

Human immunodeficiency virus infection in Northern Ireland 1980–1989

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SUMMARY

*To 31st December 1989, 71 persons are known to have attended medical practitioners in Northern Ireland with a diagnosis of Human Immunodeficiency Virus (HIV) infection. Twenty-one of these persons have had the diagnosis of Acquired Immune Deficiency Syndrome (AIDS) and 11 have died. The distribution of reports in the "at risk" categories of homosexual/bisexual males, injecting drug users, heterosexual males and females was significantly different ($p < 0.001$) from those reported in the United Kingdom as a whole. Of tests for HIV infection carried out in patients attending the genitourinary medicine department of the Royal Victoria Hospital between 1987–1989, 0.16% have been positive. The prognostic value of the T4 lymphocyte count at presentation for the subsequent development of AIDS was significant ($p = 0.0011$). The commonest AIDS indicator disease diagnosed was *Pneumocystis carinii* pneumonia which was seen in seven of the 21 patients (33%).*

INTRODUCTION

The Acquired Immune Deficiency Syndrome (AIDS) was first described in 1981¹⁻³ and was soon recognised to be behaving as an infectious disease which particularly affected homosexual or bisexual men, intravenous drug misusers, people from central Africa and haemophiliacs. These categories of persons

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became known as "high-risk groups" for development of the disease. The cause of the syndrome is now commonly accepted to be human immunodeficiency virus (HIV), first described in 1983.⁴ The pattern of the HIV epidemic has differed from country to country⁵ and even from city to city^{6,7} within a particular country. These differing emerging patterns seem to depend on local epidemiological factors specific to each area. We describe the emergence of HIV infection in Northern Ireland, and we examine the pattern of disease that develops and the management of patients.

METHODS

The data was collected from the records of the Genitourinary Medicine Departments of hospitals in Northern Ireland. Other sources were the Regional Virus Laboratory, the Northern Ireland Haemophilia Service and the Northern Ireland Blood Transfusion Service.

The Regional Virus Laboratory began anti-HIV testing in May 1985 and the Northern Ireland Blood Transfusion Service in October 1985. An anti-globulin ELISA test (Vironostika anti-HTLV-III, Organon, Teknika) is used by the Regional Virus Laboratory, and if positive, it is repeated together with two different tests — a competitive ELISA test (Vironostika anti-HIV Uniform Organon Teknika) and a gelatin particle agglutination test (Serodia-HIV Fujirebio Inc.). If these tests are all positive a further serum sample is obtained from the patient and all three tests are repeated. If the three tests are again positive only then is the patient reported as confirmed anti-HIV positive. Initially confirmatory tests were done by Dr R S Fedder of the Section of Virology, Microbiology Department, the Middlesex Hospital and University College Medical School, London, but they are now done in the Regional Virus Laboratory. Anti-HIV IgM tests were carried out on sera from two babies born to anti-HIV positive mothers by Dr P P Mortimer, Virus Reference Laboratory, Central Public Health Laboratory, Colindale, London.

Retrospective testing of haemophiliacs was done on available sera which had been stored at -20°C in the Regional Virus Laboratory and fresh sera were obtained from the Department of Haematology, Royal Victoria Hospital.

HIV p24 antigen ELISA tests (Organon Teknika) were performed on sera of those patients entering the Medical Research Council study on the use of Zidovudine in asymptomatic persons with HIV positive tests, on two babies born to anti-HIV positive mothers and on other patients when clinically indicated. All tests done were for HIV-1 antigen or antibody.

Statistical methods used were the Chi-squared test and Fisher's exact probability test.

HIV cases seen to date

The figures quoted in this article refer to those persons known to the authors who have been under medical care in Northern Ireland. Some of these persons have not been resident in Northern Ireland but visit the province on occasions. Others are persons who have been diagnosed elsewhere but moved to Northern Ireland for their care. These figures are not the same as the official figures from Northern Ireland⁸ which purport to be reports of persons with a first-ever diagnosis of HIV infection.

The first known case of HIV disease seen in Northern Ireland was diagnosed retrospectively. The patient, a 50-year-old African male, with hepatitis B infection was admitted to the Royal Victoria Hospital in 1982 with cerebral symptoms and a pyrexia of unknown origin. He developed toxic epidermal necrolysis and died within a few days. A stored sample of blood was subsequently tested when the HIV antibody test became available, and this was found to be positive. It is thought that this man died of an AIDS-related illness. Since then there have been 71 known cases of HIV infection seen in Northern Ireland to 31st December 1989.

