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Surveillance of HTLV infection in England and Wales: 1986-1992

I Simms, J H C Tosswill, A Noone, D Morgan

Summary

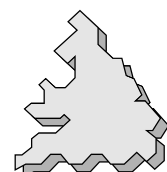
The epidemiology of infection with human T cell leukaemia/lymphoma virus (HTLV) types I and II in England and Wales between 1986 and 1992 has been studied. Two sources of data have been reviewed: reports of cases of infection received by the PHLS Communicable Disease Surveillance Centre, and information about people infected with HTLV-I and II provided on laboratory request forms sent to the Virus Reference Division of the PHLS Central Public Health Laboratory. Most patients were of Caribbean origin. The age and sex distribution of people with disease associated with HTLV-I and II in England and Wales resembles that previously recorded in the Caribbean. The data suggest that the prevalence of disease associated with HTLV infection is low in England and Wales, but case ascertainment may be incomplete.

Introduction

The human T cell leukaemia/lymphoma virus type I (HTLV-I) was the first retrovirus shown to be associated with disease in humans[1,2]. It has been linked with two distinct disease entities; adult T cell leukaemia/lymphoma, and tropical spastic paraparesis (also known as HTLV associated myelopathy)[2,3]. Adult T cell leukaemia/lymphoma is a rapidly progressive lymphoproliferative malignancy of mature T cells. It is often associated with peripheral blood involvement, cutaneous infiltration, and hypercalcaemia, and occurs in people aged 20 to 60 years. In contrast, tropical spastic paraparesis is a slowly progressive chronic disease of the nervous system that affects the lower limbs, and can also lead to incontinence and impotence. The closely related virus, HTLV-II, has not been linked definitively with disease but hairy cell leukaemia, mycosis fungoides, large granular lymphocyte leukaemia, and illnesses similar to tropical spastic paraparesis have been reported on rare occasions in people infected with HTLV-II[4-6].

The lifetime risk of developing adult T cell leukaemia/lymphoma if infected with HTLV-I is 2% to 5%, with an interval of about 30 years between acquiring the infection and developing symptoms[7-9]. The lifetime risk of developing tropical spastic paraparesis has been estimated to be 0.25%[10]. Studies of infections associated with transfusion in Japan suggest that tropical spastic paraparesis develops, on average, four years after infection[11].

Viral transmission depends on the transfer of cells, either horizontally (by blood transfusion, injecting drug use, or sexual contact) or vertically (mother to child, either perinatally or postnatally). Breast feeding is thought to be the main route of vertical transmission. Babies of seropositive mothers have a 25% probability of becoming infected if breast fed[12]. The development of tropical spastic paraparesis has been associated with infection acquired through transfusion, but adult T cell leukaemia/lymphoma has not been reported in people who have become infected in this way.



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Infection with HTLV-I is endemic in Japan, parts of West Africa, and the Caribbean where prevalences of 0% to 16%, 3.2%, and 2.4% to 5.7%, respectively, have been recorded[9,13-15]. Infection is also found in other parts of the world, either in populations that originated in the above regions or at a lower prevalence in other populations. HTLV-II infection is prevalent among injecting drug users and also seems to be endemic in some American Indian tribes[16].

It has been proposed that groups at risk of infection with HTLV-I or II should be screened in order to prevent the transmission of infection to sexual partners and the infants of infected mothers. Screening of donated blood has been introduced in Japan, the United States, and France, and is under consideration in other European countries, but neither routine nor selective screening of population groups – for example, antenatal patients – is undertaken in the United Kingdom. The prevalence in the population of infection and associated disease needs to be determined before the benefits of screening can be assessed.

Few data on infections with HTLV-I and II are available from surveys of prevalence in populations of the United Kingdom (table 1)[17-22]. Some studies have suggested that infection is restricted to black people born outside the United Kingdom. For example, in two surveys of women born inside and outside the United Kingdom of white, black African, black Caribbean, Asian, and other ethnic groups who attended antenatal clinics in inner London it was found that the women infected with HTLV-I or II were of black Caribbean origin and born outside the United Kingdom[17,18]. In contrast, all four of the HTLV-I infections detected in a large survey of blood donors in north London were in white women born in the United Kingdom[19]. Two of them had had sexual partners from the Caribbean, another had had a Japanese sexual partner who was known to be infected with HTLV-I, and the fourth may have been infected by a sexual partner from Iran. In the same survey HTLV-II infection was diagnosed in a man described as 'Anglo-Caribbean', who had been an injecting drug user and also had antibodies to both hepatitis B core antigen and hepatitis C virus. The surveys suggest that the prevalence of infection is below 5% even in groups thought to be at higher risk of infection with HTLV-I or II – such as black Caribbean people born outside the United Kingdom. This paper examines data on the epidemiology of HTLV-I and II obtained from routine reports of laboratory diagnosed infections.

