Notifications of Tuberculosis in England and Wales, 1982-1989

J M Watson, K J Fern, J D H Porter, S E Whitmore

Introduction
Notifications of tuberculosis in England and Wales increased by 1.5% in 1988, compared with 1987, and by 5.3% in 1989 over 1988. A similar reversal in the decline in reported tuberculosis cases was observed in the United States in the mid-1980s and has been attributed to the effect of the epidemic of infection with human immunodeficiency virus (HIV). This report examines the trends in tuberculosis notifications in England and Wales in recent years to determine the groups and the geographical areas in which increases have occurred and to consider whether HIV infection is likely to have played a part.

Total notifications and deaths
Mortality from tuberculosis in England and Wales has been declining from at least the middle of the last century, and notifications have declined steadily since recording began in 1913. In recent years total notifications have fallen from 7406 in 1982 to 5432 in 1989, and deaths due to tuberculosis (excluding late effects) from 564 in 1982 to 443 in 1989 (Figure 1).

Figure 1. Notifications of tuberculosis and deaths (OPCS)

Small increases in notifications have been seen in one year, compared with the previous year, in 1973 (0.7%), 1975 (1.3%), 1978 (1.6%) and 1988 (2.3%). On each occasion they have been followed by a resumption of the downward trend the next year. The provisional total for 1990 is 2.7% reduced on the equivalent figure in 1989, although still 2.4% greater than the figure in 1988. (In 1981 the Office of Population Censuses and Surveys revised its routine tuberculosis notification tables, and excluded chemoprophylaxis cases. Notifications data from 1982 onwards have therefore been presented.)
Age and sex distribution
Between 1982 and 1989 tuberculosis notifications for England and Wales fell in both males and females (Figures 2 & 3); selected age groups only have been presented for the sake of clarity. Higher rates are seen in males, apart from the under 15 years age group, and the highest rates are seen in males aged over 65 years. Small increases have been observed between 1987 and 1989 in males and females aged over 65 years, and in females 25-44 years, but such small increases have been observed before within the context of an overall downward trend.

Figure 2. Notifications: males

![Graph showing notifications: males]

Figure 3. Notifications: females

![Graph showing notifications: females]

Geographical distribution
In 1989 tuberculosis notification rates were highest in North-West Thames and North-East Thames Regions (23.7 and 22.7 per 100,000 in males respectively), followed by the West Midlands and North Western Regions (17.0 and 16.5 per 100,000 males respectively) (Figures 4 & 5). The lowest notification rates were observed in East Anglia, Wessex and South Western Regions (3.9, 5.4 and 5.4 per 100,000 males respectively). In most Regions the rate in males was higher than in females though in some Regions the rates were very similar.

Figure 4. Regional notification rates 1989 (per 100,000): males.

![Regional notification rates 1989 (per 100,000): males]

Figure 5. Regional notification rates 1989 (per 100,000): females.

![Regional notification rates 1989 (per 100,000): females]

From 1982-89 a decline in tuberculosis notification rates is seen in all Regions, but Figures 6 & 7 highlight six of the fourteen Regions where small increases have been observed between 1987 and 1989. The increases have been greatest in North-East Thames and South-East Thames (males) and West Midlands and North-West Thames (females).

When age group is also considered the increases are observed to have occurred in different age and sex groups in different Regions. Four of the most striking increases are highlighted below, but should be considered with caution in the light of the relatively small numbers and the normal variation from year to year:

1. in North-East Thames notifications increased in males aged 20-44 years (132 in 1987 to 183 in 1989).
2. in South-East Thames notifications increased in males aged 55-74 years (37 in 1987 to 62 in 1989).
3. in the West Midlands notifications increased in females aged 20-34 years (62 in 1987 to 116 in 1989) and 45-74 years (105 in 1987 to 150 in 1989).
4. in North-West Thames notifications increased in females aged 45-74 years (86 in 1987 to 126 in 1989).

The highest notification rates are generally reported from areas with high proportions of residents of Indian-subcontinent (ISC) ethnic origin and wide variations are
have been small and the significance of these is difficult to determine over a short period. The distribution of the tuberculosis cases by ethnic group in each region would provide a further indication of the factors associated with recent increases, but notifications do not include information on ethnic group.

The number of extra cases of tuberculosis as a result of the HIV epidemic that may occur in this country will depend largely upon the overlap between the population with HIV infection and the population with previous tuberculous infection. In England and Wales the highest rates of tuberculosis notifications are found in the population of ISC ethnic origin, and the lowest rates in the young white population. In contrast, almost two thirds of patients reported to CDSC with AIDS were white males aged 25-44 years, and only 1% of AIDS cases have been reported in people of Asian or Oriental ethnic origin (PHLS AIDS Centre - Communicable Disease Surveillance Centre, and Communicable Diseases (Scotland) Unit. Unpublished quarterly surveillance tables No. 9, November 1990, Table 26). Thus the potential for overlap between these two populations at present is small.

