the relation between symptoms and neurochemical deficits. Current studies of portmortem and biopsy specimens and of cerebrospinal fluid will provide more answers. New methods of assessing regional function of neurochemical systems may arise from recent technological developments in imaging which allow accurate localisation of isotope probes emitting positrons and gamma rays. Such techniques may allow more accurate selection of patients for the cholinergic and perhaps other replacement treatments. The development of techniques for selectively destroying the ascending cholinergic system in animals will allow investigation of its behavioural functions and may generate new forms of replacement treatment.

The pathogenesis and aetiology of Alzheimer's disease remain unknown territory. Molecular biological research may provide some insights into the selective vulnerability of neurones to the pathological process—perhaps a receptor or some other constituent of the cell membrane is common to affected neurones. Though abnormal neurofibrils develop in a variety of conditions, understanding the underlying genetic and transcriptional processes may give clues to aetiology. In this connection, molecular biologists may be able to exploit the fact that in trisomy 21 (Down's syndrome) Alzheimer type neuropathological changes and deficits in choline acetyltransferase develop.[4]

Current theories of aetiology include autoimmunity, aluminium toxicity, and infection by slow virus. Creutzfeld-Jacob disease is a transmissible encephalopathy of man with a long incubation period. The infective agent has not been isolated. Plaques are sometimes seen in Creutzfeld-Jacob disease and in an experimental form of scrapie, a slow virus infection of sheep. Furthermore, reductions in choline acetyltransferase and serotonin occur in some forms of experimental scrapie.[14 15] Attempts to transmit Alzheimer's disease to animals have not, however, met with success except in a few cases of the familial form.[16] Nevertheless, advances in isolating the infectious agent of Creutzfeld-Jacob disease and other spongiform encephalopathies will be of considerable relevance to research in Alzheimer's disease.

J F W DEAKIN

Senior Lecturer in Psychiatry,
University Hospital of South Manchester,
Manchester M20 8LR

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Regular Review

AIDS in Europe

P EBBESEN, R J BIGGAR, M MELBYE

The acquired immune deficiency syndrome (AIDS) includes highly lethal opportunistic infections and rare malignancies in people with no apparent reason to be immunosuppressed. It was first recognised in the United States in 1981,[1] but, in retrospect, cases had begun to appear there as early as 1978. Since its recognition, patients with the syndrome have been clearly identified in many areas of Europe. Indeed, the information we present is only a general summary of the European experience, in that accounts of cases, research, and national policies are available informally and often only anecdotally. Better information may be expected in the future when a centralised system of recording AIDS data becomes established in Europe.

First in any discussion of AIDS must be its definition. At present any of the many illnesses common in people known to be immunosuppressed might be classified as related to AIDS by one or another investigator. Apparently no common definition is being used in Europe, and this alone may account for the considerable differences in case counts observed among different nations. Epidemiologically this has conflicting results: the wider the net is cast, the more the case yield—but equally the more extraneous and confusing material is included. Since the disease spectrum seen in Europe resembles that in the United States we recommend that the definition used by the Centers for Disease Control in the United States should be used to make data concordant on the two sides of the Atlantic.

Until that has been agreed on, however, we have no choice but to accept the cases as defined by their investigators.

Secondly, how much AIDS is there? Since 1979 the number of patients diagnosed by the strict Centers for Disease Control definition has doubled every six months. Absolute counts change weekly, with about 50 cases a week now being registered by the Centers for Disease Control in the United States, but a total of at least 2000 cases had been reported by 1 September 1983. In the absence of any specific marker, episodes of illness corresponding to a broad description of AIDS may have occurred before 1979 among Europeans and Africans,[2-4] but the critical event is the dramatic epidemic increase in cases since 1979.

The European experience has mimicked the early American experience: there has been a considerable—but not yet explosive—increase in cases of AIDS in Europe. By 30 June 1983 the World Health Organisation was aware of 153 European cases, with an additional 67 cases on a "suspect" list. France led individual nations with 59 reports, followed by West Germany (24), Belgium (21), Switzerland (13), Britain (10), Denmark (10), the Netherlands (three), Sweden (three), and finally a variety of countries with one or two cases. Even this recent report understates the extent of the problem, in that we know of more identified cases than those listed for Denmark as well as other countries (and the latest count in Britain is 24).[4a]

Who is at risk? In the United States the high risk groups are homosexuals (71% of cases), intravenous drug abusers (17%), Haitians (5%), and haemophiliacs (< 1%). European investigators have reported that the same groups are at high risk.[5-11] In Europe, however, the relatively larger populations of Africans from the upper Congo basin and visitors to that area may have allowed recognition of yet another population that appears to be at high risk.[12 13] A condition such as AIDS could have long existed unrecognised in the African setting and gained entrance into America and Europe in recent years through increases in intercontinental travel. Only a definitive diagnostic test will permit us to be certain that the disease found in central Africa is a related phenomenon, since it does not share the common epidemiological profile. Studies of the high risk groups in Europe have also yielded other information of importance to the understanding of the disease. The epidemic problem in the United States was recognised only after the epidemic was well under way, beyond the point when the pattern of epidemic spread could be studied with any assurance. The concordance of lifestyle features among individuals in the high risk groups has made it difficult to dissect out the important variables that confer risk. Even the expression of the overt illness appears to be influenced by secondary factors that are partially specific to certain risk groups. Homosexual men, for example, have a disproportionately high risk of developing Kaposi's sarcoma (46% of all homosexual cases) compared with other risk groups (8% of all other cases).