Methods

Two sources of information about infections with HTLV-I and II were available for analysis, and covered the period from 1986 (when tests for the viruses became widely available) to the end of 1992. Cases of infection with HTLV-I and II are reported by microbiologists to the PHLS Communicable Disease Surveillance Centre (CDSC) as part of a voluntary system of reporting infectious diseases by laboratories for surveillance. In addition, requests for screening and/or confirmatory testing for HTLV-I and II infection from microbiology laboratories received by the Hepatitis and Retrovirus Laboratory, based at the Virus Reference Division (VRD) of the PHLS Central Public Health Laboratory, include data on the people being investigated.

Table 1 HTLV-I and II prevalence surveys in the United Kingdom

Study group	Region	HTLV-I and II prevalence		Comments
Antenatal clinic attenders[17] 3760 including white, Caribbean, African, and Asian women, born in the UK or immigrant	Inner London	0.26%		Of the 10 cases positive for HTLV-I, six were from the Caribbean, and two were from West Africa
Antenatal clinic attenders[18] 2893 including Asian, white, black African, and black Caribbean women	London	1.9% 0.7% 0.0%	Caribbean born African born UK, Asian born	All six women positive for HTLV-I were black, five were born in the Caribbean, and one was born in Africa
Blood donors[19] 4134 routine donors 2376 sickle trait screening panel donors	North London	 0% 0.08%	 (0 of 4134) (2 of 2376)	Estimated prevalence in all donors = 0.0003%
Patients attending hospital[20] 722 persons of Afro-Caribbean, African, and Asian ethnic origin, born in the UK or immigrant	West Midlands	3.6%	(7 of 192) Caribbean born	All seven patients positive for HTLV-I were born in the Caribbean
Relatives of 11 UK patients with tropical spastic paraparesis[21]	–	22% 0%	(10 of 46) Caribbean born (0 of 14) UK born	
Blood donors[22] 96720 blood donors	North London	0.004%	(5 of 96720)	Four were white women born in the UK, two of whom had Caribbean partners, one had a Chinese partner (known to be HTLV-I positive) and one had an Iranian husband. One man, born in the UK of Caribbean origin and previously an injecting drug user, was HTLV-II positive

Figure 1 Reports of infection with HTLV-I and II, 1986-92

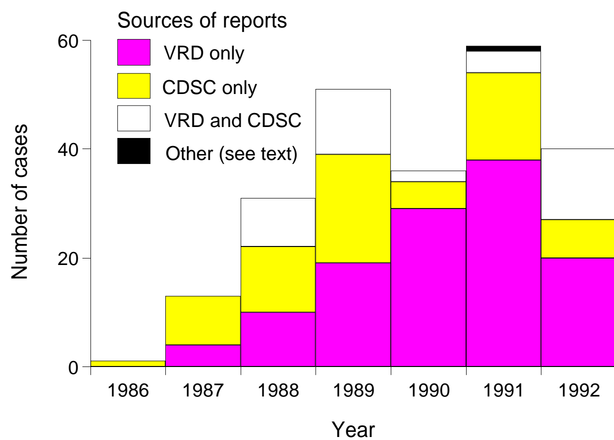
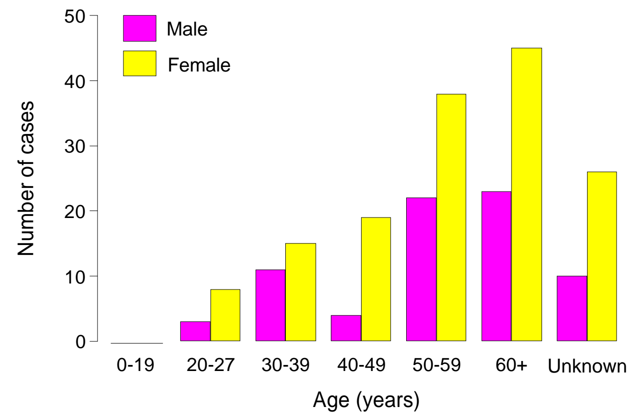