If the occurrence of tuberculosis were to be altered as a result of the HIV epidemic, increases would be expected in young adult males in the London area in particular. Although a small increase has been observed in this age and sex group in one of the Thames Regions, the increases have been confined to districts with large ISC ethnic origin populations, and have not been seen elsewhere.

Tuberculosis has been diagnosed in about 4% of AIDS cases in the United Kingdom (reported to CDSC by the end of September 1990), and other mycobacterial infections in a further 4% of cases (CDSC unpublished data). Although it is recognised that information about tuberculosis in cases of AIDS reported to CDSC is incomplete, it is unlikely that more than 6% of UK cases develop tuberculosis at any time in the course of their disease. This corresponds to about 80 new cases of tuberculosis among the estimated 1300 new cases of AIDS in the United Kingdom in 1990, rising to 120 new cases among the 2000 cases of AIDS predicted for 1992.

The extra cases of tuberculosis as a result of the HIV epidemic are unlikely to have been responsible for the increases observed in England and Wales in 1988 and 1989. Under-reporting of tuberculosis in patients with AIDS is a possibility, however. Patients with tuberculosis and HIV infection may be as infectious for tuberculosis as their non-HIV infected counterparts, and prompt treatment should be instigated and their contacts followed up. Clinicians have a statutory responsibility to notify all cases of tuberculosis, in patients with or without HIV infection, to the local proper officer, usually the Consultant in Communicable Disease Control (CCDC). Further monitoring of tuberculosis, through notifications and special detailed surveys, is essential to assess both the impact of the HIV epidemic and the contribution of the ethnic minorities to the occurrence of tuberculosis in this country.

Comment

Although small increases in total notifications of tuberculosis have been observed from one year to the next, the increase of over 5% in 1989, following an increase of 1.5% in 1988, is a cause for concern. The increases have been observed in both sexes, in younger and older adults and have been scattered across Regions up and down the country. Increases in specific sub-groups of the population observed within Regions. Between 1987 and 1989, the local authority districts with the greatest increases in notifications were also those districts with substantial populations of ISC ethnic origin. This is most apparent in a number of local authority boroughs in east London and the Midlands. By contrast significant increases have not been observed in the west London districts where many residents with HIV infection have been reported.

![Figure 6. Regional notification rates: males](image)

![Figure 7. Regional notification rates: females](image)
A national outbreak of salmonellosis from yeast flavoured products


Summary
A national outbreak of salmonellosis caused by a rare serotype occurred between July and November 1989. A total of 40 cases of Salmonella manchester infection were identified by the PHLS Division of Enteric Pathogens with a further 7 cases reported from Scotland. The median age of those affected was one year. All strains from the outbreak carried a 70mDal plasmid with a distinctive restriction endonuclease. A statistical association was found between infection and consumption of nationally distributed savoury corn snacks. Samples of autolysed yeast powder and flavourings used in the manufacture of many processed foods were also found to be positive for S. manchester.

Introduction
On 3 October 1989 CDSC was informed of a rise in the number of identifications of S. manchester by the Division of Enteric Pathogens (DEP). DEP reported that S. manchester is rarely isolated from humans in England and Wales; there were no reports in 1987 and only three in 1988. In 1989, 21 isolates had been confirmed by 3 October, 19 of which possessed a single 70mDal plasmid with a distinctive Hine II restriction endonuclease and were reported in the three months July to September. Most of the cases were geographically widespread and had occurred in young children. At the end of September 1989, S. manchester with an indistinguishable 70mDal plasmid was identified in isolates from autolysed yeast powder and cheese and onion flavouring, components of many processed and manufactured foods. The products had been submitted to a private laboratory by a food manufacturer. It was decided that CDSC should carry out an investigation to identify a vehicle or vehicles of infection.

Methods
Epidemiological
A wide ranging, detailed semi-structured questionnaire was personally administered to 10 of the 19 cases reported between July and September. Patients or, where appropriate, their parents were interviewed to determine the date of onset, duration and severity of illness and to obtain a history of all foods consumed in the week before onset.

All those affected had eaten savoury snacks in the week before onset of illness: six had eaten cheese flavoured corn snacks, manufactured by Company A and five had eaten cheese flavoured potato snacks, manufactured by Company B. Seven cases had also eaten food containing gravy powder or stock cubes and eight had eaten pork or beef sausages.

