A survey of invasive *Haemophilus influenzae* infections

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**Summary**

A survey of invasive *H. influenzae* infections has been underway in six regions of England and Wales since September 1990. In the first year, there were 433 cases of which 362 (84%) were due to *H. influenzae* type b (Hib). The majority of Hib infections were in children aged less than 5 years; there being an annual incidence of 26.4/100,000 in this age group. Meningitis occurred in 56% of cases of Hib infection. The results confirm previous evidence of the need to incorporate Hib vaccination into the childhood immunisation schedule. The ongoing survey data will provide useful information to assess the impact of an Hib immunisation programme.

**Introduction**

Infection due to *H. influenzae* is a major cause of childhood mortality and morbidity. The majority of invasive infections are due to type b capsulated strains but other capsular serotypes and non-capsulated strains also cause invasive disease. Meningitis is the most common manifestation of *H. influenzae* type b (Hib) disease; others include epiglottitis, pneumonia, septic arthritis and cellulitis. These infections are commonly associated with a bacteraemia. Bacteraemia, in the absence of invasive disease, is unusual.

There are six antigenically distinct capsular types of *H. influenzae*, designated a-f. The capsule of the type b organism consists of polyribosylribitol phosphate (PRP) which is a major virulence factor for the organism. Hib vaccines produced from PRP were first developed and evaluated in the 1970s. However, these early vaccines were ineffective in children less than 18 months of age. They have now been superseded by a second generation of Hib vaccines in which PRP is covalently linked to a carrier protein such as diphtheria toxoid. These have been found to be highly effective in infants and associated with an extremely low incidence of adverse effects. It is planned to incorporate a conjugated vaccine into the UK childhood immunisation schedule from October 1992.

Routinely available data on *H. influenzae* include statutory notifications of meningitis (available since 1982) and mortality data notified to OPCS, and voluntary laboratory reports to the PHLS Communicable Disease Surveillance Centre. A report of a survey set up in 1985 in Oxford Region estimated the annual incidence of invasive Hib infection to be 34 per 100,000 children aged 0-5 years, with 39% of cases occurring in infants under one year. Similar results were obtained in Wales where a prospective population based study has been underway in Gwynedd since 1980, and in the whole of Wales since 1988. Data from individual counties in Wales also indicated some degree of geographical variation. Both the Oxford and Welsh surveys suggest that the incidence of Hib infections, calculated from information obtained from routine sources, may significantly underestimate the impact of these diseases.

In September 1990, the Oxford and Welsh surveys were extended to include four other regions: East Anglia, Northern, North Western, and South Western. The purpose of this ongoing study is to collect clinical and laboratory data on all confirmed cases of invasive *H. influenzae* infection, in order to obtain more extensive background information.
Methods
Microbiologists in each of the participating regions were asked to report all episodes of invasive H. influenzae infection to a reference laboratory (either the Oxford Public Health Laboratory or the microbiology laboratory at Gwynedd Hospital, Bangor). Invasive infection included cellulitis, epiglotitis, menigitis, osteomyelitis, pneumonia and septic arthritis, and was defined as a case in which a) H. influenzae was isolated from a culture of normally sterile tissue or body fluid or b) Haemophilus-like Gram-negative bacilli were seen in films of normally sterile tissue or body fluid in conjunction with the detection of Hib antigen. Cases of pneumonia were accepted only if associated with positive blood cultures. Deaths outside the hospital, eg, sudden infant deaths, were included where there was a post-mortem isolate of H. influenzae from a significant source (eg, CSF).

A notification form containing clinical and laboratory data was completed for each case and forwarded, together with the isolate, to the reference laboratory. The identity of the organism and its antibiotic susceptibility were confirmed using standard techniques. H. influenzae strains were serotyped by slide agglutination using antisera to types a, b, c, d, e and f (type b antiserum supplied by the PHLS, types a, c, d, e, f antisera obtained from Wellcome Diagnostics). Where slide agglutination was difficult to interpret, counter-current immuno-electrophoresis was used to serotype strains. Strains not typable by these methods were designated non-serotypable (NT) H. influenzae.

Co-ordinating laboratories in each region were responsible for maintaining the surveillance programme and obtaining information on outcome three months after notification of a case.

Results
There were 433 cases of invasive disease caused by H. influenzae from October 1990 to September 1991 in the six regions. 362 (84%) were due to Hib, 54 (13%) to non-serotypable (NT) H. influenzae, three to H. influenzae type f and one to H. influenzae type e. The serotype was not determined in 13 cases.