Figure 2 Age and sex distribution of people infected with HTLV-I and II, 1986-92



Data from the two sources overlap and have been reconciled to create one common data set. As the confirmation of HTLV infection generally occurs during the process of diagnosis, clinical diagnoses of tropical spastic paraparesis or adult T cell leukaemia/lymphoma were rarely recorded on reports or request forms. A list of clinical terms which would be accepted as indicative of tropical spastic paraparesis or adult T cell leukaemia/lymphoma has been developed (table 2).

Results

Two hundred and thirty-one infections with HTLV-I and II were recorded during the period 1986 to 1992, with the highest annual total in 1991 (figure 1). One hundred and sixty of the cases were identified as a result of confirmatory testing carried out by VRD. Reports of 40 of these cases had been sent independently to CDSC, which also received reports of a further 70 cases. A case identified from a copy of a death certificate, on which infection with both human immunodeficiency virus and HTLV-I were recorded, was also included.

No infections with HTLV-I and II were reported in people under the age of 20. The number of reports increased with age (figure 2), and the male to female ratio was 1:2. The ethnic origin of those infected was recorded for 54% (124 of 231) of cases. Most of these were of Caribbean origin (92%; 114 of 124), six were of African origin, and the other four originated from Brazil, India, the Middle East, and Japan.

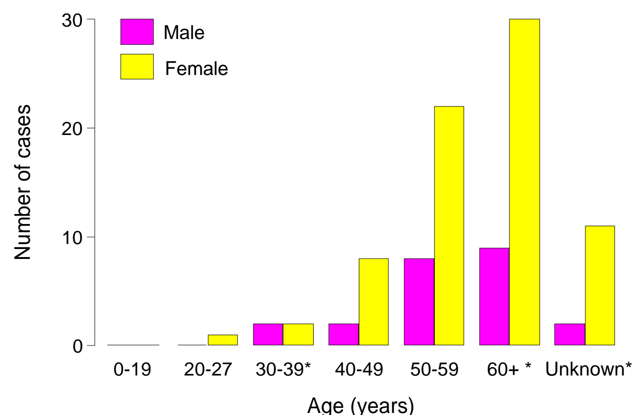
One hundred and eighty (78%) of the 231 reports or requests referred to the clinical condition of patients, which suggests that the test formed part of a diagnostic investigation. Of the remainder, 11 had been included in screening surveys, and 23 were relatives (spouse, sibling, or parent) of people known to be infected. The reason for testing was unknown in 17 cases. Of the 180 reports and requests that included a clinical record, over half (100) were compatible with a diagnosis of tropical spastic paraparesis and 44 with a diagnosis of adult T cell leukaemia/lymphoma. The remainder included 17 that were classified as 'other neurological', and 12 as 'other haematological conditions' (including two with B cell lymphomas). Seven had other infections that were probably unrelated to infection with HTLV-I and II.

The number of patients whose clinical records

Table 2 Clinical terms included in reports and used to distinguish tropical spastic paraparesis and adult T cell leukaemia/lymphoma, and other conditions reported in the investigation of HTLV-I and II infections

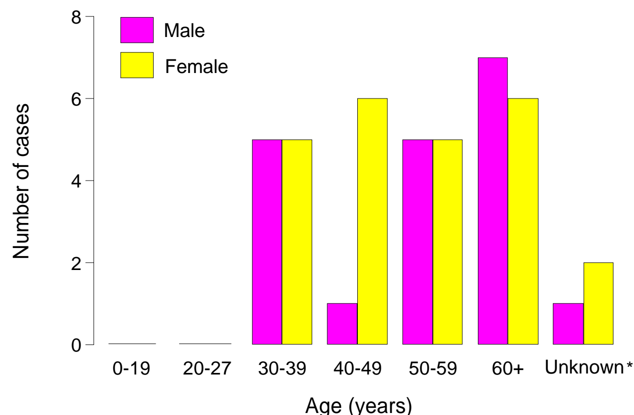
Tropical spastic paraparesis	Other neurological conditions	Adult T-cell leukaemia/lymphoma	Other haematological disease
Myopathy and paraparesis	Myopathy	Hypercalcaemia	Lymphadenopathy
Paraparesis	Central nervous system symptoms	T cell non-Hodgkin's lymphoma	B cell lymphoma
Paraplegia	Polymyositis	T cell lymphoma	
Multiple neurological or myopathic symptoms or signs	Multiple cranial nerve palsies	T cell lymphocytosis	
Myelopathy	Neurological symptoms	Non-Hodgkin's lymphoma	
Spasticity	Myositis	Acute lymphoma	
Jamaican neuropathy	Neuropathy	High grade lymphoma	
Spastic tetraparesis	Cerebrovascular accident/ pyramidal signs		
	Dementia		
	Ramsey Hunt syndrome		
	Lower motor neurone disease		
	Sensory loss		