A case-control study was undertaken to test the hypotheses that savoury corn snacks and potato snacks were associated with infection. Persons were considered to be primary cases of S. manchester infection if they had had diarrhoea since 1 July 1989, had the organism cultured from a stool specimen, had not been abroad in the week before the onset of diarrhoea, and if no other member of the household had had diarrhoea in the four weeks before the case. A control was defined as a person in the same age group, of the same sex if over 16 years of age, who lived in the same neighbourhood, had not been abroad in the week before their matched case’s onset and had not themselves had a diarrhoeal illness since 1 July 1989. Three controls per case were sought, nominated by the case or case’s parent where possible but otherwise obtained from their general practitioner.

A telephone administered questionnaire enquiry was undertaken on primary cases of S. manchester infection, excluding those interviewed in the preliminary enquiry, reported to CDSC with a date of onset from 1 July 1989, and their controls. Information was requested on personal and clinical details, foreign travel, illness in other household members and a selected food history which

References:

OPCS Monitor WR 90/52.
included the consumption of foods such as savoury snacks, including flavour and brand, gravy powder or stock cubes and pork and/or beef sausages.

Univariate analysis was carried out, using Epi-Info software, and further matched analyses, using exact binomial probabilities, were undertaken on statistical associations.

Environmental
The manufacturer’s premises were inspected by the Director of the local Public Health Laboratory and Environmental Health officers (EHOs) and a representative from the Department of Health (DoH). The source of the yeast powder and the distribution of the flavourings was documented. The factory producing the yeast powder was inspected by the Scottish Home and Health Department (SHHD), the local Environmental Health Department (EHD) and microbiologists from its parent company.

Microbiological
Microbiologists were asked to send strains of salmonella with antigenic structure 6,8:L to DEP for confirmation of serotype and plasmid characterization. The methods used for plasmid characterization were those described by Threlfall and Frost.

Results
Descriptive epidemiology
A total of 40 cases of S. manchester infection were identified between 6 July and 29 November 1989. All strains carried a 70mDal plasmid with a characteristic Hine II restriction endonuclease fingerprint. Cases were reported from every region in England and Wales as well as from Northern Ireland and the Channel Islands (Figure 1).

Figure 1. Regional distribution of reports to DEP: S. manchester

The age distribution ranged from 4 months to 70 years, median one year, with 9 cases under one year of age and 22 aged 1-5 years. A total of 34 interviews were conducted with the case or case’s parents: ten were included in the case-control study. No cases were admitted to hospital, but all saw their GP either at home or at the surgery, with three or more visits taking place for nine of the cases. The reported symptoms included diarrhoea (18), fever (14), vomiting (9), blood in stools (4) and flu-like symptoms (2). Illness lasted between three days and three months, median seven days, and days of normal activity lost, between none and eight weeks, median seven days.

On unmatched analysis a statistical association was found between infection and a history of eating savoury corn snacks from Company A, in the week before onset of illness (p=0.064). Eleven of the 18 cases had eaten cheese flavoured and one case beef flavoured corn snacks. On matched analysis, corn snacks of any flavour and cheese flavoured corn snacks from Company A were statistically associated with infection (p=0.0479 and 0.098). No other foods were statistically associated with infection.

Environmental
The cheese and onion flavouring and the autolysed yeast powder, which was a component of the flavouring, were submitted by a food manufacturer to a private laboratory in South West England as part of an increased quality assurance regimen, prompted by the finding of a salmonella of an unknown serotype in May 1989. The yeast powder was supplied to this manufacturer by a sister company of the yeast producer in Scotland which supplies over 40 major manufacturers with flavourings who in turn supply 200-300 other companies.

Microbiological
All cases of S. manchester infection included in the outbreak investigation carried a 70mDal plasmid. This plasmid was not identified in any strain of S. manchester which had been isolated in England and Wales prior to July 1989. Two separate batches of yeast powder from the Scottish factory were found to be contaminated with S. manchester with an indistinguishable plasmid and the company reported that five of 1000 samples of 25 gm of yeast powder were also positive. S. manchester was also found at the Scottish yeast producing factory following a hazard analysis (HAZOP) investigation. It was found in the roller drying area, in the drainage system of the roller drying building and in the plant producing yeast powder for the baking industry. In addition, S. oranienburg was isolated from yeast powder by the private laboratory, S. schwarzengrund was isolated from compressed yeast in the factory as well as from the factory site and together with S. manchester all three serotypes were isolated from drainage water taken from a local stream and used as a coolant in the factory.

