

Briefing

HIV and AIDS in the United Kingdom

INTRODUCTION

Since the first identification of the AIDS syndrome in Los Angeles in 1981 (and the description of the virus responsible – now termed HIV 1 – in 1983) health care professionals and policy makers across the globe have had to face the reality that the human community is facing a transmissible disease epidemic of a potential severity not experienced in living memory. Already many millions of people in sub-Saharan Africa are infected and at risk of premature death, as are considerable (if uncertain) numbers of individuals in the rest of the developing and developed world. The discovery of a new form of Human Immunodeficiency Virus in West Africa in 1985 (HIV 2) has emphasised the fact that the threat to humanity from this source may still be evolving, and could in future become even greater than it is today.

Against this background, the role of this *Briefing* is to update the 1986 OHE publication 'The AIDS Virus: forecasting its impact'. It outlines current understanding about HIV and its clinical consequences. Following this, it examines available data concerning the extent to which the virus has spread in the United Kingdom so far and then looks at possible trends in future years. The central observation of the paper is, however, that information about many key variables is inadequate at the present time to permit forecasting beyond the very short term – and even within this limited time horizon the accuracy of prediction is uncertain. It is nevertheless clear that every effort must now be made to prevent the further spread of HIV through primary prevention, mainly involving changes in sexual practices in the community.

HIV INFECTION AND ITS CONSEQUENCES

The principal target of the human immunodeficiency virus (HIV) is a subset of lymphocytes in the immune system known as helper/inducer cells. On their surface, these cells carry a particular molecule (known as CD4) to which the envelope glycoprotein of HIV attaches itself during the process of infection. Helper/inducer T lymphocytes bearing CD4 molecules play an essential role in immune response and their destruction by HIV leads to profound immunosuppression, the most severe consequence of which is the acquired immune deficiency syndrome (AIDS). At the same time, HIV also has an affinity for certain cells of the nervous system and infection with the virus may therefore be associated with neurological sequelae, most notably a progressive dementia.

HIV is a retrovirus and replicates within living cells by using the enzyme reverse transcriptase to convert its own RNA into DNA (pro-viral DNA) which is then integrated into the DNA of the host cells. The pro-viral DNA thus becomes a part of the genetic material of cells which, upon activation, programs the further manufacture of viral components and their assembly into the whole virus. The new viruses leave the cells by budding out through the cell membrane and proceed to infect other cells within the same host. It is believed that infection, once acquired, persists for life and infected subjects remain infectious to others.

Rapid advances in knowledge have been achieved since HIV was first isolated in 1983, but many uncertainties continue to surround the infection process. For example, the factors triggering the reproduction of the virus within the host have yet to be firmly established. There has been some speculation that it occurs when the 'HIV-hijacked' cells of the immune system multiply in response to the presence of other antigens. At the present time, however, it is not possible to distinguish between infections destined to remain latent and those that will give rise to illness. The precise mechanisms whereby HIV causes profound immune deficit are a further source of uncertainty. Hypotheses put forward so far include direct destruction of the affected cells in the immune system, possible auto-immune reactions and blocking of the normal interaction of the CD4 molecule with other cell types (Beverley and Sattentau, 1987). The factors determining the speed at which immuno-suppression progresses after infection and its extent have also yet to be fully elucidated.

Clinical spectrum

An incomplete picture also exists with regard to the clinical outcomes of HIV. The fact that the virus has emerged only relatively recently coupled with its potential for prolonged latency necessarily implies that currently observed patterns may alter with the passage of time. Nevertheless, even in this early phase of understanding, it is clear that HIV is associated with a very wide clinical picture. Acute infection following exposure to the virus results in the production of antibodies – sero-conversion. These antibodies, which are generally detectable within about three months of the virus being acquired, do not neutralise HIV but instead serve to indicate that infection has taken place. During this stage, some patients may experience a transient non-specific illness similar to glandular fever, involving symptoms such as generalised swelling of the lymph glands, aching muscles

and joints, sore throat and perhaps a rash. In most instances, however, acute HIV infection is sub-clinical.

Evidence available to date suggests that not all patients who sero-convert necessarily progress to chronic infection; such individuals may go into a latent phase of infection (Adler, 1987). For patients who do enter the chronic stage, the infection may be asymptomatic or it may give rise to illness of varying degrees of severity, including persistent generalised lymphadenopathy (PGL), AIDS-related complex (ARC), AIDS and various neurological manifestations.

The first in this group – PGL – is defined in terms of the presence of ‘enlarged nodes at least one centimetre in diameter in two or more (non-contiguous) extrainguinal sites that persist for at least three months in the absence of any current illness or medication known to cause enlarged nodes’. Many patients experiencing PGL have, so far, remained well but data from several prospective studies suggest that between 10 and 30 per cent of patients developing the syndrome progress to AIDS (Adler, 1987).

ARC is more serious than PGL and is diagnosed in patients with evidence of impairment to the immune system, but of a degree that does not warrant a diagnosis of AIDS (Carne, 1987). The formal definition of ARC is contained in Table 1; as this indicates, the term covers a wide range of disease states. Patients suffering these constitutional symptoms and signs over a prolonged period have a higher risk of progressing to the full AIDS syndrome than those who are antibody positive and well or suffering from PGL.

AIDS is the most serious consequence of HIV infection. It is officially diagnosed at the onset of certain opportunistic infections and/or tumours, susceptibility to which is a result of the immunodeficiency caused by the virus. The infections predominantly involve the lungs, gut and nervous system and among these pneumocystis carinii pneumonia, from the first group, is the single most frequently encountered. Kaposi’s sarcoma – a form of skin cancer that may spread to internal organs – is the most commonly observed tumour in AIDS although others such as non-Hodgkins lymphoma and squamous carcinomas of the mouth and anorectum are now being reported with increasing frequency (Adler, 1987)¹. Defined in this way,

1 A study of the 964 cases of AIDS in UK residents reported by the end of August 1987 found that pneumocystis carinii was the clinical feature reported at the time of diagnosis in 48 per cent of cases (McCormick et al 1987). Kaposi’s sarcoma was diagnosed in 21 per cent of cases. Other opportunistic infections were observed in a further 23 per cent of the patients.