Type b infections
1. Age distribution
The majority of infections (86%) were in children under five years of age (Figure 1). Figure 2 shows the distribution of Hib disease in infants. Eighty-two out of 127 (65%) infections occurred in the 6-11 month age group. Thirty-seven (10%) cases of Hib infection occurred in adults.

The estimated annual incidence was 26.4/100,000 children aged less than 5 years (Table 1). East Anglia and South Western regions and Wales had the highest incidence rates.

2. Season
The monthly occurrence of Hib infection is shown in figure 3. The highest numbers of cases were reported between October and January.

3. Diagnostic category
Meningitis was the most common diagnosis, occurring in 204/362 (56%) cases (Figure 4). Other clinical presentations included epiglotitis (48), cellulitis (31), pneumonia (22) and bone/joint infections (12). Bacteraemia with no obvious focus of invasive infection occurred in 33 (9%) cases. There were five mixed infections: meningitis and cellulitis (2), meningitis and epiglotitis (1), meningitis and septic arthritis (1), and septic arthritis and cellulitis (1). Uncommon manifestations included an infected aneurysm, endocarditis, lung abscess and pyopneumothorax.

4. Mortality
The outcome was known for 301 of the 362 cases. There were 13 recorded deaths. Seven of these occurred in adults and six in children under 15 years of age.

5. Antibiotic resistance
Ampicillin resistance was found in 54/361 (15%) Hib isolates; all these strains were beta-lactamase producers. Five out of 360 isolates (1%) were resistant to chloramphenicol. Four were resistant to both ampicillin and chloramphenicol. Ampicillin sensitivity was not known for one isolate and chloramphenicol sensitivity for two isolates.

Non-serotypable (NT) infections
There were 54 infections due to NT H. influenzae, of which 27 were in adults. Fourteen occurred in children under 5 years of age; eight of these were in infants aged less than 6 months. The age was not known in six cases.
Bacteraemia (with no detectable focus of invasive infection) was the predominant diagnosis occurring in 28/54 (52\%) cases (Figure 5), followed by pneumonia (9\%), meningitis (4\%) and epiglottitis (4\%). Other diagnoses were sudden infant death syndrome (SIDS) (2\%), cellulitis (1\%), empyema (1\%), peritonitis (1\%) pyosalpingitis (1\%), Bartholin’s abscess (1\%), haematospermia (1\%) and one case, clinical presentation unknown, where NT H. influenzae was isolated from the spleen at post mortem. The outcome was known in 45 cases, of whom 13 died (case fatality ratio: 29\%). In two of the deaths, a diagnosis of SIDS was recorded. Although NT H. influenzae was isolated from CSF and trachea in both these cases, it is not clear whether the organism was a contributory cause. Four of the 54 isolates of NT H. influenzae were resistant to ampicillin only. Two of these isolates were beta-lactamase producers. Chloramphenicol resistance was found in one isolate which was susceptible to ampicillin.

Infections due to other capsular types
There were three infections due to type f (meningitis 2, epiglottitis 1) and one due to type e (meningitis). All isolates were ampicillin and chloramphenicol sensitive. There were no recorded deaths.

Discussion
This survey covers Wales and five of the 14 English regions. The nine regions for which data are not available include the four Thames Regions and the West Midlands. While the results may not be representative of the whole country, they provide useful baseline information on which the impact of the vaccine can be assessed.

The spectrum of Hib infection is in keeping with published data from Oxford and Wales. Sixty-one per cent of cases had occurred before the second birthday, confirming the need to incorporate Hib vaccination into the current 2,3,4 month schedule. The high proportion of cases occurring between 4 and 12 months of age indicates the necessity for a catch-up programme for this group. The overall incidence in children under 5 years was lower than recent estimates. However, there was variation between regions and the maximum estimates are in keeping with the published figures. It is unclear whether the differences reflect true geographical variation or incomplete reporting. This is being further investigated. There was a high percentage of deaths in adults with Hib infection. While this is consistent with previous data, it is not certain to what extent Hib infection contributed to the outcome in these cases. More detailed follow-up is being undertaken to elucidate this.

Fifteen per cent of strains were resistant to ampicillin alone and 1\% were resistant to both ampicillin and chloramphenicol. These antibiotics are commonly used as first line agents for the treatment of childhood infections such as meningitis. Consideration should be given to using alternative antibiotics, such as cefotaxime, for the initial treatment of invasive infections likely to be caused by Hib.

Thirteen per cent of cases were due to NT H. influenzae. It is possible that some of these isolates were descendents of type b strains that had lost the ability to excrete capsule and, therefore, could not be serotyped. A study is planned in which a more advanced technique incorporating type specific DNA probes will be used to determine whether these strains are truly non-typable ie, non-capsulated, or are descended from type b strains ie, genotypically type b.