Figure 3 Tropical spastic paraparesis in people infected with HTLV-I or II: age when infection was diagnosed



* in each of these categories there was one report where the sex of the case was not known.

Figure 4 Adult T cell leukaemia/lymphoma in people infected with HTLV-I or II: age when infection was diagnosed



* in this category there was one report where the sex of the case was not known.

suggested a diagnosis of tropical spastic paraparesis increased with age, and the male to female ratio among these cases was 1:3.2 (figure 3). No trend with age was observed in cases classified as adult T cell leukaemia/lymphoma, and the male to female ratio was 1:1.1 (figure 4).

Discussion

Reporting of laboratory diagnosed HTLV-I and II infections

The reporting of HTLV infections by laboratories to CDSC is incomplete. Most of the 231 HTLV-I and II infections identified from the two sources during the period 1986 to 1992 had been confirmed at VRD. Many HTLV-I and II infections identified as a result of laboratory requests for antibody testing at VRD had not been reported to CDSC. Some cases confirmed in other laboratories may not have been ascertained by the present surveillance system. Seventy-eight per cent of the reports or requests included clinical features of infection, which shows that the data available in the United Kingdom at present refers to disease associated with HTLV-I and II rather than infections per se. It was, however, difficult to obtain a complete epidemiological picture of disease associated with HTLV-I and II from these reports. The age and ethnic group of patients were often not recorded, and the clinical information about those under investigation for disease associated with HTLV was often insufficient to make it clear whether the clinical diagnosis was tropical spastic paraparesis or adult T cell leukaemia/lymphoma. To obtain the final diagnoses, which would ideally be based on agreed case definitions for diseases associated with HTLV[23], it would be necessary to follow up laboratory reports.

The age and sex distributions of disease observed here are consistent with those described elsewhere[9,24]. Most patients were of West Indian origin, but a number of infected people originated from neither the Caribbean nor Japan. In the data reported here there are more reports of tropical spastic paraparesis than adult T cell leukaemia/lymphoma, which probably reflects the chronic nature of tropical spastic paraparesis. The pattern of HTLV-I and II disease in the United Kingdom resembles that recorded in the Caribbean, from whence most HTLV-I and II carriers in the United Kingdom originate.

Screening

Further transmission of these viruses – to, for example, sexual partners, children of infected women, or recipients of transfusions – may, in theory, be prevented by screening populations or subgroups and counselling people found to be infected with HTLV-I or II. Surveys suggest that most infections in the United Kingdom occur in people born in the Caribbean of black Caribbean ethnic groups, but in the recent survey of blood donors in north west London all four HTLV-I infections detected were in indigenous white women[22]. These findings suggest that screening selected high risk groups may have a low sensitivity. More information is needed on the prevalence of infection in the black population born in the United Kingdom, and in the white population. Data on the prevalence of HTLV-II are particularly sparse.

In the survey of north London blood donors the cost of preventing a single transmission of HTLV-I or II infection was estimated to be £30000[22]. A full cost-benefit analysis would include the costs of counselling those found to be infected, the morbidity and mortality of infections, and disease prevented. The long incubation period and low lifetime risk of disease associated with HTLV-I and II make counselling difficult, and some infected people may decide that they do not want their relatives to be screened. The data reported above suggest that relatives are not usually screened. Current clinical practice in this respect is unknown. The cost of preventing disease associated with HTLV-I and II transmitted by transfusion in a recipient's lifetime was estimated in the north London survey as £1.3m, but there is inadequate clinical data to predict the extent of disease caused by HTLV infection in Western populations.