Table 1 AIDS related complex

The AIDS related complex is diagnosed in a person who presents with any two or more signs/symptoms which have been present for three months or longer and any two or more abnormal laboratory values

Symptoms/signs

Fever: $\geq 38^{\circ}\text{C}$ intermittent/continuous
Weightloss: $>10\%$
Lymph nodes: persistent generalised lymphadenopathy
Diarrhoea intermittent/continuous
Fatigue that reduces physical activity
Night sweats

Laboratory abnormalities

Lymphopenia, leucopenia,
Thrombocytopenia
Anaemia
Reduced ratio of CD4:CD8 (>2 SD)
Reduced T helper cells (>2 SD)
Reduced blastogenesis
y Raised globulins
Cutaneous energy

Source: Adler 1987

that is according to the appearance of selected clinical markers, evidence currently available indicates that 15-20 per cent of antibody positive patients progress to AIDS within about three years of becoming infected with HIV. This proportion rises to perhaps 30 per cent at 5 years (Pinching, 1987) and may become even higher over longer periods of time. Some studies of individuals infected via blood transfusions, for example, suggest that 75 per cent or more of HIV positives may progress to AIDS up to eight years after infection.

Currently, AIDS is generally believed to be invariably fatal although the ‘shape’ of the illness preceding death varies considerably between patients. At one extreme, death may occur soon after AIDS has been diagnosed but for many patients the disease may, initially at least, follow a relapsing and remitting course. Swift diagnosis and treatment of early infections can restore patients to health and without any outward signs of disease. With time, however, the progressive loss of immune defence means that infections become less successfully treatable with antimicrobial medicines. Furthermore, organisms may emerge for which effective treatment does not exist. From this stage onwards, the patient’s condition is likely to deteriorate rapidly.

Data reported in 1986 indicate that survival varies quite markedly according to the identity of the presenting disease. An analysis of cases in the UK found a mean survival time of 21 months from presentation for patients with Kaposi’s sarcoma compared with 12.5 months for those with pneumocystis carinii. Patients suffering a combination of the two diseases were found to have the worst prognosis, with a median survival time of just 6.6 months (Marasca and McEvoy, 1986). It is possible that survival prospects have improved since these findings were reported. Physicians have now obviously gained more experience in caring for patients suffering from AIDS and in March 1987 a medicine which has been shown in clinical trials to extend survival (Fischl et al, 1987a) – zidovudine or AZT as it was formerly known – was granted a product licence permitting its use in the UK. Indeed, a recently reported study in the United States found that short-term survival at least appears to be improving, especially in patients with pneumocystis carinii (Rothenberg et al, 1987). Specifically, the one year cumulative probability of survival for these patients more than doubled between 1981 and 1985. Comparable data for the UK are therefore awaited with interest.

Finally, HIV is associated with various neurological manifestations. Approximately 30 per cent of AIDS patients suffer dementia by the later stages of their disease and as many as 75 per cent have evidence of disease of the central nervous system at necropsy (Carne, 1987a). These clinical expressions may result indirectly from the opportunistic infections and tumours seen in AIDS patients but they may also be caused by the direct action of HIV in the brain. Indeed, HIV may cause neurological disease in infected patients in whom immune defence remains intact. This observation raises the possibility that neurological features may eventually come to dominate the clinical perception of HIV related disease.

Transmission of HIV

HIV has been isolated from semen, cervical secretions, lymphocytes, cell free plasma, cerebrospinal fluid, tears, saliva, urine and breast milk. However, the concentration of the virus in these fluids shows a considerable degree of variation. HIV is also a fragile virus that survives poorly outside the body. The combined effect of these two factors is to restrict the virus to three principal routes of transmission: sexual, blood to blood and maternofetal (Pinching, 1987).

Focusing on the first of this group, the spread of the virus via sexual intercourse may occur from male to male, male to female and from female to male (for a review of the evidence see Friedland and Klein, 1987). The gathering and interpretation of information in this area are subject to

many obvious difficulties and the risks of infection cannot be estimated with any precision. It has not yet been possible to demonstrate a conclusive association between seropositivity and the length of sexual relationship, the number of sexual encounters with each partner or (for heterosexuals) specific forms of sexual practice. Current uncertainty is reflected in the wide range of estimated risks that has been reported; Pinching (1987), for example, has suggested that exposure to HIV through sexual intercourse (or the two other routes of transmission noted above) carries a 50 per cent chance of acquiring infection whereas Peto (1987) has speculated that there may be as little as one in 100 chance of infection per infectious sexual contact. Nevertheless, available evidence indicates that penetrative sexual intercourse is the most common mode of transmission and that for heterosexuals and homosexuals alike the number of sexual partners is the key factor influencing the risk of becoming infected.

The nature of blood to blood transmission has altered considerably during the last three years. Users of blood and blood products – individuals requiring blood transfusion and haemophiliacs – are at virtually zero risk of infection now that measures have been taken to safeguard the blood supply. A twin strategy of demanding abstention of individuals belonging to high risk groups from donating blood and screening all donors for HIV has been adopted and the Chief Medical Officer at the Department of Health has calculated that 'the risk of a blood donation containing undetectable AIDS virus is about one in a million' (Acheson, 1987). Haemophiliacs are now additionally protected by the virus-destroying heat treatment that is applied during the production of the blood-clotting agent, Factor VIII. These developments mean that the sharing of contaminated needles by injecting drug abusers has become the principal means of blood to blood transmission of HIV.

The virus may also be transmitted from an infected mother to her child. Infection can be effected in utero but may also be acquired from maternal blood at parturition. It is also possible that the virus might be transmitted via breast milk although only one case has so far been reported (Ziegler et al, 1985) and further evidence is awaited.

At the same time as epidemiological investigation has identified sexual intercourse, intravenous drug abuse and maternofetal transmission as the three key means of spread of HIV, it has also established that ordinary social contact with sero-positive subjects entails no risk of infection. For example, Friedland and his colleagues (1986) found that only one of 101 close but non-sexual contacts of 39 AIDS patients sharing the same household for at least three months had evidence of HIV infection (and in this isolated case the virus appeared to have been acquired perinatally). More recently, support for the belief that HIV is not spread through close contact other than sexual or blood exposures has emerged from another study carried out in the United States which found that unaffected siblings of children with AIDS or ARC did not develop antibodies to the virus (Fischl et al, 1987).