In comparison with invasive infections caused by Hib, those associated with NT H. influenzae usually arise in young infants or older adults with some underlying disease or structural abnormality. The predominance of bacteraemia and pneumonia is consistent with this and contrasts with Hib where meningitis and epiglottitis were the most common clinical presentations. The mortality was also higher in patients with non-serotypable infections compared with Hib infection.

Vaccination is likely to reduce the incidence of Hib disease dramatically, provided that good coverage can be achieved. However, the epidemiology of the disease may change as a consequence. In particular, an upward shift in the age distribution of the disease may occur, with implications for future vaccination policy. In some parts of the world, capsular types other than type b (notably type a), against which there are no vaccines, are also associated with invasive infections such as meningitis and pneumonia. It is possible that, under the influence of an immunisation programme, these serotypes may assume greater importance in this country. There is a need to continue the surveillance of H. influenzae infection following implementation of Hib immunisation in October 1992, so that its impact can be accurately assessed.

Strategies for the control of infection also include chemoprophylaxis, guidelines for which have recently been published. Late cases and recurrences may occur despite prophylaxis and, therefore, vaccination should also be considered for pre-school children who are household contacts of a case or room contacts, where two or more cases of Hib disease have occurred in a playgroup, nursery or creche within 120 days. In addition, vaccination should be considered for

![Figure 3 Distribution of Hib infection by month, October 1990 – September 1991](chart)

Table 1 Annual incidence of Hib infection by region for children under 5 years old

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Incidence/100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Anglia</td>
<td>41</td>
<td>30.7</td>
</tr>
<tr>
<td>Northern</td>
<td>40</td>
<td>20.1</td>
</tr>
<tr>
<td>North Western</td>
<td>60</td>
<td>21.5</td>
</tr>
<tr>
<td>Oxford</td>
<td>43</td>
<td>24.1</td>
</tr>
<tr>
<td>South Western</td>
<td>67</td>
<td>33.3</td>
</tr>
<tr>
<td>Wales</td>
<td>61</td>
<td>33.2</td>
</tr>
<tr>
<td>Overall</td>
<td>312</td>
<td>26.4</td>
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</tbody>
</table>

* Based on OPCS resident population mid-year estimates for 1990
Bone/joint infections 3%

published later this year.

Committee on Vaccination and Immunisation and will be

on Hib vaccination is currently being considered by the Joint

Maidenhead, Berks SL6 7BU, tel: 0628 785291). Detailed guidance

Merieux UK Ltd (Clivemont House, Clivemont Road,

Vaccine (PRP-T) is available on a named patient basis from

only a single dose. Vaccine is not indicated for adult contacts.

at monthly intervals; those aged 13 months and over require

Children aged 2-12 months should receive three doses of vaccine

maintaining the database.

R16

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among infants and children two months or age and older.


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An outbreak of hepatitis A

In early 1990, a public health laboratory reported six cases of hepatitis A occurring in five children and a teacher from the same locality and with dates of onset within a six week period.

Investigation

Case finding was extended by alerting local general practitioners, informing parents of children at local schools and reviewing other cases diagnosed by local laboratories. A case was defined as a person with serological or salivary evidence of recent infection with hepatitis A virus (HAV), with or without jaundice, having a connection with the locality and a date of onset between 1 December 1989 and 1 April 1990, where appropriate. Blood samples were taken from all suspected cases and immediate family members and tested for IgG and IgM anti-HAV. Saliva specimens were obtained, using the salivette technique, from 315 adults and children who had been in contact through school, home or social events. They were analysed for IgG and IgM anti-HAV by antibody capture radioimmunoassay (GACRIA and MACRIA).

Cases or their parents were interviewed using a detailed semi-structured questionnaire to obtain clinical, food and social histories. Local toilets and sources of food, milk and water were investigated.

Results

Fourteen serologically confirmed clinical cases (8 children, 6 adults) were identified, and 10 asymptomatic cases (9 children, 1 adult) were ascertained by serological or salivary testing. The epidemic curve for the 14 clinical cases is shown in Figure 1. Eight of the asymptomatic cases were family contacts of five clinical cases. The children attended six different schools. The first adult clinical case was a primary school teacher; the remaining adult cases had dates of onset in late February and March and thus may have acquired their infection from the children.