Table I shows the epidemiological risk categories (as classified by the Communicable Disease Surveillance Centre) into which these persons belonged. Thirty-four (48.5%) were homosexual/bisexual males and eight (11.4%) were females with only heterosexual intercourse as their risk factor. Heterosexual males accounted for six cases (8.6%). Four injecting drug users were seen (5.7%). The percentages for these groups of known epidemiology reported in the U.K.⁸ were: homosexual/bisexual males — 58.8%; females with heterosexual intercourse — 5.0%; male heterosexual — 3.9%; injecting drug users — 18.6%. The different distribution of our cases in these four categories is statistically significant ($p < 0.001$). One person has been classified as unknown category. Fig 1 illustrates the numbers of new cases seen each year by sex and risk factors.

The 16 haemophiliacs (22.5%) identified as infected with the virus in 1985 when HIV antibody testing became available have been cared for by the Northern Ireland Haemophilia Service. Of the 55 remaining persons 49 (69%) have been cared for by the genitourinary medicine services. The remaining six (8.5%) have been cared for by other agencies.

TABLE I

Cumulative totals of HIV-1 antibody positive persons seen in Northern Ireland by exposure category to 31st December 1989

<i>Exposure category</i>	<i>Male</i>	<i>Female</i>	<i>Total</i>
Homosexual/bisexual male	34	—	34
Injecting drug user	2	2	4
Homosexual/bisexual male and injecting drug user	—	—	—
Haemophiliac	16	—	16
Blood/components recipient	1	—	1
<i>Heterosexual contact:</i>			
Partner(s) with above risk factor(s)	—	1	1
Others*			
Possibly infected abroad	4	2	6
No evidence of exposure abroad	2	5	7
Undetermined	—	—	—
Child of at-risk/infected parent	—	—	—
Multiple risks	—	1	1
Other/undetermined	1	—	1
Totals	60	11	71

*Partner(s) not known to have above risk factor(s).

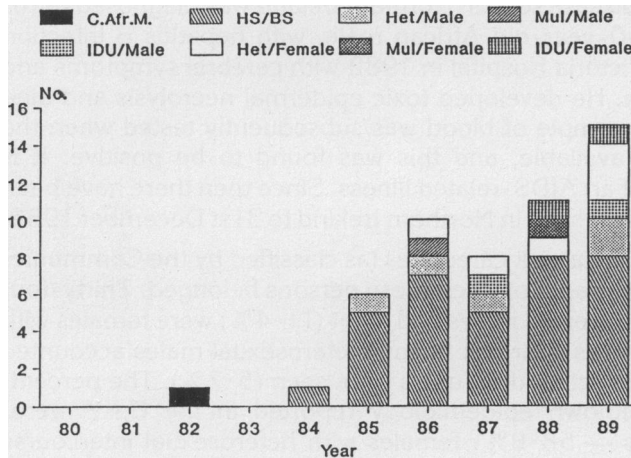


Fig 1. HIV positive persons identified each year 1980 – 1989 by sex and risk category (excludes 16 male haemophiliacs diagnosed 1985).

C.Afr.M = central African male;
 IDU = Injecting drug user;
 HS/BS = Homosexual/ bisexual male;
 Het. = Heterosexual;
 Mul. = Multiple risk factors.

To 31st December 1989, 21 persons with the Acquired Immune Deficiency Syndrome have been looked after in Northern Ireland; of these 11 have died. Table II shows the risk categories to which these patients belonged. Fig 2 illustrates the new cases of AIDS diagnosed each year. The first two cases in females were seen in 1989.