Even professionals engaged in the care of AIDS and other HIV infected patients do not appear to be significantly at risk of becoming infected. In the United Kingdom, a prospective study of 150 health care workers accidentally exposed to HIV through needlestick injuries, splashes and other means found no evidence of sero-conversion (McEvoy et al, 1987). Larger scale studies in the United States have similarly indicated that the risks facing workers in the health care setting are very low (McCray, 1986) and it has been estimated that the risk of acquiring HIV infection from a single accidental exposure is probably less than one per cent. Nevertheless, by mid-1987 seven cases of occupationally acquired infection had been documented worldwide (McEvoy et al, 1987) and their occurrence, though clearly extremely rare events, underscores the need for high standards of clinical practice and hygiene to be employed at all times in order to avoid inadvertent infection.

CURRENT NUMBERS

At any given point in time, the human immunodeficiency virus is responsible for a spectrum of clinical manifestations and within each of these the severity of experienced illness varies to a considerable degree. However, the only comprehensive data that are currently available concern patients in whom the virus has caused the development of the full AIDS syndrome. Clinical cases of AIDS are reported in strict confidence to the Communicable Disease Surveillance Centre in England and the Communicable Disease Unit in Scotland under a voluntary system of monitoring which began in 1982. The system employs the strict criteria compiled by the US Centres for Disease Control in Atlanta and recommended by the World Health Organisation for classifying and recording the UK case reports.

The data have to be interpreted with a certain amount of caution, not least because of periodic revisions in the criteria defining a case of AIDS. Indeed, recent changes giving new emphasis to the results of laboratory tests for HIV infection will mean that an unknown number of cases excluded under previous criteria may now be registrable (Lancet, 1987). In addition, published figures relating to the immediately current period are susceptible to the effects of late reporting. Nevertheless, the surveillance data released each month by the Department of Health and Social Security (DHSS) are a valuable source of information and the latest available figures show that 1,170 cases of AIDS had been reported in the UK up to the end of November 1987.

Table 2 provides an analysis of this cumulative total by patient characteristic. The vast majority of cases so far (97 per cent) have involved males and within this group 87 per cent have been classified as homosexual or bisexual males. Haemophiliacs comprise the second largest grouping. Up to the end of November 1987, 68 of the 1,200 haemophiliacs estimated to have been infected with HIV had developed AIDS. However, this figure represents less than six per cent of total cases to date. The remaining groups are even less numerically significant with the largest of these – individuals believed to have acquired HIV through heterosexual intercourse – yet to account for even four per cent of the cumulative total of cases.

The table also shows that 665 (57 per cent) of the cases reported between 1982 and the end of November 1987 have already died. This total is two and a quarter times the figure that had been recorded at the start of 1987. In other words,

Table 2 UK AIDS cases by patient characteristic cumulative totals up to the end of November 1987

	Males	Females	Total	Deaths
Homo/Bisexual	986	–	986	553
Intravenous drug abuser (IVDA)	12	5	17	8
Homosexual and IVDA	17	–	17	8
Haemophilia	67	1	68	51
Recipient of Blood: Abroad	9	7	16	10
UK	6	2	8	7
Heterosexual: Possibly infected abroad	23	11	34	14
UK (no evidence of being infected abroad)	3	6	9	7
Child of HIV positive mother	5	8	13	6
Other	–	1	1	1
Undetermined	1	–	1	–
TOTALS	1129	41	1170	665

Source: DHSS

56 per cent of *all* deaths from AIDS in the UK have been concentrated in the first 11 months of 1987. The data reveal that, on average, the UK is currently recording slightly more than one death from AIDS every day.

Putting the mortality from AIDS into perspective is confronted by a number of difficulties. The fatalities to date have been unevenly distributed over the five year period since the start of the surveillance system. Furthermore, information concerning the age at which these deaths have occurred is not published with the routine AIDS data. However, if it is assumed that 97 per cent of AIDS fatalities involve males² and that these cases are aged between 25 and 44 years, then the projected total of AIDS deaths for 1987 (406)³ is approximately equivalent to one death in every 26 at these ages. If deaths from injuries and poisonings are excluded from the total, AIDS fatalities may currently be estimated to be equivalent to one death in every 17 from natural causes among males aged 25-44 years.

Prevalence of HIV

Information about the current numbers of AIDS cases and fatalities offers only a limited insight into the burden generated by HIV. In order to gauge the full impact of the virus, both now and in the immediate future, data are required showing the prevalence of the virus in the community at the present time. In this regard, the DHSS reports each quarter data collected by the Communicable Disease Surveillance Centre and the latest available figures cover the period from the introduction of HIV antibody tests for general use in October 1985 to the end of September 1987.

Table 3 provides an analysis by geographical region of the 7,500 positive HIV tests reported so far to the monitoring system. The figures are incomplete because under and late reporting are known to occur. In addition, they cannot be regarded as an accurate guide to geographical prevalence patterns since individuals may undergo testing in a region other than that in which he or she usually lives. Furthermore, laboratories that undertake the reporting of cases to the monitoring system may in some instances be located in regions other than those in which the tests were actually carried out. Nevertheless, the data serve a useful purpose in dispelling any complacency that this particular health problem is confined to the London area alone. Although only 24 per cent of AIDS cases to date have been reported from outside the four Thames regions of the NHS, nearly 50 per cent of HIV positive test results have been recorded in the non-London regions⁴.

The data are analysed from the perspective of patient characteristic in Table 4. It is immediately apparent that the composition of the known HIV antibody positive population differs markedly from that of the current AIDS population shown in Table 2. Thus, whereas homosexual/bisexual males account for 84 per cent of cases of AIDS to date, they contribute only 45 per cent of the HIV antibody positive numbers at the present time. The data have to be treated with some caution not only for the reasons already noted, but also because of the problem of overlap – that is, some AIDS cases will be included in the figures for HIV antibody positive cases. Nevertheless, the central point to emerge from the data is that the composition (by patient characteristic) of the future AIDS caseload will be different from that being seen today and this could have important implications for the provision of care.

Most notably, the data suggest that more cases of the full AIDS syndrome can be expected among intravenous drug

Table 3 Cumulative totals of HIV antibody positive persons (up to end September 1987) and cases of AIDS (up to end November 1987) by geographical region.

	HIV positives	AIDS cases
ENGLAND		
Regional Health Authority		
Northern	228	31
Yorkshire	218	17
Trent	206	19
East Anglia	140	17
NW Thames	2,035	515
NE Thames	1,205	226
SE Thames	692	111
SW Thames	166	39
Wessex	188	24
Oxford	264	21
South Western	174	19
West Midlands	294	19
Mersey	91	15
North Western	234	38
WALES	61	18
NORTHERN IRELAND	50	4
SCOTLAND	1,311	37
TOTAL	7,557	1,170

Source: DHSS

Table 4 Cumulative totals of HIV antibody positive persons reported up to end September 1987, by patient characteristic, United Kingdom.

