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1. Prevalence and prognosis of HTLV III infection

There is suggestive evidence that many, and perhaps most, infected individuals may suffer a continuing slow decline in T4 lymphocyte count. If this is so, the rate of appearance of new cases of persistent generalised lymphadenopathy (PGL) and AIDS so far observed in the few small cohorts of seropositive homosexual men that have been followed for more than 3 years may persist or even increase with the passage of time. The data so far published are thus consistent with the prediction that many, and possibly the majority, of seropositive individuals will eventually die of AIDS. Whether this is so cannot be inferred from available data, and a systematic international collation of these results should be organised to attempt to project the eventual prognosis by conventional actuarial analysis. The number of seropositive individuals may still be doubling every six months or so in Britain, and it has been suggested that in the U.S. this number may already approach one million. Such estimates, and the possibility that a similar number may eventually die even if the epidemic is halted, indicate the scale of the research effort that should be mounted. The prevalence of seropositivity among homosexual men attending a London STD clinic rose from 2% in 1982 to over 20% in 1984, and seems likely now to be very much higher. Recent U.S. data on numbers of AIDS cases suggest that a similar epidemic among heterosexuals may be appearing, as has already occurred in Africa.

The possibility that a high proportion of seropositive individuals will develop AIDS is a reasonable "most pessimistic"

assumption, but it is not clear what the corresponding "most optimistic" estimate should be. The observed risk in long-term (i.e. about 4 years) follow-up of seropositive homosexual men is of the order of 5%-10%, and as the evidence tends to suggest that further cases will occur in these cohorts the risk can hardly be less than 10%. Data on AIDS are often obscured by the inclusion of more recently infected men in the denominator. Even the fact that AIDS is always, or almost always, fatal is still not universally appreciated, as only half the diagnosed cases have so far died.

2. The spread of HTLV III infection in the heterosexual community

2.1 Haemophiliacs

The seropositive rate is already high among haemophiliacs and among homosexual men in U.S. cities where HTLV III is now prevalent. Only a minority, if any, of the general population may be capable of mounting an effective immune response to initial infection, and it seems likely that the chronic infection that ensues constitutes a permanent infective carrier state. The major unanswered question is therefore the likelihood that transmission will occur in relation to frequency and type of sexual practice or other forms of contact. There is some evidence that a substantial proportion of AIDS patients' wives are infected, but this requires confirmation. This question could be answered quickly and easily in Britain through the Haemophilia Society. Heterosexual contacts of unmarried haemophiliacs should be even more informative, as any that

are seropositive could be asked about their other sexual contacts. The likelihood of female to male transmission is not known, and the seropositivity rate in male consorts of infected women is difficult to study in other circumstances, as many infected women are likely to be drug users or to have bisexual partners.

2.2 The general population

The pattern of the HTLV III epidemic among homosexuals seems likely to provide a model for the course that any epidemic in the heterosexual community will follow. The U.S. epidemic appears to have begun in New York among extremely promiscuous homosexual men, and then spread successively to other cities and areas, and to less promiscuous homosexuals. If a rapid spread of infection is going to occur among heterosexuals, it is therefore likely that an appreciable proportion of promiscuous heterosexuals in New York are already infected, and that a detectable seropositivity rate may soon appear in promiscuous heterosexuals in London. The most informative group to study may therefore be heterosexuals of both sexes who are treated for other venereal diseases. This is easy to do through STD clinics, where blood samples on all (or a sample of) heterosexual patients attending clinics throughout Britain should be taken and stored every six months or so, beginning immediately. This would be more difficult in New York and other large cities in the U.S., as they do not have an analogous network of STD clinics, but it should certainly be attempted, perhaps through one of the U.S. national health care schemes.

Routine population-based blood-sampling would also be valuable, but would be difficult to organise. Blood donors and other subgroups in which routine samples are available (e.g. those attending BUPA clinics) are worth monitoring but are probably not representative. If a detectable increase in seropositivity is observed in heterosexuals attending STD clinics, however, more systematic national monitoring should be established.

2.3 Personal contact studies

Every opportunity to study sexual and family contacts of seropositive heterosexual individuals should be exploited. These include haemophiliacs, heterosexual seropositive STD clinic patients, and of course all heterosexual AIDS patients. A network of skilled interviewers is needed to conduct this sensitive contact tracing. STD clinics already have such staff, and epidemiology groups conducting population-based case-control or genetic tracing studies could also contribute useful expertise.

3. Organisation of research

The research outlined above needs to be implemented immediately, and this cannot be achieved unless it is centrally coordinated and adequate staff and funds are provided. The MRC Working Group on AIDS has the necessary expertise to do this, but the present system, under which separate laboratories, clinics and haemophilia groups conduct limited studies with individual, unco-ordinated and usually inadequate grants is not satisfactory. Certain specific facilities and arrangements are needed immediately, including:

- i) Enough interviewers to conduct contact tracing of all heterosexual seropositive or AIDS cases. Many of these should be based in selected STD clinics, but some might be based at the Communicable Disease Surveillance Centre of the Public Health Laboratory, where a clinical epidemiologist should be appointed to co-ordinate work on all notified AIDS cases, and perhaps also on haemophiliacs (see below).
- ii) Facilities for storage of the large numbers of blood samples that would be collected. The freezers should obviously be accessible to those who take blood (clinics and interviewers), but a central data base recording details of all samples, interviews and contacts should also be maintained.
- iii) Adequate routine laboratory facilities for the analysis of blood and other samples both by antibody detection and by direct assay for the virus.
- iv) The work on haemophiliacs, although regionally based, must be nationally co-ordinated and funded. This would presumably be arranged by the researchers who are already involved in this work, perhaps in collaboration with the CDSC.
- v) A formal arrangement for co-ordination and exchange of research between Britain and the U.S. should be established, perhaps through a joint committee. The prevalence and evolution of seropositivity in American heterosexuals with other STDs is of particular importance to Britain, as it may provide one or two years' advance warning of the British experience.
- vi) The epidemic among homosexuals is not yet at as high a level in other towns as in London, and local centres offering confidential serum testing and information might still reduce the eventual numbers affected.