Decisions about screening strategies and the information needed for cost-benefit analyses of possible interventions would be improved by a more complete description of the epidemiology of infection with HTLV-I and II and their associated diseases. It is proposed that current surveillance is strengthened by increased ascertainment of cases and through follow up of reported infections to collect standardised clinical data.

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Correction: Outbreak forum: food poisoning at a masonic lodge. J P Wright, et al.

In the CDR Review of 29 April 1994, the attack rates (for those who had eaten cream and mayonnaise) in the first two rows of table 1 (page R59) were inadvertently transposed.

Measles in secondary school children: implications for vaccination policy

N Calvert, F Cutts, E Miller, D Brown, J Munro

Summary

The reported incidence of measles in children of secondary school age rose in 1992, after a progressive decline between 1988 and 1991. This rise was maintained in 1993. Several school and community based outbreaks of measles have occurred in the United Kingdom. This paper reports the investigation of an outbreak of measles based in a secondary school, which took place in 1992.

Thirty clinical cases were detected among the school's 840 pupils and 10 sporadic cases occurred outside the school. Twenty-one of the school cases provided samples of serum, in 19 of which measles IgM was detected. The overall attack rate was 3.6%, with no significant differences attributable to age and sex. Vaccine efficacy was about 90%.

This outbreak is one of the first to be described in the United Kingdom, although other countries (notably the United States) have reported measles in teenagers. The small degree of spread in the community may reflect the current high uptake of measles, mumps, and rubella vaccine and the catch up campaign that took place in 1988. The feasibility and cost effectiveness of various policy options to prevent future outbreaks in secondary schools are now being evaluated.

Introduction

The United Kingdom introduced measles vaccine into the routine schedule of childhood immunisation 25 years ago. For the first 15 years measles vaccination was not well implemented and coverage remained at around 50%[1]. This level of vaccination did not change the age distribution of cases and the highest incidence continued to be in children under 5 years of age[1]. Serological surveillance in 1986 and 1987 showed that, with coverage of measles vaccine at 70%, most children acquired immunity through disease or vaccination before school entry and only 5% of children over 10 lacked measles antibody[2]. In recent years coverage has increased steadily to over 90%. Measles, mumps, and rubella (MMR) vaccine was introduced in 1988, and many preschool children who had already received measles vaccine have also received MMR vaccine as part of the catch up programme.

Notifications of measles in the United Kingdom have fallen dramatically, particularly since 1988. The proportion of cases being notified in older children has risen, but the absolute numbers are small. Areas where vaccine coverage is very high have reported outbreaks that mainly affected children over 9 years old[3], or increases in the proportion of cases in this age group[4]. Concerns have been raised that further outbreaks will occur in secondary schoolchildren, as has been documented extensively in the United States[5].

We report the investigation of a measles outbreak that mainly affected teenagers at a comprehensive school (school A) in the Copeland district of West Cumbria, and discuss the implications for policies to eliminate measles. At the time of the outbreak, 840 pupils aged between 11 and 19 years were enrolled at the school. Measles vaccine was introduced in the district (population 72 000) in 1968 and coverage rose quickly to over 70% by 1972. MMR vaccine was introduced in 1988. Catch up vaccination of children aged 2 to 4 years was conducted by general practitioners and of schoolgirls aged 5 to 11 years by school nurses, but these were local initiatives and not national policy. Since 1988 over 97% of children are estimated to have received MMR vaccine in the second year of life. The number of cases of measles in Copeland district fell steadily, from 107 cases in 1986 to 12 in 1991.

Investigation

On 23 March 1992 a child became ill with measles, the first of 30 at school A. In the following two months 40 cases were notified to the Department of Public Health Medicine, West Cumbria Health Authority. The health authority wrote to local general practitioners on 15 April, alerting them to the potential outbreak and requesting prompt notification of cases. Questionnaires were posted to the parents of all notified cases and asked about clinical symptoms and signs, vaccination status, and history of contact with other cases of measles. Cases were asked to visit their general practitioners to have a blood test (10ml samples of venous blood were taken for serological assays).