Patient characteristic	Male	Female	Unknown	Total
Homosexual/bisexual	3,381	0	0	3,381
IVDA	760	400	24	1,184
Homosexual and IVDA	45	0	0	45
Haemophilia	1,056	4	1	1,061
Recipient of blood	41	28	1	70
Heterosexual contact	150	164	8	322
Child of HIV antibody positive mother*	25	21	28	74
Several or other risks or no information	1,204	88	128	1,420
TOTAL	6,662	705	190	7,557

* The presence of antibodies in a baby's blood is not an accurate guide to infection

Source: DHSS

abusers in future years. By the end of November 1987 this group had accounted for only 17 (1.5 per cent) of the 1,170 cases of AIDS reported to the surveillance system. Yet the information contained in Table 4 shows that intravenous drug abusers make up 16 per cent of the known infected population at the present time. This group will therefore become increasingly prominent in future AIDS case mixes, a development that will have significance for patient management since these individuals do not usually have the support of the informal care networks enjoyed by the male homosexual community.

The trend will also serve to modify contemporary patterns in two other ways. First, the data to the end of September 1987 show that 34 per cent of the known 1,184 HIV positive subjects infected through intravenous drug abuse are female. In all of the other patient groups combined, females account for less than five per cent of identified HIV positive cases at present. Intravenous drug abuse is consequently one of the principal conduits for

2 The data published by the DHSS do not provide a breakdown of fatalities by sex and this proportion is employed as males account for 97 per cent of all AIDS cases.

3 The 11 months total of 372 deaths to the end of November 1987, averages out at nearly 34 per month, or an estimated 406 for the year as a whole.

4 Furthermore, the analysis by McCormick and colleagues (1987) of 964 UK AIDS cases found that although 75 per cent had been reported from the Thames regions of the NHS, 'only' 66 per cent of the total number of patients gave a residential address in the Thames/London region.

growth in the numbers of AIDS cases among women in the future.⁵

Second, the cases of HIV infection linked to intravenous drug abuse known at present may also have an important impact on the future geographical distribution of AIDS cases. This observation reflects the fact that 756 (64 per cent) of the 1,184 currently identified cases in the UK have been reported in Scotland. Indeed, intravenous drug abusers are by far the most numerically significant element within the identified HIV positive population in Scotland – by the end of September 1987 they accounted for 58 per cent of all Scottish HIV positive cases compared with 7 per cent in the rest of the UK. Most new Scottish cases of AIDS in the immediate future may therefore be expected to stem from drug abuse whilst elsewhere in the UK homosexual/bisexual behaviour will continue to be the predominant source.

Haemophiliacs and individuals believed to have been infected via heterosexual intercourse comprise the third and fourth largest groups in Table 4. Focusing on the former, about 1,200 haemophiliacs are HIV antibody positive. Although it is not known how many of this group will eventually progress to AIDS, further infections should not occur because of the measures that have been taken to safeguard supplies of blood and blood products.

Within the heterosexual grouping, published data for the UK, excluding Scotland, indicate that in 21 per cent of cases infection appears to have been acquired through sexual contact with individuals belonging to the currently recognised high risk groups. A further 58 per cent of known HIV positives in the heterosexual group comprise, *inter alia*, 'persons without other identified risks from countries where heterosexual transmission is believed to play an important role.' The prevalence of HIV in the UK heterosexual population at the present time is therefore very small. Nevertheless, complacency would be inappropriate. The 322 HIV positive cases reported by the end of September 1987 represented an increase of nearly 80 per cent over the figure published just six months earlier.

Although the foregoing data offer some valuable insights into the spread of HIV infection in the community, they suffer from a number of minor limitations – some of which have already been noted – and the much more substantial problem of understatement. Obviously, not everybody who has been infected with HIV has presented for testing, not least because it is possible for an individual to be unaware that he or she has been infected with the virus.⁶ Consequently, there is no doubt that the information collected by the HIV surveillance system understates the prevalence of infection in the population. What is not clear, however, is the magnitude of this understatement.

Many suggestions have been put forward about the true prevalence of HIV infection in the UK. About one year ago the Department of Health estimated that as many as 30,000 people might be infected with the virus. At the time, however, it was conceded that the figure could be wrong by up to 50 per cent in either direction (Newton, 1987) and experts called to give evidence to the Social Services Committee (1987) described the estimate as 'a complete guess'.

Currently, the Department of Health considers that 40,000 people may be HIV antibody positive. The British Medical Association believes that prevalence may be higher at 50,000. Alternatively, Gallwey (1987) has suggested that only one in 10 of those infected have been identified and on this basis the current total may now be nearer 75,000. Yet other estimates claim that between 100,000 and 250,000 people may be carrying the virus today (Social Services Committee, 1987).

5 Heterosexual transmission is also important in this context. The data to the end of September 1987 show that 51 per cent of the 322 HIV positive cases believed to have become infected through heterosexual contact are female.

6 In addition, the absence of curative therapy coupled with the potentially severe social and economic costs of a positive test are powerful disincentives for individuals who suspect they might be infected not to present for investigation.

Against this background of uncertainty, an alternative approach to gaining a more accurate understanding of the spread of HIV might be thought to lie in detailed analyses of specific populations. Yet here, too, little if any progress is possible because of the lack of appropriate information. Focusing on homosexual males – the group accounting for 84 per cent of current AIDS cases – a survey by Carne and co-workers (1987) found a prevalence of HIV antibodies among those attending a London sexually-transmitted-disease clinic of 25.3 per cent in November/December 1986. Setting aside the confusion generated by reports of different rates from other parts of the country, it is not known how representative clinic attendees are of the rest of the homosexual community nor, indeed, is it clear what the size of the latter might be. Similar observations apply in the context of intravenous drug abusers, among samples of whom HIV prevalence rates have been found to vary from over 50 per cent in Edinburgh to about 10 per cent in London (Adler, 1987a).⁷

Yet, even if more accurate information about the prevalence of HIV now present in the community did become available, the task of predicting the burden that would flow from this pool of infection would still be confounded by the ambiguities surrounding the clinical consequences of the virus. Focusing on AIDS alone, there is much uncertainty about the latency period between infection and the development of the syndrome. Recent statistical analyses have suggested mean incubation periods as wide apart as 4.5 years (Lui et al, 1986) and 15 years (Rees, 1987). Investigating cases infected via blood transfusion, Medley and co-workers (1987) have shown that the mean incubation period may vary significantly according to the age at which infection is acquired. It is also possible that latency may be influenced by the nature and scale of the infectious challenge. At present, the data base needed to clarify these issues inevitably does not exist. And alongside this problem there are of course additional uncertainties concerning the nature and timing of the other consequences of HIV infection and the possibility that some sero-positive subjects may never develop HIV related disease.