Information from the questionnaires indicated that nine of the early cases had frequented the same fish and chip shop but salivary testing of five staff and their family members did not reveal any association with the shop (Table 1). During the investigation, it became clear that the index case, who lived in a nearby town and attended a different school, had been present at a chess tournament, 25 days before the onset of his illness, in which six asymptomatic cases had participated (four of whom were detected by salivary testing – table 1). No common foods or other sources of infection were identified. The schools did not share catering facilities. The local water supply did not show evidence of microbiological contamination.

Discussion

The investigation suggested a point source (followed by person-to-person transmission) associated with a chess tournament which took place three and a half weeks before the index case developed hepatitis. The tournament was held in a church hall, where it may have been difficult to maintain good hygiene during refreshment breaks. In contrast to other experience, there was no evidence of significant transmission within the six schools attended by 16 of the cases. Salivary testing enabled susceptible contacts to be identified and treated with normal human immunoglobulin.

The long incubation period, the occurrence of asymptomatic cases, and serial transmission of the virus over a long period, can complicate the investigation of outbreaks of hepatitis A. A case-control study was not undertaken as no hypothesis was forthcoming from the initial investigation. The possible source of this outbreak only came to light when a boy from an adjacent town was interviewed and revealed his connection with a chess tournament. The possible source of this outbreak only came to light when a boy from an adjacent town was interviewed and revealed his connection with a chess tournament.
with the chess club. Salivary testing of the other chess club participants revealed a further four subclinical cases in addition to two identified serologically.

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**Hospital-acquired cryptosporidiosis**

In early 1991, an outbreak of cryptosporidiosis occurred among nurses treating a man with AIDS in a hospital in Wales. This patient was admitted in an advanced stage of the disease (CDC stage IV), with cryptosporidiosis, oral candidiasis, facial and peri-anal herpes infections and signs of early dementia. His immune status was poor, with a CD4 lymphocyte count of between 68 and zero cells/cu.mm. He was receiving zidovudine, cotrimoxazole, and fluconazole. He had profuse watery diarrhoea and vomiting which proved difficult to control. Large numbers of cryptosporidia were detected in stool and vomit samples. At one stage, the patient was producing over six litres of watery stool which, coupled with intractable vomiting and the dementia, led to significant environmental contamination.

The patient was nursed by trained nursing staff in a single room with its own bathroom and toilet in a modern, purpose built, infectious diseases unit. Eleven days after the patient was admitted, one of the nursing staff involved in his care became ill with diarrhoea and, because of the patient’s cryptosporidial infection, an investigation was instigated of all staff involved.

**Investigation and results**

A review of nursing records and staff interviews revealed sixteen members of the nursing staff with symptoms including nausea, vomiting, abdominal pain, diarrhoea, headache and fever. Stool samples were examined, using the phenol-auramine technique, from nine nurses, five of whom were positive for Cryptosporidium and had diarrhoea (Figure 2). These five were designated as cases. Their diarrhoea was sudden in onset, frequent, watery, yellowish and offensive. The duration of symptoms varied from three to twenty days. Two relatives of the patient and his partner, all of whom had spent time with him in the unit and with whom he had lived prior to admission, were symptomatic but were not screened.

Examination of nursing procedures during management of the patient did not reveal any obvious lapses. Procedures likely to involve gross contamination, such as cleaning up after episodes of incontinence or vomiting, were carried out wearing impermeable protective clothing, including eye protection. The only contact one infected nurse had with the patient was when she assisted him back to bed after he had visited the toilet. None of the medical or domestic staff is known to have become infected. Transmission to other patients in the unit, or to staff family contacts, is not known to have occurred.

**Discussion**

This outbreak was identified following investigation of staff, irrespective of symptoms, after one nurse had reported ill. As hospitals become involved in the care of increasing numbers...
of AIDS patients, units need to be particularly vigilant in the management of patients with cryptosporidiosis. The oocysts of Cryptosporidium are resistant to many of the usual disinfectants and the infective dose is thought to be small. AIDS patients suffering from cryptosporidiosis, especially those with dementia, impose severe demands on nursing staff. Cryptosporidia have been previously reported in vomit and this may be an important source of infection.

A number of outbreaks of cryptosporidiosis in hospitals have been reported. These include one where serological studies suggested increased exposure among the staff involved in the care of an AIDS patient with cryptosporidiosis even though oocysts were not identified in stool specimens. Environmental contamination and poor hygiene have been identified as important factors in transmission in several nosocomial outbreaks.