TABLE II

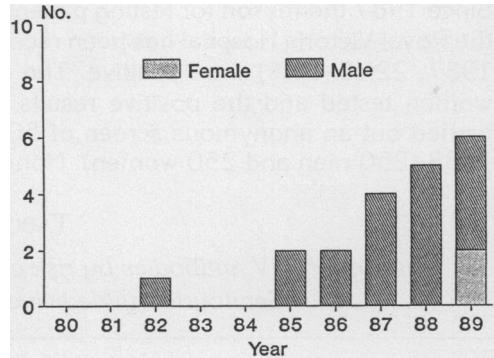
Cumulative totals of AIDS cases (deaths) seen in Northern Ireland by exposure category to 31st December 1989

Exposure category	Male	Female	Total
Homosexual/bisexual male	15 (11)	—	15 (11)
Injecting drug user	—	—	—
Homosexual/bisexual male and injecting drug user	—	—	—
Haemophiliac	—	—	—
Blood components recipient: abroad	1	—	1
UK			
<i>Heterosexual contact:</i>			
Partner(s) with above risk factor(s)	—	—	—
Others*			
Known exposure abroad	3	1	4
No evidence of exposure abroad	—	1	1
Child of at-risk/infected parent	—	—	—
Multiple risks	—	—	—
Other/undetermined	—	—	—
Totals	19 (11)	2	21 (11)

*Partner(s) not known to have above risk factor(s).

Figures in brackets are positive results.

Fig 2. Number of new cases of the Acquired Immune Deficiency Syndrome seen per year 1980–1989 in Northern Ireland.



Testing

The Northern Ireland Blood Transfusion Service has screened approximately 65,000 donors per year, about 15% of whom are new donors. Of these, four persons have tested positive — two men, one of whom was known to be homosexual and two women. Subsequent contact tracing showed that one male partner of this homosexual man and the bisexual husband of one of the women also had a positive test.

The Regional Virus Laboratory has tested 9,093 other blood samples for HIV antibodies. One hundred and twenty-three patients with coagulation defects who had received treatment with blood products were tested and 16 were positive (13.8%). If only severely affected patients (less than 0.02 units/decilitre factor VIII) are included this rises to 25%. Stored sera were available on 11 of the 16 positive patients and when tested showed that seroconversion occurred between 1983 and 1985. The source of seroconversion in one patient in 1985 was traced to a batch of heat treated factor VIII which was found retrospectively to be contaminated with HIV (Fig 3).

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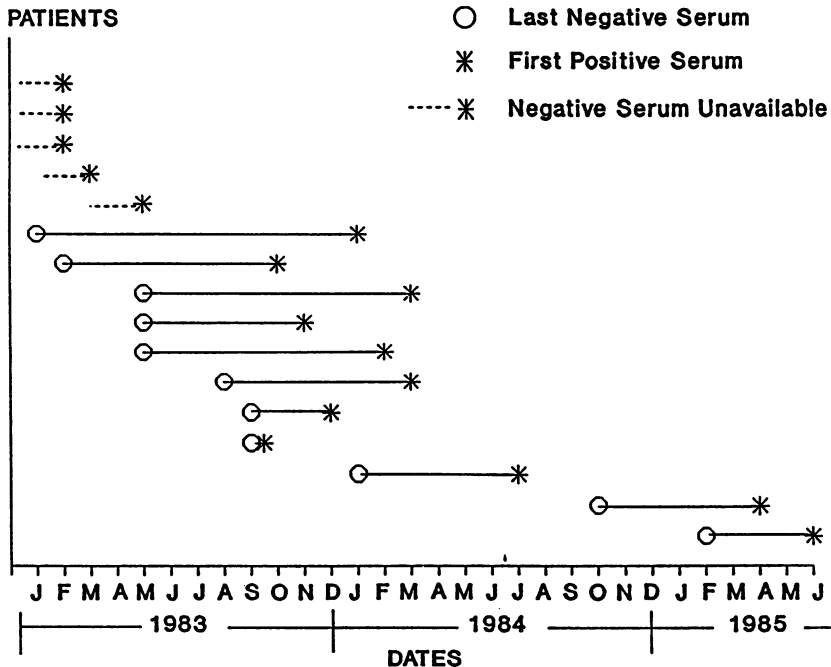


Fig 3. Time of anti-HIV-1 seroconversion in 16 haemophilic patients.