THE FUTURE

It follows from these observations that if the clinical burden associated with current levels of infection in the community cannot be predicted with any confidence then longer term developments must lie even deeper in the realms of uncertainty. How the virus might spread in future years will depend on a diverse range of variables about which only relatively crude speculation is possible at the present time. From a 'technical' perspective, for example, it has been suggested that HIV is developing new strains at a pace that could serve to thwart efforts to develop an effective vaccine and defeat the measures currently employed to protect blood supplies against contamination. Changes in the virus might also increase the power to infect of those body fluids that are not thought to pose a hazard at the present time.

7 Some commentators have argued that a more accurate understanding of the prevalence of HIV than is available at the present time could be gained by introducing a system of anonymised screening of blood samples – obtained for other investigative purposes – for the virus. This approach would certainly yield information regarding the numbers infected and permit trends over time to be measured. But some evidence presented to the Social Services Committee Enquiry into AIDS (1987) suggested that testing in this way would not enable identification of risk groups and without this information accurate epidemiological models cannot be constructed. For this and various other reasons the Committee was unable to recommend the general use of anonymised screening, but debate continues about the need for a measure of this sort so that some degree of precision might be introduced into planning for the likely impact of the virus. Recently, for example, Black and his colleagues (1987) have called for the introduction of a system of testing all pregnant women for HIV sero-positivity. In conjunction with responses to a brief questionnaire giving a few personal details, the results would provide 'a sensitive index of the rate at which the epidemic is entering the heterosexual population in each area'. The system would ensure anonymity and women would have the choice of whether or not to learn the result of the blood test.

Alternatively, mutation of the virus could act to diminish rather than increase its infectiousness (Schild, 1987).

More fundamentally, future changes in the incidence of infection will reflect the extent to which individuals modify their lifestyles in order to avoid the risk of becoming infected with HIV. Current understanding is that HIV is essentially a sexually transmitted infection (Friedland and Klein, 1987). The message that needs to be conveyed is therefore straightforward. Sexual contact with an infected person generates a risk of acquiring HIV infection and as the prevalence of infection increases, so too does the likelihood of infection in a random partner. Risk may be eliminated by confining sexual contact to one uninfected partner. In other circumstances, for example, where more than one partner is taken and infection status is unknown, risk may be reduced by the use of condoms.

The virus does not discriminate between different types of sexual practice. Consequently, 'the sexually active population as a whole should be regarded as possibly at risk and should receive practical advice about how infection can be avoided' (Acheson, 1986).⁸ To this end, the government launched a publicity drive, based on newspaper advertisements, in March and April 1986. The initiative was, however, widely attacked as unimaginative and for being conducted on too limited a scale to be effective. In response to these criticisms, a new £20 million campaign was established in November 1986 with the objective of raising public awareness about AIDS and to dispel myths about the ways it can be spread. It has employed television, radio, cinema and newspaper advertisements whilst information leaflets have been distributed to all 23.5 million households in Britain. More recent strands of the campaign have been aimed specifically at intravenous drug abusers with the objective of discouraging the habit altogether, or at least promoting safer practices by dissuading people from sharing equipment.

The government's measures are being complemented by private and voluntary sector initiatives, and of course the extensive discussion of AIDS and HIV, albeit of variable quality, throughout the entire news media has also helped to raise awareness. Several studies have been undertaken to assess the impact of these multi-source efforts but the evidence available to date has tended to paint a rather confusing picture. Focusing just on the government's contribution, for example, the Director of the World Health Organisation's AIDS Programme has described the official UK campaign as a model for other countries (Mann, 1987) whereas a prominent psychologist involved directly in counselling patients has argued that it appears to have raised considerable anxieties in groups at lower risk while having little impact on those at higher risk (Miller, 1987).

The government's monitoring of its own campaign, carried out via surveys conducted between February 1986 and February 1987, has concluded that 'there is considerable evidence. . . that major progress has been made over the year in terms of the objectives of the government's publicity campaign to increase awareness and knowledge, to change attitudes and thereby to modify behaviour' (DHSS, 1987). Specifically, interviewees' responses indicated 'major increases in knowledge of the ways in which AIDS can be transmitted' and that 'many substantial changes have occurred in public attitudes'. The findings also appeared to show that 'there have been major changes in the claimed sexual behaviour of homosexuals.'

The observations concerning progress in public knowledge about the virus have been broadly corroborated by other research, for example, a study carried out between June and December 1986 by the Department of

Community Medicine at the University of Southampton (Campbell and Waters, 1987). However, the key requirement for preventing the spread of HIV is that this understanding should be translated into appropriate behavioural change and in this respect several surveys conducted during 1987 have produced less sanguine findings (Anon, 1987). For example, a MORI poll of just over 1,000 people aged between 16 and 54 years, commissioned by the Independent Broadcasting Authority and carried out during March, found there had been no apparent reduction in promiscuous behaviour since a previous investigation in December 1986. It showed that 2 per cent of the population reported having had sexual intercourse with four or more people in the previous two months, one per cent with three partners and one per cent with two partners.

A BBC/Gallup survey conducted in April 1987 was also unable to detect signs of appreciable behaviour change to counter the threat posed by AIDS. Further, about one-third of the sample admitting to three or more sexual partners during the previous year did not consider a change in their sexual behaviour necessary. It was unclear whether this finding stemmed from confidence on the part of the respondents concerned that their sexual practices were safe or whether it reflected a disregard for, or even ignorance of, the messages of the AIDS information campaign.

More optimistic trends have emerged, however, from several surveys focusing on homosexual males. For example, Carne and co-workers (1987) have reported a reduction in the number of sexual partners as well as shifts towards safer sexual practices among samples of homosexual/bisexual men attending the sexually transmitted disease clinic of a London teaching hospital. Between 1982 and 1984, the prevalence of HIV antibodies in this group grew by 7.4 per cent per annum but the rate of increase fell to 1.8 per cent between 1984 and November/December 1986. Over the same period, there was a fall in the gonorrhoea rate – an indicator of alterations in sexual behaviour since it is one of the most prevalent sexually transmitted diseases and has a short incubation period – from 15.3 per cent to 5.1 per cent.