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Comment
Cryptosporidial infection causes self-limiting diarrhoea in immunocompetent people but a more severe and chronic illness occurs in patients with AIDS who may produce several litres of watery stool daily. The biliary tract and respiratory system can also be involved. Spread is thought to be faecal-oral but the oocysts can survive for some time, and spread via fomites may be important although nosocomial outbreaks are uncommon. Patients with chronic, severe cryptosporidial diarrhoea may be inpatients for several weeks and a typical AIDS ward may have a number of such patients at any one time. In a recently described nosocomial outbreak the source was identified as an ice machine which was probably contaminated by a confused, incontinent patient. Patients with cryptosporidiosis should be nursed in a single room with the usual enteric precautions, careful room cleaning when the patient is discharged home, and, as on any ward, nurses should be encouraged to report any diarrhoeal illness they may suffer and provide stool samples for analysis. Antidiarrhoeal agents help to improve the quality of life for the patient and may also facilitate nursing care. Paromomycin has been recently described as of potential benefit for severe cryptosporidiosis in AIDS patients and may help to reduce the risk of transmission to other staff.

Raw eggs and body builders
Several cases of Salmonella enteritidis phage type 4 infection were reported in July 1991 associated with a single gymnasium (gym 1).

Investigation and results
A case was defined as an individual who attended gym 1 between 24 June and 6 July and who developed diarrhoea with vomiting, abdominal pain, and fever or headache, and had a positive stool culture for S. enteritidis. Five cases were identified; three were admitted to hospital and two treated by their general practitioners. Four were body builders and one was a footballer. There were four men and one woman with ages ranging from 21-43 years. Each became ill within 24 hours of a visit to gym 1, during which a protein enriched raw egg health drink was consumed.

Thirteen other regular attenders at the gym completed questionnaires. Nine had consumed the egg protein drink and one had developed diarrhoea but no stool sample had been taken from him and he was classed as a presumptive case. About ten regular attenders refused to co-operate but none of them was known to have been ill. Four of the confirmed cases had consumed the egg protein drink on only one occasion (28 June) and became ill on the following day. The remaining confirmed case and the presumed case consumed this drink at least twice a week but shared a drink on 4 July and became ill the day after. No other common exposure was found.

Inspection of gym 1 revealed reasonable standards of hygiene. A limited range of foods was available. These were pre-packed snacks, tinned soft drinks, and hot drinks from a vending machine. The only food which contained raw items was the egg protein drink. It was made up by the gym owner who had not suffered from gastrointestinal symptoms in the months before, during, or in the ten days after the period when the outbreak occurred. He had not been abroad for several years and a stool sample taken from him was negative. None of his household had had a gastrointestinal illness in the relevant period.

A sample of the protein powder used to make the drinks was taken from the top layer of an opened container (which
had been used for the drink consumed by the cases on both occasions). This sample, together with 22 eggs found on the premises and swabs taken from the mixer used to prepare the drinks, was sent for microbiological examination. *S. enteritidis* PT4 was grown from the sample of protein powder. No isolations were made from the eggs or from the food mixer.

The sources of the components of the protein drink were traced (Figure 3). The protein powder had been bought from another local gym (gym 2) which had obtained it directly from the manufacturer. Samples of three unopened batches bought by gym 2 in June (part of which was resold to gym 1) were obtained from the manufacturer, whose premises were inspected by the local environmental health department. No growth was obtained from these samples and standards of hygiene at the factory were good. The ten members of gym 2 who regularly consumed the protein drink without raw egg were questioned. None had suffered any gastrointestinal illness during the relevant period. All other consumers of the powder were identified (gymys 3-10) and were visited by local environmental health officers: no further illness was discovered as a result.

The supply route of the eggs is also shown in the figure. The eggs were bought from a market stall that obtained supplies from several farms. One farm was identified as a major source of the eggs (farm A) and this was investigated by the Ministry of Agriculture, Fisheries and Food. *S. enteritidis* PT4 was isolated from the laying flock which was then compulsorily slaughtered.

**Discussion**

The vehicle of infection in this outbreak appears to have been the egg protein drink. The possible sources of the organism were the eggs, the powder, or cross contamination, either from the gym owner or another source in the gym. The protein powder found to contain *S. enteritidis* PT4 appears to have been contaminated after it had arrived at gym 1. Asymptomatic food handlers are an uncommon source of non-typhoid salmonellas. The only raw food available at gym 1 was the eggs used in the drink, and one of the flocks that produced eggs for the market stall which supplied this gymnasium was found to be carrying a similar organism.

The Chief Medical Officer issued a warning to the public concerning the danger of consuming raw eggs in August 1988, and at least one report on the risk of this practice has appeared in a body building magazine. This outbreak and several anecdotal reports suggest, however, that consumption of raw eggs by body builders continues. The results of this investigation highlighted the continued dangers attendant on this practice.