Seven cases of S. manchester infection were also reported from the Communicable Diseases (Scotland) Unit: two children and one adult were from one household, the remainder were sporadic cases in young adults from different parts of Scotland. Strains from these cases all had a plasmid indistinguishable from isolates from elsewhere in the UK but were not included in CDSC’s case-control study.

Analytical epidemiology
Eighteen cases and 42 controls were included in the case-control study. No cases were admitted to hospital, but all saw their GP either at home or at the surgery, with three or more visits taking place for nine of the cases. The reported symptoms included diarrhoea (18), fever (14), vomiting (9), blood in stools (4) and flu-like symptoms (2). Illness lasted between three days and three months, median seven days, and days of normal activity lost, between none and eight weeks, median seven days.

On unmatched analysis a statistical association was found between infection and a history of eating savoury corn snacks from Company A, in the week before onset of illness (p=0.064). Eleven of the 18 cases had eaten cheese flavoured and one case beef flavoured corn snacks. On matched analysis, corn snacks of any flavour and cheese flavoured corn snacks from Company A were statistically associated with infection (p=0.0479 and 0.098). No other foods were statistically associated with infection.
S. manchester was also found in three different food items. Garlic flavoured croutons produced in the north of England, cheese and onion crisps produced in Northern Ireland and chicken and vegetable ‘cup a soup’ produced in the north of England all contained contaminated yeast powder.

**Control Measures**

All deliveries of yeast powder from the distributing company to customers were stopped voluntarily in August 1989 when a salmonella confirmed in September by DEP as S. manchester was identified in the sample from the food manufacturer. Production of yeast powder at the Scottish factory was stopped and investigations begun by the Scottish Home and Health Department (SHHD) and the local Environmental Health Department. An increased sampling regime of all yeast powders was introduced at the factory in September, followed by a more rigorous sampling procedure in October and closure of the factory. The factory was subject to a hazard analysis investigation by the company, SHHD and the EHD. A customer alert programme was prepared by the distributors advising companies not to use powder manufactured between May and October 1989 and letters informing the companies and the Chief Environmental Health Officers of this were distributed by the DoH and the distributing company on October 13 1989. The factory in Scotland was reopened at the end of October following approval to restart production of autolysed yeast powder providing distribution of the powder was subject to a positive release procedure. In November 1989 all autolysed yeast powder produced by the Scottish factory was recalled and the factory again closed, because a sample from Northern Ireland, which had been produced in September prior to the hazard analysis, was found to be contaminated with S. manchester despite the rigorous positive release regime. All customers and CEHOs were informed.

All the recommendations following the investigation at the Scottish factory were implemented, including prevention of possible contamination by river water. Production of yeast powder was restarted in February 1990.

**Discussion**

S. manchester is a rare serotype. Only 49 reports were received by CDSC between 1965 and 1985. There was a rise in 1986, when 35 sporadic isolates were received, before the number of reports declined to none in 1987 and three in 1988.

The Scottish factory commenced testing yeast products for salmonellas in 1976 and found its first isolate in 1982. Salmonella was also detected in 1986 but it is not known what the serotype was, or what control measures were implemented at the factory as this had occurred under previous management. Investigations in 1989 revealed cross contamination in the roller drying area and a risk of cross contamination in the bagging process of yeast powder. In addition, the finding of salmonellas in the river water used for cooling purposes indicated a possible recycling of salmonella from river to plant over a considerable period of time.

Yeast powder is not considered to be a natural reservoir of salmonellas. Two previous outbreaks have been recorded, both in the USA. In the first in 1955\(^9\), a hospital associated outbreak of salmonellosis was traced to the consumption of contaminated dried yeast included in tube feeding formulas. Three salmonella species were isolated from the dried inactive yeast, S. oranienburg, S. montevideo and S. senftenberg. Investigations showed that these micro-organisms were being introduced from the air outside the building through a ventilating duct. In the second S. schwarzenburg and S. montevideo were associated with an outbreak in 1964\(^9\) which involved 23 institutions for the mentally handicapped in nine American States. In this outbreak the yeast powder was part of a food supplement which also contained dried cotton seed protein contaminated with S. tenessee and S. simsbury. Isolations were made from the production lines and/or the final products at both plants.

In the British investigation, S. schwarzenburg together with S. oranienburg were also found at the factory site and in the drainage water taken from a local stream. The latter serotype has previously been identified in isolates from black pepper\(^9\), a condiment also used to flavour many processed foods.

Many dried foods may be subject to the same hazards of low level contamination by potentially pathogenic organisms and may be responsible for a proportion of sporadic cases of salmonellosis, the origin of which are infrequently recognized.