Some degree of caution has, of course, to be exercised in interpreting the information that has been gathered so far about the public's understanding of, and response to, HIV infection and AIDS. Individuals vary considerably in their willingness to answer fully and accurately questions dealing with highly sensitive and personal issues. Further complications arise from the apparent inconsistencies in survey findings, although these may often reflect variations in such factors as questionnaire design, composition of the sample population and the timing of fieldwork. Nevertheless, the present position would appear to be that a widespread understanding of the hazards of HIV and of the ways it is transmitted has been created by the combined information efforts of many different agencies but that this progress has yet to be matched by changes in sexual behaviour on an appropriate scale. In reality, comparatively little is known about contemporary patterns of sexual activity – especially the numbers practising safe sex – and this area was clearly identified by a recent meeting of the Royal Statistical Society on the statistical aspects of HIV infection as one in which there is an urgent need for more and better data (Altman, 1987). Nevertheless, the evidence available at present is a cause for concern and in 1988 the Health Education Authority, which took over responsibility for AIDS information campaigns from the Department of Health in October 1987, will launch a fresh initiative in an attempt to encourage changes in sexual behaviour.

Forecasts

Attempts to forecast the likely future burden of HIV in the UK are therefore fraught with difficulty. Many of the key variables that will influence future patterns are, at the present time, unknown quantities. The number of people currently carrying the virus, the typical duration and

⁸ At the present time, HIV appears to be largely confined to specific high risk groups. However, via sexual activity, certain members of these groups – especially bisexual males and intravenous drug abusers – might act as bridges for the infection to cross into the wider population. In particular, there is concern that in order to finance drug taking some HIV positive drug abusers may resort to prostitution and thereby risk passing on the virus to their clients. Once the infection has entered the heterosexual community, the likelihood is that it will be self-sustaining (Anderson, 1987).

intensity of infectiousness of HIV sero-positives, the extent of these individuals' sexual interaction with other as yet infection-free members of the population, the precise levels of risk of acquiring infection entailed in these contacts and how far 'appropriate' change in sexual behaviour can be achieved are all major sources of uncertainty. Deficiencies in these and other key areas of knowledge have not, however, deterred attempts to predict the spread of the virus, but more often the numbers of AIDS cases, many years into the future.

Of the many examples that might be quoted, one of the most recently published forecasts is that constructed by Wilkie (1987). The model assumes that 5 per cent of males are homosexual and that AIDS does not spread significantly into the heterosexual community. On this basis, it is predicted that the peak of the epidemic will be reached in 1998 when there will be 63,000 sick from AIDS and another 48,000 dying. Thereafter, it is estimated that a further 7,600 deaths will occur each year.

A possible scenario of even more calamitous proportions is suggested by the Christian Medical Fellowship in a new book entitled 'The 20th Century Plague' (Collier, 1987). It is argued that 'if lifestyles involving multiple sexual partners, extramarital relationships and certain homosexual practices do not change, if intravenous drug addicts continue to share infected needles and syringes, and prostitution still goes on' and if safer sex campaigns fail then the virus will spread unchecked within the population. This could mean 3 million people infected with HIV in the UK by 1991, rising to 12 million by 1994. At this later point, it is estimated that 'there would only be between 120,000 and 240,000 cases of AIDS in Britain. Most of the rest of the 12 million would be symptomless. But they would represent a time-bomb waiting to go off by the end of the century.'

Given the considerable measure of uncertainty that surrounds many of the factors that will determine the potential spread of HIV in the future, it is not clear how useful 'forecasts' of this nature really are. More moderately, and arguably in much closer accord with the information currently available, Anderson and May (1987) are only prepared to go as far as to suggest that heterosexual transmission could well spread AIDS within relatively promiscuous sub-groups. Beyond this, the possibility of much more disseminated epidemic would 'depend on whether a significant fraction of the people infected with HIV remain as carriers who show no symptoms and never develop AIDS, essentially for the rest of their sexually active lives. If this is so, then modest levels of promiscuity could result in HIV infection spreading slowly, over decades, among people who would not think of themselves as promiscuous.'

This observation is offered by Anderson and May as a 'guess' and as such underscores the uncertainties of the present time. Elsewhere, the first of these authors, in collaboration with other workers, has demonstrated that even more finely focused attempts at forecasting are unable to yield confident insights into the future. Confining attention to HIV transmission within the male homosexual community in the UK, Anderson and his colleagues (1987) constructed a mathematical model with the objective of gauging the minimum size of the future AIDS epidemic. It was assumed that transmission ceased at the end of 1986, but even on this restricted basis the model's predictions were found to range considerably according to the values given to critical parameters such as the mean incubation period of HIV and the proportion of sero-positive subjects progressing to AIDS. In discussing the findings, it was suggested that it may take as much as 30-50 years' longitudinal study to obtain the necessary data in these and other key areas.

Against this background, the policy of the UK government is that 'predictions should be made only as and when justified by the available scientific data' (Newton, 1987a). Provisional forecasts for the short-term have, nevertheless, been produced by the Communicable Disease Surveillance Centre. Extrapolating from previous

trends, Tillett and McEvoy (1986) have estimated that there will be 3,000 new cases of AIDS in the UK in 1988. This projection is based on only five years' data and is inevitably subject to potentially wide margins of error. Indeed, latest available figures suggest that it may possibly overstate the total for 1988. During the 11 months to the end of November 1987, 560 cases of AIDS were reported to the surveillance system. The monthly average implied by this figure yields an estimated total for the whole of 1987 of 611. This sum implies a cumulative total at the end of 1987 of 1,221 cases, which is twice that recorded by the end of 1986. If it is assumed that a further doubling of the caseload will occur during 1988, then 'only' about 1,200 new cases of AIDS may be expected during the latter year.

It should be noted, however, that this analysis may be flawed because of the existence of various drawbacks in the available data. Late reporting of AIDS may mean, for example, that the true number of cases diagnosed during a given year – the basis of the predictions by Tillett and McEvoy – is greater than the number reported to the surveillance system over the 12 months in question. Consequently, it is possible that the projected figure of 3,000 new AIDS cases in 1988 may turn out to be accurate. Further, it is intriguing to note that if this is so, and the annual doubling trend is maintained, then 12,000 new cases may be anticipated in 1990, a total that can also be obtained by assuming that about one quarter of the 40,000-50,000 people currently believed to be HIV antibody positive will progress to AIDS in three years. However, superficially satisfying as this confluence of forecasts may be, the underlying reality is that at the present time there exists a fundamental lack of information about the prevalence of the virus in the community and its eventual effects.