Transmissible agent

In particular, promiscuity and anonymous sexual contact have been implicated, but is that because the number of partners is greater, or because of more venereal disease, or because of the exposure to the antigens of seminal fluid, or because of sex associated nitrite inhalant drugs and cocaine? All of these possibilities have had their advocates. The European experience, however, is that cases have arisen particularly among people with direct or indirect exposure to high risk areas, which suggests that it is contact with a case or with "carriers" from high risk areas that confers exceptional risk.[14 15] We conclude that when promiscuity has been found to be a factor it is because of an increased opportunity to be exposed to a transmissible agent.

We and others have used the immunological marker of abnormally low helper to suppressor ratios as a possible indicator of risk of AIDS.[16-19] Neither this marker nor any other laboratory marker is of proved relevance to AIDS, but the ratio is virtually always abnormally low in patients with AIDS. We have found a correlation between healthy homosexuals possessing a low ratio and having had homosexual experience in the United States in 1980-1. A similar link has been observed among healthy Dutch haemophiliacs, in whom the proportion with low ratios was higher among those men who used factor VIII from the United States as opposed to that from European sources.[20]

The sum of these observations suggests that a transmissible agent has been involved in the spread of this condition from the United States to Europe. The similarity of the high risk groups to those seen in hepatitis[21] even suggests a similar route of transmission, although hepatitis viruses have not been implicated in the cause of AIDS by either epidemiological or laboratory investigations.

What agent is implicated in AIDS is another question. Different investigators have their own candidates,[22-28] but the most interesting recent contender for the role has emerged from a European laboratory. A French team from the Pasteur Institute in Paris has described evidence of a retrovirus that is antigenically distinct from the earlier described HTLV retroviruses.[29] If confirmed, this agent will be of interest to virologists regardless of its relation to AIDS, but among the candidates for causing AIDS it rates higher by virtue of being lymphotropic and lympholytic for helper cells. Such an agent may, however, be present and unrelated to AIDS, a passenger carried along with the homosexual lifestyle exposures, much as we believe cytomegalovirus probably is.[30 31]

Future prospects?

In the larger context, how will AIDS develop in Europe, given that the course is unchecked by decisive medical intervention? In the same manner as syphilis closed down the communal bath houses of sixteenth century Europe, AIDS has already modified sexual behaviour—but not so far to the extent of limiting the spread of the disease. The factor that is most likely to influence the ultimate size of the outbreak will be the number of people exposed to high risk. We must expect that the size of the pool of susceptibles in Europe is similar to that in the United States and that—in the absence of control measures yet to be discovered—we could have an outbreak equal in size to that in the United States.

Any progressive increase in cases such as has occurred in the United States has implications for medical planners and research workers in Europe, raising issues that we can foresee but for which we have no answers. The hospitals of a major disease focus such as New York City (45% of all cases) have been inundated with patients requiring complex and expensive long term care. Facilities for both care and research have been strained, especially in light of concern among some investigators that contamination of their equipment might prohibit its use on other patients. Personnel in New York and elsewhere have resigned from units that care for patients with AIDS and that do laboratory work related to AIDS. Although the evidence strongly indicates that AIDS cannot be transmitted by casual contact, and there has been no documentation of

transmission from cases of AIDS to health care workers, these concerns should be anticipated and dealt with.

On a more optimistic note, medical history has many examples of epidemics that have suddenly blighted a community only to burn out without any formal public health intervention as the pool of susceptibles became exhausted. If such a historical prospective is applicable only a small fraction of the exposed will ever develop illness of any kind, much less a lethal variety. There is ample evidence that AIDS is not easily transmissible to those outside the defined risk groups. Even after several years of diligent searching, only about 6% of cases fitting a description of AIDS fall outside a known risk group,[32] and many of these may have been classified in this way because of erroneous or incomplete information.

There is, however, no reason for complaisance. AIDS appears to be increasing exponentially, and the prognosis of those with disease is dismal. Each patient with AIDS in the United States requires two to three months of care in hospital, often in intensive care facilities. The cost of the hospital care alone of patients with AIDS will exceed $100 million in the United States next year.[33] Though the number of cases of AIDS in Europe is, fortunately, far smaller, these estimates provide sobering portents for the future. The health planners and science resource managers of Europe must make use of whatever lag time exists between the epidemic curves in the United States and Europe to prepare the necessary support for the coming needs—both clinical and research needs.

P EBBESEN
Chief

M MELBYE
Research fellow

Institute of Cancer Research,
Radiumstationen,
DK 8000 Aarhus,
Denmark

R J BIGGAR
Epidemiologist

National Cancer Institute,
Bethesda,
Maryland,
USA

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