It is interesting to note that all three outbreaks associated with yeast powder affected vulnerable populations. The outbreak associated with S. manchester in 1989 mainly affected young children. Many of them were from lower social class families whose diet contained a high proportion of processed foods. From their packaging it is obvious that a large proportion of snack foods are targeted towards young children, and autolysed yeast powder and yeast extract powders are used in hundreds of different foods including savoury crisps, snacks, biscuits, processed meats and baby food products. Savoury corn snacks from Company A were statistically associated with illness in the case-control study. It was not possible, however, to exonerate the many other products which contained yeast powder or flavourings. Since the yeast producing company had taken steps to recall possibly contaminated yeast powder or flavourings from their customers at the time the association with the savoury corn snacks was established, it was felt to be inappropriate to withdraw these or any other end food product. However, a few companies withdrew their products based on a perceived contamination risk.

The incident highlighted the value of a laboratory surveillance scheme in detecting the small number of cases over several weeks from a wide geographic area which had resulted from low dose contamination of a nationally distributed product.
Acknowledgements
We would like to thank the yeast producer, the Scottish Home and Health Department, the Communicable Diseases (Scotland) Unit and the Department of Health England for their help in this outbreak investigation.

CA Joseph MSc
EM Mitchell MFPHM
JM Cowden MFPHM
JC Bruce BSc
CE Hine MFPHM
R Wallis MFPHM
Field Services Division and Gastrointestinal Disease Section, CDSC

MLM Hall BSc
EJ Threlfall PhD
Division of Enteric Pathogens, CPHL

References
1. Dean AD, Dean JA, Burton JH, Dicker RC. Epi Info, Version 5: a wordprocessing, database and statistical program for epidemiology on microcomputers. Centres for Disease Control, Atlanta, Georgia, USA 1990.

HIV-2 in the United Kingdom - A Review

B G Evans, O N Gill, S R Gleave, P P Mortimer, J V Parry

Summary
Human immunodeficiency virus type 2 (HIV-2) was first recognised in 1986 and subsequently the infection was shown to be widespread in West Africa. There have been few case reports from countries outside the African continent. In North America and Europe the highest number of infections have been in Portugal and France.

Twelve HIV-2 infections have been identified in the United Kingdom (UK) and nine of the twelve had some connection with Africa, mostly West Africa; in three cases only “sub-Saharan Africa” was stated on the report, and one was from Mozambique. The other three HIV-2 infections were identified as follows: one in stored sera from a man who died in 1978, one in a child from Portugal who was diagnosed in the UK as having Acquired Immune Deficiency Syndrome (AIDS) in 1985, and one in a homosexual man who was tested unlinked and anonymously in London in 1987. It is not known how many of the total number of UK HIV-2 infections are represented by these twelve, but among large numbers of blood donors and people attending genitourinary medicine clinics the occurrence of infection was rare.

Background
Recognition of the virus
A new retrovirus, subsequently known as HIV-2, was first isolated from West African AIDS patients in 1986 although serological evidence suggesting the existence of a second human immunodeficiency virus was published in 1985. HIV-2 is very closely related to the simian immunodeficiency virus which causes AIDS-like disease in captive macaques. Whether macaques became infected via sooty mangabey monkeys, which have been shown to be infected both in captivity and in the wild with a very similar virus, or via human strains, is not known. There is evidence that human HIV-2 infection existed in West Africa as early as 1966 though some dispute this. The high prevalence of antibody in older age groups in West Africa has been used to argue that HIV-2 was not recently introduced, but studies have shown the prevalence of antibody to be closely related to certain behavioural risks. This and the failure to recognise AIDS in West Africa prior to 1986 suggest a more recent introduction.

Clinical Features
The range of opportunistic infections and malignancies, and the wasting and dementia associated with progressive HIV-1 infection are also present in HIV-2 disease. The lower proportion of HIV-2 infected people in West Africa as early as 1966 though some dispute this. The high prevalence of antibody in older age groups in West Africa has been used to argue that HIV-2 was not recently introduced, but studies have shown the prevalence of antibody to be closely related to certain behavioural risks. This and the failure to recognise AIDS in West Africa prior to 1986 suggest a more recent introduction.