PROGRESS IN VACCINES AND MEDICINES

A further source of uncertainty bedevilling attempts to forecast the course and impact of HIV infection lies in the role that vaccines and medicines will come to play in containing and treating the virus. Theoretically, progress in these two areas might pull in opposite directions. The development of an effective vaccine could offer the potential for eliminating further spread of HIV whereas the evolution of survival-promoting but non-curative medicines could, if they have no (or relatively little) impact on infectiousness, serve to expand the pool of HIV contagion within the community. Such developments are, however, speculative, despite the substantial academic and industrial research efforts that are currently being channelled into such areas. (The Medical Research Council is currently engaged on a £14.5 million research programme and it has been estimated that the British based pharmaceutical industry alone is spending about £40 million per year on AIDS related research.)

Nevertheless, since the identification of HIV 1 in 1983 the scientific community has made impressive steps forward in understanding the virus and its pathological effects in humans. In practical terms this has already led to the availability of a number of tests for HIV antibody and the recent development of assays capable of detecting HIV 1 itself. In the near future tests capable of distinguishing between antibodies to 'core' antigens within the virus, as opposed to those on the outer envelope, are due to become available.

In time, tests for HIV 2 should also be developed. Such techniques are of course vital if epidemiologists are to be able to track the spread of the infection in populations. They also have an indirect therapeutic/preventative role. The availability of tests for HIV 1 has already helped to change the behaviour of many sero-positive individuals, both in terms of encouraging them to adopt 'healthier' lifestyles and in leading them to protect the interests of others to whom they might pass on the infection.

In the context of anti-viral medicines, the only product so far available for the purpose of actively inhibiting HIV infection in man is, as already noted, zidovudine. This is similar to thymidine, one of the four substances used to

form DNA nucleotides. Under the control of an enzyme known as reverse transcriptase, the RNA within HIV acts as a template against which a DNA copy is made, eventually to be integrated with the genetic material of the human host cell. Zidovudine inhibits reverse transcriptase in creating a DNA copy chain, because when it is taken up instead of thymidine it lacks the 'link' necessary for other molecules to attach themselves. This interrupts the HIV replication process, leaving parts of the viral RNA exposed to the degrading action of host cell enzymes.

Clinically, this medicine has shown itself capable of extending the life expectancy of patients with the AIDS syndrome, and it is to a degree at least effective in the context of HIV dementia. Its potential for extending the period of symptom free life amongst non-symptomatic people with HIV infection is unproven: interest has naturally been expressed in this possibility, but since zidovudine can cause significant side effects – most notably anaemia serious enough to demand blood transfusions – a cautious approach to investigating the medicine's role is regarded as advisable.

Currently a key focus of research is combination therapy, in which the effects of zidovudine may be enhanced by the simultaneous use of other agents. Many experimental medicines with actions related to those of zidovudine are also under investigation by both government and industry funded researchers, who hope to identify less toxic therapies for the future.

In the relatively near future the recent achievement of a British company in producing large quantities of HIV reverse transcriptase through recombinant DNA techniques, and in obtaining the enzyme in crystalline form, should open the way to a detailed understanding of its molecular structure. Differences between the latter and that of human cell DNA polymerases may then be systematically exploited in attempts to produce new medicines which selectively block HIV replication. However, inhibition of reverse transcription is only one of the approaches to HIV chemotherapy that have been identified (Mitsuya & Broder, 1987; Hall, 1987; Yarchoan and Broder, 1987). Other potentially vulnerable stages of the HIV replication cycle include:

Cell entry

HIV binds to CD4 receptors on the surface of T4 lymphocytes and other cells, and subsequently gains entry to the target cell. If this initial invasion can be prevented, infection may be halted. A substance known as peptide-T has been tested in this context, but with disappointing results. The lipid containing medicine AL721 from the Weizman Institute in Israel may have an effect in this area, reducing viral/CD4 binding through creating distortions in the HIV envelope (Heley, 1987).

RNA uncoating

The anti-viral medicine amantadine probably functions (in the context of influenza A) via an inhibition of viral ability to 'uncoat' its genetic content after entry into a target cell. It is theoretically possible that similar effects could be achieved in respect of HIV/retroviruses.

Integration of DNA copies of viral RNA with host DNA, and the subsequent transcription of the former to messenger RNA

The experimental medicine ribovirine may inhibit the 'capping' of messenger RNA – and hence the later production of viral proteins – more than it affects the corresponding functions of human cells (Hirsch and Kaplan, 1987). However, it is not officially approved for the purpose of treating AIDS.

Viral protein assembly

It is possible that the chemical signals (peptides) which activate T4 lymphocytes also boost synthesis of viral components (Gallo, 1987). Greater understanding of this could open the way to new therapies, although these could

interfere with normal immunological processes. A less hazardous route to therapy may thus be to try to disrupt the formation of specific viral proteins, such as the protease enzyme responsible for 'cutting up' the proteins produced by the three main genes that encode for the components of HIV. Researchers in the pharmaceutical industry have already identified potent inhibitors of this enzyme *in vitro*. Other identified proteins appear to have a regulatory role in the process of assembly which might be vulnerable to disruption.

In addition it may be possible to prevent or alleviate the ill-effects of HIV infection through treatments aimed at correcting or modifying its impact on the immune system. The pharmaceutical industry in Britain and elsewhere is investigating a range of substances (lymphokines) which T4 lymphocytes can produce in order to 'orchestrate' immune system responses. They include interferons and interleukins, together with other potential 'immunomodulators' such as Colony Stimulation Factor (CSF) and Tumor Necrosis Factor (TNF) (PMA, 1987). The possibility that auto-immune reactions are involved in syndromes such as AIDS is also being investigated.

With regard to vaccine development, French researchers are already involved in a human vaccine trial in Africa, and in America several companies have put forward, or are preparing, candidate vaccines for consideration for trials. In Britain the Medical Research Council is also involved in this field, in particular through the work of Jarrett in Glasgow (MRC, 1987).

Although it is commonly assumed that the role of vaccines will be in essence one of primary prevention, they may in practice also prove significant in maintaining HIV sero-positive individuals in an indefinitely prolonged state of freedom from symptoms (that is, maintaining viral latency). Indeed, techniques based on passive and/or active immunisation may ultimately be able to eliminate viral material from infected subjects (Salk, 1987).