**References**


**Comment**

The descriptive epidemiology suggests a common source for this outbreak with the likelihood that the health drink prepared at the gymnasium was the vehicle of infection. The only food item from which the organism was isolated was the protein powder. The sample was taken from the top of a container of powder which may have been cross contaminated. The investigation suggested that raw eggs were the source of infection. This conclusion is supported by the finding of *S. enteritidis* PT4 in one of the laying flocks supplying the market stall from which the implicated eggs were obtained. Data published by the PHLS and the State Veterinary Service indicate that foods containing eggs were suspected in 55 of the reported outbreaks in which a food vehicle was specified between October 1990 and September 1991. Despite previous warnings, it is clear that certain groups of athletes are still using ‘health’ drinks containing raw eggs and thereby putting themselves at risk. CDCs and EHOs should consider the need to contact gymnasia in their areas to remind them of the risk.
Voluntary testing to measure HIV prevalence in sexually transmitted disease clinics

A Noone, J Y Mortimer and collaborators*

Summary
Voluntary HIV testing was used to study the extent of HIV-1 infection in patients attending sexually transmitted disease (STD) clinics in England and Wales between 1985 and 1990. Homosexual and bisexual men and 10-20% of heterosexual men and women were invited to complete a study record and have an HIV-1 antibody test. The rate of newly diagnosed HIV-1 infection was higher in homosexual and bisexual men than in heterosexual clinic attenders. It was also higher in patients attending clinics in the South East compared with those attending clinics in other regions. From 1988 onwards, HIV infection was identified in heterosexual men and women who did not report behavioural risk factors associated with increased risk of HIV transmission. In the early years of the study, the proportion that agreed to complete a study record and have an HIV-1 antibody test was high in all groups. This proportion declined in those attending clinics in the South East, particularly among heterosexual men and women, less than 50% of whom agreed to take part in the study in 1989 and 1990. The decline in acceptance rate made voluntary testing unsuitable for monitoring trends in HIV infection. Unlinked anonymous HIV testing, which minimises the effect of participation bias, has become the method of choice for monitoring the prevalence of HIV infection.

Introduction
The need to monitor the extent of infection with human immunodeficiency virus (HIV) in the general population was recognised at an early stage of the epidemic in the UK. At that time, surveillance based on voluntary testing of individuals following counselling was the only widely accepted method for HIV prevalence monitoring. In 1985, the year in which HIV antibody testing became widely available, a study was instigated of patients attending STD clinics in England and Wales. It was argued that the prevalence of HIV infection in patients attending STD clinics, who had, on average, more sexual partners than the general population, would indicate the upper limit of prevalence in the population over time and serve as an early warning system of the wider spread of infection. This collaborative survey of STD clinic attenders continued until March 1990 and results for 1985-1988 have been published elsewhere1,2. This paper updates these results and presents an overview of the study in the light of developments in practice and attitudes towards the surveillance of HIV infection in more recent years.

Methods
Between 1985 and 1990, homosexual/bisexual men and heterosexual men and women attending selected STD clinics in England and Wales were invited to complete a study record and consent to an HIV antibody test after appropriate counselling. The study started in four clinics in 1985 and extended to seven in 1986, and fourteen from 1987 onwards. It ceased at the end of March 1990.

All homosexual patients with one or more episodes of sexually transmitted disease in a calendar year were included in the study. A 10% sample of heterosexual men and women attending with one or more episodes of sexually transmitted disease in the calendar year was included in 1986 and a 20% sample was included from 1987 onwards. Heterosexual patients attending only for an HIV-1 antibody test were excluded. Patients found to be positive for HIV-1 antibody in a previous calendar year were also excluded.

The study record completed by the patient included information on age, sex, selected symptoms, sexual orientation, number of sexual partners, travel abroad, and, from 1988, a history of injecting drug use. Data on current and past clinical diagnoses were entered on the study record by clinic staff. Screening tests for antibodies to HIV-1 were carried out at local laboratories using ELISA and gelatin particle agglutination assays. Confirmatory tests were performed at reference public health laboratories using competitive or capture radio-immunoassays or further ELISAs (supplemented when needed by western blotting).

The participation rate was the proportion of those who agreed to complete the study record and have an HIV-1 antibody test. Prevalence was defined as the proportion of first-positive HIV-1 antibody tests in those participating in the calendar year. As in earlier reports, results were stratified into two geographical groups – South East Thames (Brighton and Dulwich clinics) and Other regions (all other clinics) to reflect the marked difference in the extent of the epidemic of HIV infection.