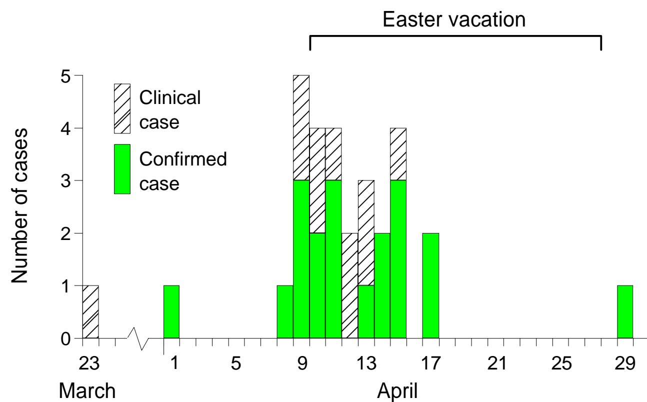
It was feared that a measles outbreak might disrupt important examinations, and a vaccination campaign was planned to halt the spread of the epidemic. Health authorities, as purchasers, have no direct control over community services. The need to identify funding and organise meetings caused delay, and resulted in the vaccinations being carried out after the Easter holidays.

On 7 and 8 May 1992 a limited vaccination campaign was conducted at school A, the source of most of the notified cases. Seven hundred and forty-six (89%) of the children enrolled at the school were vaccinated. The main reason that pupils were not vaccinated was absence from school on the days when the vaccine was administered. Vaccination details of children who attended the school were obtained from the child health computer.

Table 1 Measles cases and attack rates at school A by age

Age (years)	Number of children	Clinical cases		Confirmed cases	
		Number	Attack rate (%)	Number	Attack rate (%)
12 to 13	173	11	6.4	5	2.9
14	183	13	7.1	9	4.9
15	160	4	2.5	4	2.5
16	166	–	0.0	–	0.0
17	94	2	2.1	1	1.1
18 to 19	64	–	0.0	–	0.0
Total	840	30	3.6	19	2.3

Figure Onset of measles at school A



Laboratory assays

Serum was tested for measles-specific IgM and IgG using an established antibody capture radioimmunoassay[6]. The assay is based on virus grown in tissue culture and a measles-specific monoclonal antibody. Samples were considered positive for measles-specific IgM if the ratio of test to negative control reactivity (T/N) exceeded 3.0 and for measles-specific IgG if the T/N ratio exceeded 2.1.

Data analysis

We defined a case of measles as 'clinical' if there was a history of fever and rash and at least one of the following: cough, conjunctivitis, or coryza[7]. A 'confirmed' case of measles had, in addition, a positive serum IgM. We estimated attack rates for all cases, and separately for confirmed cases. Vaccine efficacy (VE) was estimated using the formula:

$$VE = \frac{ARU - ARV \times 100\%}{ARU} = (1 - RR) \times 100$$

in which ARU and ARV are the attack rates in unvaccinated and vaccinated children respectively, and RR is the relative risk (ARV/ARU). We calculated Taylor Series confidence intervals around the relative risk[8], and derived the vaccine efficacy. Epi Info was used to process data from the study.

Results

Vaccine coverage

Copeland district has achieved coverage higher than the national average for measles and, more recently, MMR vaccines. The estimated coverage has been over 80% since 1980, and over 90% since 1983. Among cohorts of secondary school age, measles vaccine coverage was 73% to 80% for children born in 1975 to 1981 and 86% to 90% for those born in 1982 to 1983. Of those born in 1983, a quarter had also received MMR vaccine. The records for some individuals are incomplete. In school A, in children born between 1973 and 1981, measles vaccination was documented for only 63% of pupils, 15% had an unknown vaccination status, and 22% had not been vaccinated.

Description of the outbreak

Forty cases of measles were reported from March to May 1992, all of which fulfilled the criteria for clinical measles. Samples of serum were obtained from 27 cases. Cases confirmed by serology were found in three schools: school A (of 30 cases, 21 provided samples and 19 were confirmed), school B (all three reported cases were confirmed), and school C (both reported cases were confirmed). Two other secondary schools each reported one case but samples of serum were not obtained. In addition, two cases were reported in preschool children but not confirmed, and one confirmed case occurred in a 48 year old.

The first case, which was confirmed serologically, developed in a previously vaccinated boy of 11 at school B on 16 March 1992. The second case, the index case at school A, developed on 23 March in a girl of 12 who had received measles vaccine at the age of 16 months. Her symptoms fulfilled the clinical case definition, but no serological tests were performed. The second case at school A (confirmed) developed nine days later in a girl of 15 who had received measles vaccine at the age of 18 months.