However, although the goal of an effective protective vaccine (or vaccines) is clearly a desirable ideal, its achievement could prove elusive. So far animal trials have proved disappointing in as much as circulating antibodies raised to viral envelope components do not seem to confer adequate HIV protection. A complex response involving cellular immunity is almost certainly necessary for this to be achieved. And it is possible that the variability of HIV strains (out of a total genome of 9,500 nucleotides some variants of HIV 1 differ by as much as 1000) will defeat an immunisation based approach, despite some encouraging indications that infection with one HIV strain protects against others.

Finally, the testing of vaccines for human use will prove long and complex. Any suggestion, therefore, that advances in this area can be expected in the next few years to be shown to have a protective effect against HIV infection should be treated with reserve.

CONCLUSION

Despite the uncertainty that surrounds the spread of HIV in the foreseeable future, there is little doubt that its impact on the community could potentially be substantial. In the context of AIDS mortality, Osborn (1987) has commented from United States' experience that 'we are losing a generation of well-trained and exceptionally talented young men and humanity cannot afford to lose an iota of trained talent in these troubled times.'

In the United Kingdom, deaths from AIDS so far are only about one-fortieth of the total recorded in the United States but they are steadily gaining greater significance. In the 11 months to the end of November 1987, 372 AIDS deaths were recorded, suggesting a possible total for the year as a whole of 406 deaths. If it is assumed that the mean age of death from AIDS is 35 years, then current annual fatalities may be estimated to be responsible for more than 12,000 lost years of potential working life. If it is further assumed that all of these deaths occur in England and Wales

Table 5 Years of potential working life lost due to deaths in 1985 from certain causes, males, England and Wales.

Cause of death	Years lost (thousands)
Malignant neoplasms	205.5
Trachea, bronchus, lung	49.0
Digestive organs	49.3
Circulatory system disease	264.8
Coronary heart disease	195.4
Cerebrovascular disease	33.4
Diseases of respiratory system	50.3
Congenital anomalies	59.2
Conditions in perinatal period	67.3
Accidental deaths	156.7
Road accidents	97.4
Suicide	56.9
All causes	1028.5

Source: Office of Population Censuses and Surveys

and involve males⁹, then comparisons may be drawn between AIDS and other causes of premature death. It is clear from Table 5 that at present AIDS mortality generates a level of loss that is small compared to most diseases and almost insignificant in relation to such major contemporary problems as coronary heart disease and accidents. However, if the current annual rate of increase in AIDS deaths is maintained (the total rose almost 2.4 fold during 1987) then about 5,500 deaths from this cause may be anticipated in 1990. If this prediction proves correct, the loss of potential working life generated by 1990's AIDS fatalities will total more than 165,000 years, a toll second only to coronary heart disease in Table 5 (assuming the values for these other causes do not alter significantly between 1985 and 1990).

HIV also has major resource implications for the National Health Service. Attention has so far tended to focus principally on the hospital expenditures incurred in treating HIV positive subjects who have progressed to the full AIDS syndrome. However, the costs reported from this sector of the health service have shown quite a considerable degree of variation. In 1986, Johnson and her colleagues calculated the costs of in-patient and out-patient care for an AIDS patient between diagnosis and death at nearly £7,000.

Subsequently, £10,000-£20,000 became the most frequently quoted estimate of the expenditure involved with a progressive shift towards the upper end of the range over time. Indeed, in the recent House of Commons debate on health, the Parliamentary Under-Secretary for Health stated the cost to be about £20,000 per patient per year (Currie, 1987). It is not clear whether this figure takes into account the costs of treatment with zidovudine which are now estimated at around £4,000 per patient per year (Marsh, 1987).

It should of course be emphasised that AIDS patients do not require hospital care alone. Indeed, researchers at St. Mary's Hospital in London have recently described a theoretical package of care for the 'average' adult AIDS patient in which only one month of the survival period of one year is spent as a hospital in-patient (Cunningham and Griffiths, 1987). Other elements of the package draw upon day care treatment facilities as well as the home help, district nursing, hospice at home and various other services. In total, the per capita cost of the care package is estimated to be slightly more than £27,000.¹⁰

If this sum is applied to the estimated out-turn number of AIDS cases for 1987 (611), the cost of providing care for

the year's cohort of new patients may be calculated to be £16.5 million. In 1988, this sum could rise five fold to £81 million if the Communicable Disease Surveillance Centre's prediction of 3,000 new cases is fulfilled. This expenditure figure is equivalent to the cost of providing acute hospital in-patient treatment for 128,000 non-AIDS patients – a total equivalent to about one-fifth of the current hospital waiting list in Britain.

It is difficult to judge how accurate these estimates might be. The fundamental uncertainties concerning the future number of AIDS cases has already been discussed in detail. In addition, the use of average data disguises the fact that the shape of the AIDS illness – and hence the costs of care – can vary quite markedly between patients. Changes in the approach to care – forced by an increasing caseload or as a concomitant of pharmaceutical progress – may serve to alter per capita case costs. Finally, the estimates presented above disregard the costs arising from the treatment of non-AIDS manifestations of HIV infection as well as those directly and indirectly generated by testing for the virus.

Despite these cautionary observations, it is clear that HIV could have very serious resource implications for a health service that is already experiencing severe financial pressures. The potential impact of HIV in this respect coupled with the immense human and social costs accompanying the spread of the infection underpin the urgent need to win both the battle against the epidemic and the war against the virus (Hall, 1987a). In the present absence of an effective vaccine or treatment, the former depends on an appropriate public response to health education about the nature of HIV and how infection can be avoided. The latter is a more distant prospect but the worldwide efforts of the academic and industrial research communities, often working in collaboration, suggest that more effective drug treatments at least are a real possibility (Healy, 1987). In addition to saving lives and reducing suffering, such innovations may also play an important role in helping to limit further dissemination of the virus by reducing the infectivity of individuals already infected.

⁹ These are currently acceptable assumptions since the true proportions in fact lie between 95 and 100 per cent.

¹⁰ This figure includes the cost of zidovudine treatment which at the time of preparing the estimate was £5,200.

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*This Briefing was prepared by Nicholas Wells.
David Taylor contributed the section on vaccines and medicines.*

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Office of Health Economics

12 Whitehall London SW1A 2DY.

Telephone: 01-930 9203.