Since 1987 the reason for testing patients at the Genitourinary Medicine Clinic in the Royal Victoria Hospital has been recorded. Of the 1433 tests carried out since 1987, 22 (0.16%) were positive. The epidemiological categories for men and women tested and the positive results are shown in Table III. In addition we carried out an anonymous screen of 500 consecutive attenders at this clinic in 1988 (250 men and 250 women). None of these tests was positive.¹⁰

TABLE III
*Testing for HIV antibodies by risk categories in Royal Victoria Hospital
Genitourinary Medicine Clinic — 1987–1989*

<i>Male</i>	<i>1987</i>	<i>1988</i>	<i>1989</i>	<i>Total</i>
Homosexual	85 (2)	60 (4)	41 (2)	186 (8)
Bisexual	24	9 (1)	11 (1)	44 (2)
Heterosexual with risk factor	41 (1)	23	25 (1)	89 (2)
Injecting drug users	6 (1)	5	4 (1)	15 (2)
Anxiety	244	203	152 (1)	599 (1)
Needlestick injury	1	2	0	3 (0)
			Total:	936 (15)
<i>Female</i>	<i>1987</i>	<i>1988</i>	<i>1989</i>	<i>Total</i>
Bisexual contact	7	4	2	13 (0)
Heterosexual with risk factors	17 (1)	11 (1)	14 (1)	42 (3)
Injecting drug user	0	0	2 (1)	2 (1)
Prostitute/IDU	0	1 (1)	0	1 (1)
Anxiety	159	126	145 (2)	430 (2)
Children	2	1	0	3 (0)
Unknown	4	0	0	4 (0)
Needlestick (unknown source)	0	2	0	2
			Total:	497 (7)

Figures in brackets are positive results.

Of the remaining 7,160 tests from various sources in hospital and general practice, three male patients were found to be positive; one male with heterosexual contact in central Africa, one heterosexual male with a history of blood transfusion in the USA prior to HIV screening of blood, and one having had heterosexual contact in Amsterdam. This last patient had positive serology for syphilis and hepatitis B which are both much commoner infections in homosexual men — as we have not seen this man at the clinic there may be doubt about this epidemiological information. It should be noted that the positive tests do not correlate with the positive diagnoses shown in Fig 1, as six of these persons had had positive tests outside Northern Ireland which were not repeated.

Five persons have suffered needlestick injuries from HIV positive patients — three doctors in the genitourinary medicine service and two nurses in the haemophilia services. None of these has seroconverted during follow-up of between three to 12 months. Two infants have been born to mothers with HIV infection; neither of these has been shown to have become infected on follow-up.

HIV disease

Manifestations of HIV disease are classified according to revised guidelines laid down by the Communicable Disease Centre (CDC) in Atlanta, USA¹¹ (Table IV). Category 1 was only recognised in 1985¹² and was at first thought to be an unusual event, although it has now been recognised in over 50% of cases in some series.¹³ Common manifestations are fever, sore throat, lymphadenopathy, macular rash (especially involving the trunk), arthralgia, myalgia and headaches.^{13, 14} This illness usually occurs within a few weeks of infection and predates the seroconversion of the HIV antibody test. It has been suggested that the more severe and prolonged this acute illness the worse is the prognosis, with a more rapid decline in T helper cells and onset of late HIV disease.¹³ We have not observed this illness as yet in any of our patients, although retrospectively several reported prior illnesses which would have fitted. One patient had been referred to a medical outpatient department with this illness, but not surprisingly at that time the diagnosis was not made; this is an illness which medical practitioners need to be aware of today.

TABLE IV

CDC classification of human immunodeficiency virus disease manifestation

Group I	Acute infection
Group II	Asymptomatic infection
Group III	Persistent generalised lymphadenopathy
Group IV	Other disease
Subgroup A	Constitutional disease
Subgroup B	Neurologic disease
Subgroup C	Secondary infectious diseases
Category C – 1	Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
Category C – 2	Other specified secondary infectious diseases
Subgroup D	Secondary cancers
Subgroup E	Other conditions

The majority of patients probably have little or no early symptoms, and those who do invariably recover and become asymptomatic (Group II). Persistent generalised lymphadenopathy (Group III) is defined as the persistence for over three months of two or more extra-inguinal lymph nodes greater than one centimetre in size in persons at risk of HIV infection and having no other cause for lymphadenopathy. This was felt initially to have prognostic significance but recent work suggests this is not the case.¹⁵ Onset of late HIV disease (Group IV)

is often marked by constitutional symptoms of malaise, indolent fever, profuse night sweats, loss of appetite, persistent diarrhoea and mucocutaneous manifestations which include ichthyosis, seborrhoeic dermatitis and deterioration or re-emergence of disorders such as fungal infections (often atypical), acne, psoriasis and eczema. These conditions are by no means specific. More suspicious disorders are recurrent and persistent herpetic infections especially perianal disease in homosexual/bisexual males. Herpes zoster which is more severe than usual, often multidermal or even bilateral and which responds poorly to treatment, facial molluscum contagiosum in adults, oral candidiasis and hairy leukoplakia¹⁶ (a condition said to be specific to HIV infected persons appearing as white plaque-like lesions on the lateral borders of the tongue) are all suspicious. We have seen each of these conditions in our patients except for psoriasis. Some patients had consulted general practitioners, hospital doctors and dentists with many of these problems, sometimes for longer than two years before being diagnosed as HIV positive, so it is necessary today for all medical disciplines to have a high level of awareness of the possible significance of such disorders.