Distribution of infection
HIV-2 is present in many West African countries and in some it is a more common cause of AIDS than HIV-1, although in certain of these countries the prevalence of HIV-1 is also increasing. In one major 1987 survey in Guinea-Bissau the following prevalence rates of HIV-2 infection were observed: 9% of prenatal women, 8% of
women attending a family planning clinic, 4% of applicants for scholarships, 9% of blood donors, 37% of female prostitutes, 5% of police officers, 16% of outpatients suspected of having tuberculosis, and 55% of patients clinically suspected of having an AIDS indicator disease. HIV-2 AIDS cases and asymptomatic infections have been described from Central, Eastern and Southern Africa\textsuperscript{4,17,34,35}, but these have been relatively few compared with the large numbers of HIV-1 infections locally.

A few HIV-2 infections have been reported in many European countries\textsuperscript{36}. Relatively more HIV-2 infections have been reported from France and Portugal, though in France the numbers are small compared with HIV-1\textsuperscript{37}. Of the 348 AIDS cases in Portugal to the end of 1989, 44 (13%) were caused by HIV-2 and over two thirds of these had contact with, or were from Africa, but 14 had no known African contact. Among 9905 sera collected from high risk persons or from patients with AIDS or suspected HIV disease in Portugal, 174 (1.8%) were seropositive for HIV-2\textsuperscript{38}.

HIV-2 was first described in Brazil in 1987\textsuperscript{23}, in the United States in 1988\textsuperscript{34,35}, and in Canada in 1989\textsuperscript{36}. So far, eighteen HIV-2 infections have been identified in the United States\textsuperscript{37}. The fifteen for whom information was available were either recent immigrants from, or travellers to West Africa, or had had sexual contact with West Africans. The low HIV-2 prevalence in the United States has been confirmed by the absence of infection in over 10,000 members of selected high risk groups who were tested by January 1990\textsuperscript{39}.

Since no infected blood had been detected in 20 million donations in the United States between 1987 and 1989, a recent review\textsuperscript{27} concluded that screening for HIV-2 was not warranted. Samples were tested for HIV-2, however, only if they were reactive on testing for HIV-1.

Transmission
The predominant mode of HIV-2 transmission is through sexual intercourse between men and women. A high infection rate was found amongst female sex workers in Senegal\textsuperscript{30} and 10 of 25 HIV-2 infected spouses in Guinea-Bissau were also infected\textsuperscript{1}. Sexual transmission of HIV-2 between men and women has been documented in Europe\textsuperscript{30}.

Transmission of HIV-2 has also been reported through sexual intercourse between men\textsuperscript{34,35}, blood transfusion and blood factor treatment\textsuperscript{35}, injecting drug use\textsuperscript{35}, and from mother to child\textsuperscript{34,35}. The rate of vertical HIV-2 transmission from mother to child is uncertain and some studies suggest that it might be quite low\textsuperscript{36}. To date HIV-2 infection of a health care worker following an accidental occupational exposure has not been reported.

Heat inactivates HIV-2 as it does HIV-1\textsuperscript{37} and hence clotting factor concentrates which are now routinely heat inactivated are likely to be free of HIV-2 infectivity.

Progression
Despite the high prevalence of HIV-2 infection in West Africa there have been many fewer AIDS cases recognised there compared with East and Central Africa where HIV-1 predominates. This could imply that HIV-2 is less pathogenic than HIV-1 but whether this is so remains an open question\textsuperscript{38}.

A year after 62 HIV-2 infected persons were identified through a random household survey in Guinea-Bissau, seven (11%) had died, mostly from illnesses compatible with a diagnosis of AIDS\textsuperscript{9}. In comparison only 16 (1.3%) of 1261 uninfected persons had died suggesting a relatively high progression rate to AIDS for HIV-2 infection. In a French study\textsuperscript{37}, however, of 35 HIV-2 infected adults with a mean follow-up of 19 months the clinical status remained stable in 23 out of 25 patients with CDC group II and group III illness. Two West African studies\textsuperscript{38,39} showed that in hospitalised patients with symptomatic HIV disease a larger proportion were anti-HIV-1 positive than would have been expected from the observed seroprevalence of the two viruses in the general population. A three year follow up of 43 HIV-2 infected individuals in Guinea-Bissau\textsuperscript{39} showed 12% progressed to AIDS, but the authors thought this was less than would have been expected for HIV-1 infected persons.

Thus some studies have shown that HIV-2 is as pathogenic as HIV-1, but most suggest a slower infection progression rate for HIV-2. A 1989 review\textsuperscript{40} concluded that although HIV-1 and HIV-2 infected AIDS patients have similar disease patterns it may be that in HIV-2 infections the asymptomatic state lasts longer so that a smaller proportion develop AIDS within a given interval. Longer term cohort studies will be essential to establish the rate of progression of HIV-2 infection to AIDS.

