among persons reattending the clinic, and 3) the frequency of HIV antigenemia in persons seroconverting from antibody negative to antibody positive.

# PATIENTS AND METHODS

### Patients

In the period June 1984 to October 1985, 1182 males and 155 females who attended a public health STD clinic in central Copenhagen were tested for HIV antibodies. These included individuals attending due to a suspicion of STD, or controls following treatment for such, and individuals only requesting an HIV antibody test. All homosexual/bisexual males identifying themselves as such were offered an HIV antibody test, whereas other patients were only tested on request. We have no precise information concerning the sexual habits of the latter group of patients, but it is estimated that more than 90% of the investigated males were homosexual/bisexual males. The persons reattending the

clinic were either patients treated for STD and controlled for treatment efficiency according to routine procedures or persons belonging to known risk groups, who were generally advised to have another HIV antibody test performed within a 3 month period. Persons found HIV antibody positive were either followed at the STD clinic or referred to the associated dermatological department.

HIV antibody and antigen tests

The HIV antibody tests were performed with an enzyme-linked immunosorbent assay (ELISA) and confirmed by an immunoblotting test (IBT), as previously described (7). HIV antigen was detected with a capture ELISA, as previously described (8).

## RESULTS

Altogether 1337 persons were investigated. 155 were females and 5 (3.2%) of these, all intravenous drug abusers, were HIV antibody positive (ab+). 1182 were males, 308 (26.1%) were ab+ and 874 (73.9%) were antibody negative (ab-). 412 of the males were investigated more than once, and among these 237 were ab- at entry, but only 197 remained ab- during the study period, thus 40 males seroconverted from ab- to ab+. Data on these patients are given in Table I. Since the mean follow-up period of these 40 patients was 7.1 months (median: 7.0 months, range: 3-16 months), the seroconversion rate is estimated to be 2.4% per month.

From 37 of the seroconverting patients, samples were available for HIV antigen testing. 18 of these were HIV antigen negative (ag-) in both the latest ab- and the first ab+ serum. The mean follow-up period of these was 6.2 months (median: 6.0, range: 3-12). The remaining 19 patients were HIV antigen positive (ag+) in latest ab- serum, 10 of these were ag+ in the first ab+ serum and 9 were ag- in the first ab+ serum. The mean follow-up period of these 19 patients was 7.4 months (median: 7.2, range: 3-16). No significant difference was found between the mean follow-up periods of those who were either ag+ or ag- in the latest ab- serum.

Table I. Epidemiological and serological data on 40 males seroconverting from HIV antibody negative to antibody positive

rige (mean, range), years	33 (18–53)	
syed. Whether the presence of HIV		
Sexual habits		
Homosexual	36	
Bisexual	5	
Heterosexual	1	
Cause for admittance		
STD	22	
HIV antibody test	18	
Mean (range) duration of the period between	7.0.10	
the latest ab- and first ab+ sample, months	7.1 (3–16)	
Initially ab- and tested more than once	237	
Seroconversion rate per month, %	2.4	
HIV antigen testing		
Persons with available samples	21	
(a) ag- in latest ab- and first ab+ samples	18	
(b) ag+ in latest ab- and first ab+ samples	10	
(c) ag+ in latest ab- but not in first ab+ sample	9	

Intravenous drug abuser.

Clinical data on the 40 patients were retrospectively evaluated. 5 patients had skin symptoms indicative of an acute HIV infection (9), 7 patients had generalized lymphadenopathy and 5 patients had experienced episodes of a mononucleosis-like disease. None of these symptoms were significantly associated with the absence or presence of HIV antigen in serum. Further, no significant association was found between HIV antigen and the cause for admittance to the clinic. By 20 months of follow-up, none of the patients have developed AIDS or ARC.

# DISCUSSION

The monthly seroconversion rate, 2.4% (1.7–3.1%, 95% confidence limits) is approximately of the same order as previously described in two Danish studies (10, 11) which found 2.9% seroconverting during a 21-week period in 1982–83, and 1.2% and 0.7% during one 5- and one 9-month period, in 1981–83. This might suggest that the efforts made during 1984–85 to modify the sexual behaviour of risk group individuals have been far from effective.

The duration of the latency period from seroconversion to development of AIDS is not known. We did not find any (0.0–8.8%,. 97.5% confidence limits) developing AIDS or ARC during 20 months of follow-up, which accords with other studies (12, 13, 14). One study found none of 15 seroconverters progressing to AIDS during one year of follow-up, the second found no AIDS cases among 66 persons with a mean follow-up of 17 months after seroconversion, and the third likewise did not observe in 1985 any AIDS cases among 15 persons seroconverting in 1981–82.

Only a minor part of the seroconversions in this study were associated with clinical symptoms, which is similar to reports by others (15, 16). However, in these studies 36% and 46%, respectively, had generalized lymphadenopathy, 53% had so in a third study (12) as had 18% in our study. Therefore, it seems that a large proportion of seroconverters develop lymphadenopathy during the acute HIV infection or in close connection herewith.

We found that 51% of the persons had detectable HIV antigen in the latest antibody negative sample. This is considerably higher than found by others (17, 18), in which 15% and 14%, respectively, were ag+ in the latest ab- sample. The reason for this difference is not obvious, but the most probable explanation might be differing sensitivity and specificity of the antibody and antigen tests employed. Whether the presence of HIV antigen in serum during primary infection has any implications regarding the subsequent course of the infection and thus the counselling of the patients is currently not known. However, the high frequency of antigen in ab- samples found in this study emphasizes the need for caution when counselling high-risk group ab- persons as to the infectivity of the individual patient.