Results
Homosexual and bisexual men
Throughout the period of the study, the prevalence of antibodies to HIV-1 was higher in homosexual/bisexual men tested at the two clinics in South East Thames than among those tested at clinics in other regions (Figure 1). In both groups of clinics the highest prevalence of first positive HIV-1 antibody tests was recorded in 1986 and fell thereafter.

Very few patients refused to participate in 1985. Participation rates then declined in the South East from 98% in 1986 to 69% in 1990 (Figure 2). In other regions, the proportion agreeing to participate changed very little in the course of the study.

Comparisons between men accepting and refusing the HIV-1 antibody test in 1987, 1988, 1989 and 1990 suggested a greater willingness for homosexual/bisexual men at higher risk of infection to have the test. For example, among homosexual men attending clinics in South East Thames in 1989, those with five or more sexual partners in the previous twelve months, and men with a history of injecting drug use, were more likely to have an HIV-1 antibody test (Table 1).

Heterosexual men and women
The rates of newly recognised HIV-1 infection in heterosexual men and women were higher in South East Thames than in other regions during the period of the survey (Figure 1). The

* Listed on page R24.
numbers of HIV positive individuals identified were small and there were no obvious trends in these rates in either group during the study period.

Ten of 5517 heterosexual men attending STD clinics were found to have antibodies to HIV-1 in 1989. Five of these – two in the South East and three in other regions – did not have a major risk factor although two of these men reported ten or more sexual partners in the previous twelve months. The other five had had sexual partners in or from countries where HIV infection most commonly results from heterosexual transmission ie, WHO Pattern II countries. Four of the six heterosexual men found to be HIV-1 antibody positive in 1990 were injecting drug users; three of these attended clinics in the South East. Of the other two, one had had sexual partners in a WHO Pattern II country and the other did not report a major risk.

Four of 4706 heterosexual women were found to have antibodies to HIV-1 in 1989. Two of these attended clinics in the South East: one reported injecting drug use but for the other, who had had only one sexual partner in the previous year, no major risk factor was identified. One of the remaining two women had a sexual partner who injected drugs, and the other was from a WHO Pattern II country. None of the heterosexual women in the South East, who accepted the test in 1990, was HIV-1 antibody positive. No major risk factor was reported by the only HIV-1 antibody positive woman identified at a clinic outside the South East that year.

A decline in participation among heterosexual men and women was observed between 1986 and 1990. This was most marked in the South East where, by 1990, only 45% of heterosexual men and 34% of heterosexual women who were invited to take part agreed to complete a study record and have an HIV-1 antibody test (Figure 2).

Comparisons of heterosexual men and women, agreeing or refusing to have an HIV-1 antibody test, with respect to history of injecting drug use and number of sexual partners, suggested (as for homosexual/bisexual men) that those at greater risk of infection were more likely to accept the test (Table 1).

Discussion
Between 1985 and 1988, a high proportion of eligible clinic attenders took part in the study, making this a useful method of monitoring HIV-1 infection in groups of sexually active individuals. These high participation rates were achieved at a time when there was considerable controversy about HIV testing – a positive test result could have severe psychological consequences for an individual and result in practical difficulties eg, in retaining employment or securing a mortgage. Low and declining rates of acceptance of HIV antibody tests were observed.
in a national survey of HIV infection and STDs in homosexual/bisexual men attending STD clinics in the UK; rates fell from 55% in the last quarter of 1986, in 117 participating clinics, to 42% in the last quarter of 1988, in 131 participating clinics. In the same survey, test acceptance in clinics in the Thames regions fell from 47% (18 participating clinics) to 30% (27 participating clinics). The decline in participation observed in our study may have been partly a consequence of this debate. It is also possible that staff were unable to maintain the extra commitment of time and effort involved in a voluntary testing programme over a long period.

This study reports on rates of newly identified HIV-1 infections in patients attending STD clinics who agreed to have an HIV-1 antibody test. In 1986 and 1987 in South East Thames, these rates were 15% in homosexual/bisexual men, 1.5% in heterosexual men and 1.0% in heterosexual women. Anonymous testing of attenders at one London clinic gave a prevalence of HIV-1 infection of 25% among homosexual/bisexual men in the same period. The prevalence of HIV-1 infection among heterosexual men and women was 0.5% in 1986 and 1.0% in 1987. While HIV-1 prevalence in homosexual/bisexual men may have been higher in this particular London clinic than in the two clinics involved in the study reported here, rates of newly identified infections will be an incomplete indicator of the prevalence of antibody to HIV-1, especially among homosexual/bisexual men. An unknown number of clinic attenders who had already had positive tests in previous years were not included in our study.