Testing for HIV-2 in the United Kingdom
In the spring of 1987 the PHLS Virus Reference Laboratory (VRL) began testing for anti-HIV-2 specimens that had either given equivocal results by anti-HIV-1 tests or were from individuals at high risk of HIV-2 infection. Testing was done using an anti-HIV-2 specific assay up to December 1988 and then all samples were tested using a combined anti-HIV-1/2 HIV-assay. Other sera also tested for HIV-2 at VRL included specimens referred where the clinical history was suggestive of HIV disease but the anti-HIV-1 screening assay is negative, or where borderline positive results were obtained for anti-HIV-1. A total of 3417 sera from these sources was tested early in 1988\textsuperscript{41} without confirming any HIV-2 infections.

Since September 1986, UK blood donors who have lived in, or visited Africa and had sex with men or women living there have been asked not to donate blood. This lessens the risk of donors giving blood in the window period for HIV infection prior to seroconversion. The wording of the leaflet is such that donors from West African countries should exclude themselves.

In July 1987 a research project was begun in which four Blood Transfusion Centres in England referred to the VRL specimens from donors who had visited Africa on any occasion since 1977. This was later modified to include only those who had visited West Africa. In 1988 all Blood Transfusion Centres adopted this procedure. Once found to be anti-HIV-2 negative, donors who had not revisited West Africa were not subsequently screened for HIV-2 when donating. Of the 15,000 donations referred for anti-HIV-2 testing between June 1988 and July 1990, there was
none in which HIV-2 infection was confirmed. [Mortimer JY - personal communication]

From July 1990 combined anti-HIV-1/HIV-2 testing of all donations was introduced in the UK Blood Transfusion Service. In the initial two months there were no HIV-2 antibody positive results in 475,000 tests. Since then approximately 250,000 donations have been tested each month and only one HIV-2 infected donor was detected by the end of 1990. [Rawlinson VI - personal communication]

Early in 1990, an unlinked anonymous HIV prevalence monitoring programme began in England and Wales. A series of surveys is underway including a pilot survey of 30,000 genitourinary medicine clinic attenders, a pilot survey of 60,000 hospital patients, and a survey of 120,000 women attending ante-natal clinics. All specimens collected for this programme are to be tested initially with a combined anti-HIV-1/HIV-2 assay.

Recognised HIV-2 infections in the United Kingdom

In 1990 laboratories which were known to have tested specimens that were positive for HIV-2 were contacted and asked for information on known HIV-2 infections. The two laboratories, which until recently undertook all confirmatory testing for HIV-2, were included. In addition, a literature search was undertaken and blood transfusion centres supplied information on two HIV-2 infected donors. Therefore it is likely that most, if not all, recognised HIV-2 infections in the UK are summarised in the Table.

Of the twelve cases of HIV-2 infection, five were related to West Africa. In another three the African connection was not specified other than “sub-Saharan” and a further case was from Mozambique. One was a child who had a blood transfusion in Portugal and had come to the UK for diagnosis and treatment of AIDS. Two reports were in men who had sex with men, including one where the sexual contacts were both in the UK and South East Asia. The other man was tested in an unlinked and anonymous study so that further information was not available.

Conclusions

Cross reactions with anti-HIV-2 are common in some of the screening tests used for anti HIV-149. The degree of cross reactivity, however, depends on the screening test and can vary considerably. One such cross reaction was the means by which a UK blood donor was diagnosed as being infected with HIV-2.

Combined anti-HIV-1/HIV-2 assays are as sensitive as anti-HIV-1 assays in screening for anti-HIV-1. They are also reasonably sensitive for anti-HIV-2. Although it depends on the type of HIV-1 test used for the comparison, the specificity of combined testing is not much lower than for HIV-1 only assays50. Combined tests are only marginally more expensive to use than HIV-1 only tests - the increase in expense being associated with confirmatory testing of the extra specimens reactive on initial testing due to the slightly lower specificity of the combined test and the need to confirm or exclude both HIV-1 and HIV-2.

In May 1989 the AIDS Laboratory Diagnostic Working Group advised combined screening in diagnostic laboratories in the UK. Several types of combined screening test are available and these have recently been evaluated50,51.

There seems no reason why combined testing should not become the norm in laboratory practice for HIV testing in the UK. The number of HIV-2 positives diagnosed will almost certainly be small but testing technology and confirmatory expertise exists and it seems appropriate to use it.