AIDS indicator diseases which led to a classification of AIDS¹⁷ for the 21 cases we have managed are shown in Table V along with diseases diagnosed and treated after the indicator disease. *Pneumocystis carinii* has been the commonest diagnosis accounting for 33% of the indicator diseases, which is not significantly different from the overall figure of 50% reported from the rest of the UK.⁸ The longest surviving AIDS patient we have seen is a man with Kaposi's sarcoma, first diagnosed in California in 1985. This man is alive and well at the time of writing this article. The median survival of the 11 patients who have died has been 11 months from the time of initial diagnosis of AIDS, which compares with 9–10 months up to 1987, rising to 18 months in 1987 for patients in England and Wales.¹⁸

TABLE V
Indicator disease for AIDS diagnosis in 21 patients

	<i>Initial diagnosis</i>	<i>Subsequent diagnosis</i>
<i>Pneumocystis carinii</i> pneumonia	7	3
Kaposi's sarcoma	2	—
Oesophageal candida	3	—
Cytomegalovirus infection	2	2
Persistent herpes simplex infection	2	2
Cryptosporidiosis	1	—
HIV encephalopathy	1	—
Cerebral lymphoma	1	3
Intracerebral toxoplasmosis	—	2
Myelitis	—	2
Severe peripheral neuropathy	—	1
Mycobacterium avium intracellular hepatitis	—	1
Unknown	2	—

Unfortunately, no post-mortems have been available in Northern Ireland because of the inadequacy of mortuary facilities. This has precluded us from making additional subsequent diagnoses which undoubtedly have been missed, or confirming some of our presumptive diagnoses such as intracerebral toxoplasma and lymphomas.

Of the 16 haemophilic patients infected, three have died, one by suicide, one from liver failure unrelated to HIV infection and one in whom HIV infection was contributory. None have had evidence of opportunist infections other than oral candidiasis affecting four and pityriasis versicolor affecting one. Two patients have required treatment for HIV-associated thrombocytopenia, three patients have required treatment with antiviral agents, and the remaining 10 are asymptomatic patients in category CDC II.

Prognosis

Predicting the prognosis for people with HIV disease using laboratory markers has been the subject of intensive research since the disease was first described. A recent study by Fahey et al¹⁹ looked at eight parameters, and concluded that the most useful laboratory markers were the total T4 lymphocyte count, serum beta-2-microglobulin and serum neopterin. Of these three laboratory markers only serial T4 lymphocyte counts have been carried out routinely on HIV positive patients by the genitourinary medical services. Some authors have noted that a T cell count level less than $200 \times 10^6/l$ at the time of presentation is highly predictive of development of an AIDS indicator disease.^{15, 20} In 30 patients followed up in the genitourinary medicine clinic this parameter gave a good indication of the likely development of AIDS within a 24 month follow-up ($p = 0.0011$ Fisher's exact probability test). Nineteen were not evaluated as they either presented to us with AIDS (8), have been lost to follow-up (5), or were temporary visitors to Northern Ireland and were not assessed (6). (Table VI). Use of such markers is of value today along with the clinical state of the patient, as they allow the clinician to make logical decisions on the introduction of antiviral and prophylactic therapy.