From 1988 onwards, there was evidence of HIV-1 infection in heterosexual men and women in the UK who did not report major risk factors. Evidence from named test monitoring confirms this impression of a slow but sustained increase in the numbers infected with HIV-1 through sexual intercourse with partners of the opposite sex who themselves do not fall into major risk categories.

The potential for participation bias limits the value of voluntary testing as a means of assessing the extent of HIV infection. This has been shown in several studies of attenders at antenatal and STD clinics in which HIV antibody prevalence was seriously underestimated by voluntary testing. In this study there was no evidence that those at higher risk of infection refused the HIV-1 antibody test, disproportionately, between 1986 and 1990, but the very low levels of participation in 1989 and 1990, especially in South East Thames, made the method unreliable as a means of monitoring HIV infection. At the same time, a consensus had emerged in the UK in support of the use of the unlinked anonymous method of HIV surveillance which, while limiting the epidemiological information that can be gained, minimises participation bias. In 1990, a pilot unlinked anonymous serosurvey of STD clinic attenders began at five clinics in England and Wales. In those countries where anonymous testing is currently unacceptable on legal or ethical grounds, voluntary testing remains the only means of surveillance of HIV infection; a multicentre survey of voluntary testing of STD clinic attenders is in progress in several European countries.

Since 1989, the benefits of HIV testing of symptom-free individuals have become clearer and include the opportunity to monitor CD4 lymphocyte counts and to instigate chemoprophylaxis for opportunistic infections. Routine voluntary testing, ie, the offer of an HIV-1 antibody test to all patients attending STD clinics, has been widely advocated, not only because of these benefits, but because of the opportunity to counsel patients on the prevention of all STDs. HIV antibody test acceptance rates of between 70% and 92% have been reported from STD clinics in the United States and Australia. In the UK, only a proportion of HIV-1 infected people are known to the doctors treating them, supporting the case for HIV testing to be offered to all patients attending STD clinics where the prevalence of HIV-1 infection is high. There is a need

### Table 1 Characteristics of patients invited to have an HIV-1 antibody test in 1989

<table>
<thead>
<tr>
<th>Subgroups and area</th>
<th>Agreed to HIV-1 antibody test</th>
<th>Number</th>
<th>History of injecting drug use</th>
<th>&gt;5 sexual partners in past 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>% (number)</td>
<td>% (number)</td>
</tr>
<tr>
<td>Homosexual/bisexual men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South East Thames</td>
<td>Yes</td>
<td>261</td>
<td>16.6 % (47)</td>
<td>21.6 % (48)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>125</td>
<td>4.4 % (5)</td>
<td>4.3 % (5)</td>
</tr>
<tr>
<td>Other regions</td>
<td>Yes</td>
<td>877</td>
<td>12.9 % (159)</td>
<td>11.3 % (90)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>173</td>
<td>19.9 % (36)</td>
<td>14.0 % (21)</td>
</tr>
<tr>
<td>Heterosexual men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South East Thames</td>
<td>Yes</td>
<td>604</td>
<td>9.3 % (46)</td>
<td>10.1 % (58)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>738</td>
<td>5.0 % (6)</td>
<td>2.9 % (21)</td>
</tr>
<tr>
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<td>Yes</td>
<td>4913</td>
<td>6.2 % (117)</td>
<td>6.8 % (304)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1725</td>
<td>1.4 % (18)</td>
<td>5.0 % (82)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South East Thames</td>
<td>Yes</td>
<td>602</td>
<td>11.1 % (28)</td>
<td>4.3 % (25)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>839</td>
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<td>0.4 % (3)</td>
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<td>Other regions</td>
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<td>4104</td>
<td>1.4 % (64)</td>
<td>2.7 % (109)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1489</td>
<td>0.3 % (4)</td>
<td>1.0 % (14)</td>
</tr>
</tbody>
</table>

§ This number excludes those whose age, history of injecting drug use or number of sexual partners was not known.

* p <0.05 or ** p <0.01 for the difference between proportions of patients accepting and refusing the test.
for research on attitudes to HIV antibody testing if this is to be implemented. Recent evidence suggests that heterosexual patients attending STD clinics still have concerns about confidentiality of the test result and the financial implications of a positive test26.

Unlinked anonymous HIV serosurveys have become the method of choice in monitoring population trends in HIV infection, but voluntary HIV testing continues to have an important role20 in identifying infected individuals and monitoring the progress of infection so that timely treatment can be initiated.

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Acknowledgement
This study was designed and coordinated by Dr Sheila Polakoff, Hepatitis Epidemiology Unit, PHLS Central Public Health Laboratory, London.

References