In the event of a positive or unexpected negative reaction arising during the course of combined anti-HIV-1/HIV-2 testing, the test should be repeated at least in duplicate by the same kit on the original sample. If one or more of the repeated tests is positive the sample should be referred to a confirmatory laboratory. All eight designated confirmatory laboratories in England and Wales are equipped to confirm anti-HIV-1 reactivity and several possess the means to identify HIV-2 infections. Because HIV-1 is many times more common than HIV-2 in the UK, most of the confirmatory laboratories will confirm HIV

<table>
<thead>
<tr>
<th>Travel history/exposure category</th>
<th>Sex</th>
<th>Age group</th>
<th>Date of diagnosis of HIV-2 infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>From Portugal, blood transfusion recipient</td>
<td>M</td>
<td>5-9</td>
<td>1985 died from AIDS (Cryptococcal meningitis)</td>
</tr>
<tr>
<td>Homosexual</td>
<td>M</td>
<td>30-40</td>
<td>1987 unlinked anonymous test</td>
</tr>
<tr>
<td>From Portugal, resident of Guinea-Bissau for 10 years</td>
<td>M</td>
<td>40-49</td>
<td>1988 serological diagnosis, AIDS 1978</td>
</tr>
<tr>
<td>Heterosexual contact in W Africa</td>
<td>F</td>
<td>20-29</td>
<td>1988</td>
</tr>
<tr>
<td>From sub-Saharan Africa</td>
<td>F</td>
<td>Reproductive age</td>
<td>1988 unlinked anonymous test</td>
</tr>
<tr>
<td>From Mozambique</td>
<td>M</td>
<td>40-49</td>
<td>1989</td>
</tr>
<tr>
<td>Homosexual contacts in UK and SE Asia</td>
<td>M</td>
<td>40-49</td>
<td>1989</td>
</tr>
<tr>
<td>From sub-Saharan Africa</td>
<td>F</td>
<td>Reproductive age</td>
<td>1989 unlinked anonymous test</td>
</tr>
<tr>
<td>From France, heterosexual contacts in Africa</td>
<td>M</td>
<td>40-49</td>
<td>1989 AIDS, died 1990</td>
</tr>
<tr>
<td>From Mali</td>
<td>F</td>
<td>30-39</td>
<td>1990</td>
</tr>
<tr>
<td>Heterosexual contacts and blood transfusion in W Africa</td>
<td>M</td>
<td>50-60</td>
<td>1990 died from liver failure: not AIDS</td>
</tr>
<tr>
<td>From Niger, heterosexual contact</td>
<td>M</td>
<td>40-49</td>
<td>1990</td>
</tr>
</tbody>
</table>
infection by testing referred samples by two or more independent combined anti-HIV-1/HIV-2 assays, and then attempt to identify them as HIV-1 by use of a type-specific competitive assay. Lack of, or weak, reactivity in an HIV-1 specific assay signals the need for a specific assay for anti-HIV-2. This may be a type specific competitive assay, an indirect peptide-based assay or an immunoblot. A second sample should be tested from all individuals whose first sample was repeatedly reactive in the initial assay to ensure that misdiagnosis does not occur because of clerical errors.

Each of the known HIV-2 infected persons reported so far in the UK have had a major risk factor for HIV-2 infection. The overall prevalence of HIV-2 infection is probably very low because the occurrence of infection has been rare among large numbers of blood donors and persons attending genitourinary medicine clinics. Should the prevalence of HIV-2 infection increase, this should be recognised quickly through the unlinked anonymous HIV prevalence monitoring programme, particularly through the survey of genitourinary medicine clinic attenders.

Since there is no difference in the methods of transmission between HIV-1 and HIV-2, recommended health promotion measures to limit HIV-1 spread will also reduce transmission of HIV-2. Moreover, continued self exclusion of high risk donors, testing of blood donations and heat treatment of blood factor concentrates will prevent HIV-2 transmission by blood transfusion or treatment with blood concentrates.

B G Evans  FFPHM  
Consultant Epidemiologist  
O N Gill  FFPHM  
Consultant Epidemiologist  
S R Gleave  BSc  
Scientific Officer  
PHLS AIDS Centre  at CDSC  

PP Mortimer  FRCPath  
Director  
J V Parry  PhD  
Grade C Clinical Scientist  
PHLS Virus Reference Laboratory  

Acknowledgements

The authors would like to thank the following centres for permission to quote results given in the Table, Brentwood Blood Transfusion Centre, Farnborough Laboratory and Dulwich PHL, Hospital for Tropical Diseases London, Leeds PHL, Lewisham Blood Transfusion Centre, Northwick Park Hospital, Oxford PHL, St. Bartholomews Hospital Virology Department, St Marys Hospital Virology Dept, University College and Middlesex School of Medicine Department of Medical Microbiology - Division of Virology.

References

24. CDC. AIDS due to HIV-2 infection - New Jersey.