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### REFERENCES

- Coffin J, Haase A, Levy JA, Montagnier L, Oroszlan S, Teich N, Temin H, Toyoshima K, Varmus H, Vogt P, Weiss R. Human immunodeficiency viruses. Science 1986; 232:697.
- WHO Collaborating Center on AIDS. AIDS surveillance in Europe. WHO, Paris, France, Report 8, 1986.
- Stevens CE, Taylor PE, Zang EA, Morrison JM, Harley EJ, de Cordoba SR, Bacono C, Ting RCY, Bodner AJ, Sarngadharan MG, Gallo RC, Rubenstein P. Human T-cell lymphotropic virus

- type III infection in a cohort of homosexual men in New York City. JAMA 1986; 255: 2167-2172.
- 4. Robertson JR, Bucknall AB, Welsby PD, Roberts JJK, Inglis JM, Peutherer JF, Brettle RP. Epidemic of AIDS related virus (HTLV-III/LAV) infection among intravenous abusers. Brit Med J 1986; 292: 527-529.
- 5. Kroon S, Gerstoft J, Petersen CS, Dickmeiss E, Lindhardt BØ. T-lymphocyte subsets among Danish heroin addicts. Eur J Sex Trans Dis 1985; 3: 17-21.
- Gerstoft J, Lindhardt BØ, Petersen CS, Kroon S, Ullman S, Møller S, Nielsen JO, Dickmiess E. Antibodies to human T-cell lymphotropic virus type III in promiscuous healthy homosexual men. Relation to immunological and clinical findings. Eur J Clin Invest 1985; 15: 290-295.
- Lindhardt BØ, Ulrich K, Ryder L, Dickmeiss E, Sørensen H, Jørgensen J, Jersild C, Grunnet N. HTLV-III antibody testing in three Danish blood banks. Vox Sang 1986; 51(S1): 9-14.
- Gaub J, Petersen C, Poulsen AG, Mathiesen L, Ulrich K, Lindhardt BØ, Faber V, Gerstoft J. Hofmann B, Lernestedt JO, Nielsen JO, Nielsen CM, Platz P. The effect of Foscarnet (phosphonoformate) on human immunodeficiency virus isolation, T-cell subsets and lymphocyte function in AIDS patients. AIDS 1987; 1:27-33.
- Wantzin GL, Lindhardt BØ, Weissmann K, Ulrich K. Acute HTLV-III infection associated with exanthema diagnosed by seroconversion. Brit J Dermatol 1986; 115: 601-606.
- 10. Hofmann B, Platz P, Ødum N, Ryder LP, Svejgaard A, Pedersen NS, Nielsen JO, Faber V, Sprechler HH, Oehlenschlager J, van der Berg T, Kørner EA, Gerstoft J, Kryger P, Saxinger C. Occurrence of anti HTLV-III antibodies in Danish high risk homosexuals in 1982-83. Seroconversion rate and risk of AIDS. AIDS Research 1986; 2: 1-3.
- 11. Melbye M, Biggar RJ, Ebbesen P, Sarngadharan MG, Weiss SH, Gallo RC, Blattner WA. Seroepidemiology of HTLV-III in Danish homosexual men: prevalence, transmission, and disease outcome. Brit Med J 1984; 289: 573-575.
- 12. Weber JN, Rogers LA, Scott K, Berrie E, Harris JRW, Wadsworth J, Moshtael O, McManus T, Jeffries DJ, Pinching AJ. Three-year prospective study of HTLV-III/LAV infection in homosexual men. Lancet 1986; i: 1179-1182.
- 13. Goedert JJ, Biggar RJ, Weiss SH, Eyster ME, Melbye M, Wilson S, Ginzburg HM, Grossman RJ, diGioia RA, Sanchez WC, Giron JA, Ebbesen P, Gallo RC, Blattner WA. Three-year incidence of AIDS in five cohorts of HTLV-III-infected risk group members. Science 1986; 231: 992-995.
- 14. Coutinho RA, Krone WJA, Smit L, Albrecht-van Lent P, van der Noordaa J, Schaesberg W. Goudsmit J. Introduction of lymphadenopathy associated virus or human T lymphotropic virus (LAV/HTLV-III) into the male homosexual community in Amsterdam. Genitourin Med 1986; 62: 38-43.
- 15. Fox R, Eldred LJ, Fuchs EJ, Kaslow RA, Visscher BR, Ho M, Phair JP, Polk BF. Clinical manifestations of acute infection with human immunodeficiency virus in a cohort of gay men. AIDS 1987; 1:35-38.
- 16. Boyko WJ, Schechter MT, Craib KJP, Willoughby B, Douglas B, Sestak P, McLeod WA, O'Shaughnessy M. The Vancouver Lymphadenopathy-AIDS study: 7. Clinical and laboratory features of 87 cases of primary HIV infection. Can Med Assoc J 1987; 137: 109-113.
- 17. Allain JP, Paul DB, Laurian Y, Senn D. Serological markers in early stages of human immunodeficiency virus infection in haemophiliacs. Lancet 1986; ii: 1233-1236.
- 18. Goudsmit J, Paul DA, Lange JMA, Speelman H, van der Noordaa J, van der Helm HJ, de Wolf F, Epstein LG, Krone WJA, Wolters EC, Oleske JM, Coutinho RA. Expression of human immunodeficiency virus antigen (HIV-Ag) in serum and cerebrospinal fluid during acute and chronic infection. Lancet 1986; ii: 177-180.