TABLE VI

Development of AIDS diagnosis (in brackets) in 30 patients related to T4 cell count at HIV diagnosis (p value calculated using Fisher's exact probability test)

Follow-up	T4 cell count		
	$> 200 \times 10^6/L$	$< 200 \times 10^6/L$	
0 - 12 months	4 (0)	4 (2)	NS
13 - 24 months	6 (0)	1 (1)	NS
24+ months	11 (2)	4 (4)	$p = 0.00011$

Antiviral therapy and prophylaxis

The only anti-HIV drug licenced in the United Kingdom is azidothymidine (AZT). It acts as an inhibitor of reverse transcription which is a vital step in the life cycle of retroviruses and as a chain terminator in proviral DNA synthesis.²¹ It has been

shown that azidothymidine inhibits the replication of virus which can lead to clinical improvement, and objective improvement in laboratory markers.²²⁻²⁴ Unfortunately, the side-effects of this drug may require dose reduction or discontinuation. The most serious side-effect commonly seen is bone marrow suppression with a reduction in both red and white cell counts. Serious side-effects are more common in persons in more advanced stages of the disease. This would be in keeping with our experience of this drug, as nine out of 10 patients treated for aids have had to have dose reduction or complete withdrawal. On the other hand, there seems to be evidence that HIV positive persons who are asymptomatic and have good laboratory parameters are more tolerant of this drug.²⁵ The Medical Research Council in conjunction with the French research authority INSERM are presently conducting a multi-centre, double-blind study (Concorde Trial), comparing azidothymidine with placebo in asymptomatic persons with HIV infection. The Royal Victoria Hospital Genitourinary Medicine Clinic is a centre in this study and nine patients have been entered for a mean of 44 weeks (range 3 to 59). So far none have had to have dosage reduction because of haematological problems. No information is yet available on progression of disease, but a similar study in America has indicated efficacy in this respect.

Management

Patients other than haemophiliacs with HIV infection have mostly been managed as outpatients by the Genitourinary Medicine Service at the Royal Victoria Hospital, although some attend genitourinary clinics held in Altnagelvin and Coleraine hospitals. These patients have open access to the clinics and the counselling and social services provided at these centres. A designated HIV clinic is in operation at the Royal Victoria Hospital. Inpatient management has mostly been handled by the genitourinary medicine physicians, with close co-operation with relevant specialists, mostly gastroenterology, immunology, neurology and respiratory medicine. Some initial misgivings were voiced by nursing, paramedical and ancillary staff in the care of patients and handling of specimens, but with explanation of the epidemiology of the infection, familiarity with day to day management, and the advent of the EHSSB staff education programme,²⁶ these have largely been allayed, and our experience compares favourably with that of our colleagues in England and Wales.

With a few exceptions, all our patients have consented to their general practitioners being notified of their diagnosis, and in only one instance did that doctor not wish to care for the patient because of the HIV infection. We have now successfully managed three patients with AIDS in the community with the co-operation of the general practitioners, community nursing and social services. Two of these patients received terminal care at home. Co-operation from the funeral services has been exemplary, both in the community and for patients who died in hospital.

CONCLUSION

In Northern Ireland we have been relatively fortunate in having fewer cases of HIV infection reported per 100,000 of population (4.1 per 10^5) than in any other region in the UK.⁸ We can only speculate on the reasons for this difference. Homosexual men in the past have left Northern Ireland to express their sexuality in a more liberal and anonymous community such as London. Another factor is

the low incidence of injecting drug misuse in Northern Ireland which is borne out from a number of sources.²⁷ Both these factors may have conspired to give a disproportionate number of heterosexually transmitted cases of HIV infection. Comparing the overall figures for patients with coagulation defects for the United Kingdom to those for Northern Ireland there is a 41% HIV positive rate with an increase to 59% for severely affected patients,⁹ compared to 15.8% and 25% respectively. The lower figure for infection of haemophiliacs in Northern Ireland may be explained by the use of more factor VIII derived from European sources. All factor VIII products became infected eventually but the European material became contaminated at a later date compared to that imported from the United States of America.

Entering the 1990's is a time of hope for better treatment of HIV disease, with a consequent improvement of quality of life and survival time for those infected. Forward predictions of the number of cases up to 1993 for England and Wales have been revised downwards for homosexual males, which reflects a marked change of sexual behaviour in this group of people. Little is known of the sexual behaviour of the population of Northern Ireland, although one study indicated little change in homosexual risk behaviour in Northern Ireland over the period 1981 – 1987 despite a greater awareness in this population of HIV infection and a significantly greater resolve to change sexual behaviour because of perceived risk.²⁸ Because of this, and the fact that comparison between Northern Ireland and England and Wales may not be valid, we have chosen not to make projections for the 1990's in Northern Ireland. With the foregoing evidence, an awareness of HIV disease in the community is essential for all medical practitioners, and we express the hope that people in our population will recognise the risk of HIV transmission and take appropriate action in their own lives to avoid infection.

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