Investigation at school A

Parents of all 30 affected children who attended school A responded to the questionnaire. No history has been obtained of contact between the first three cases at school A; the cases arose in different year groups. The epidemic curve at school A (figure) shows several generations of measles transmission. The peak occurred just before the Easter vacation (10 to 27 April), and only one case occurred after the break. The limited campaign of vaccination was conducted when the epidemic was almost over.

All of the 21 samples of serum obtained from cases at school A were positive for measles-specific IgG. Nineteen were positive for serum IgM. One had an equivocal result to the serum IgM assay; this child was reported to be unvaccinated. Measles attack rates by age and sex of children at school A are shown in tables 1 and 2. The attack rates for males and females were not significantly different. The estimated vaccine efficacy at school A was 90% (95% confidence interval: 75% to 96% for all clinical cases, and 70% to 97% for confirmed cases only) (table 3).

Discussion

This small outbreak occurred mainly in one comprehensive school. The cohorts affected were those born before a high level of coverage (>90%) was reached, and before MMR vaccine was introduced in the district. The overall attack rate was low, even among the unvaccinated children, possibly because of natural immunity acquired through previous infection with measles, or because the Easter vacation interrupted the epidemic before the supply of susceptible children was exhausted. The vaccination campaign seems not to have contributed tohalting

Table 2 Measles attack rate at school A by sex

Sex	Number of children	Clinical cases		Confirmed cases	
		Number	Attack rate (%)	Number	Attack rate (%)
Male	418	14	3.3	11	2.6
Female	416	16	3.8	8	1.9
Not stated	6	–	0.0	–	0.0
Total	840	30	3.6	19	2.3

Table 3 Estimated vaccine efficacy at school A

Vaccine status	Number of children	Clinical cases			Confirmed cases		
		number	attack rate (%)	vaccine efficacy (%) (95% confidence limits)	number	attack rate (%)	vaccine efficacy (%) (95% confidence limits)
Vaccinated	529	6	1.1	90 (75-96)	4	0.8	90 (70-97)
Unvaccinated	186	21	11.3	–	13	7.0	–
Not known	125	3	2.4	79 (30-94)	2	1.6	75 (<0-94)

the epidemic.

Unlike many school outbreaks in the United States, this outbreak was largely confined to one school; only sporadic cases occurred outside school A. The lack of spread among preschool children may reflect the current high level of coverage by MMR vaccine and the effectiveness of the catch up programme in 1988, which contrasts with the low level of coverage by measles vaccine among preschool children in the United States[9]. The lack of measles transmission in other schools, where one or two cases occurred, may be because of the holiday period, but a further study is in progress to assess the level of susceptibility to measles in another school in West Cumbria.

In this outbreak the clinical case definition of measles proved to be an accurate guide to case identification, as measles was confirmed serologically in 25 out of 27 cases tested (93%). It is unclear why the other two cases could not be confirmed, as both were unvaccinated children from whom samples were collected within three weeks of the onset of illness. Laboratory investigations are important in the surveillance of measles. A recent pilot study in the United Kingdom[6] – which included children from this outbreak – has shown that measles-specific IgM can be detected reliably in saliva samples. This is a potentially valuable tool for the diagnosis of measles.

The estimated efficacy of measles vaccine was within expected limits. The attack rate of measles in children whose vaccination status was unknown was between those of vaccinated and unvaccinated groups, which suggests that some were vaccinated and others were not. Vaccine failure does not seem to have been the main cause of this outbreak, as cases occurred most commonly in unvaccinated children, but it is notable that the first two cases at school A occurred in vaccinated children.

Implications for vaccination policy

Over 90% of children born in the United Kingdom since 1983 have received either measles or MMR vaccine, so the potential for outbreaks among older children is likely to be a temporary phenomenon. The question of policy is whether to wait for older children to acquire immunity through natural infection or to conduct extra vaccination activities to immunise them. As more children in the community become protected with MMR vaccine it may take longer for those who have not been vaccinated to acquire natural immunity.

In the United States selective vaccination of susceptible children – those with no history of disease or vaccination – has failed to prevent outbreaks because of the inaccuracy of the histories obtained[10-12] and the inability to detect children in whom vaccines have failed who have contributed to outbreaks in highly vaccinated populations[13-15]. The high proportion of children in this study whose vaccination status was undocumented suggests that selective vaccination would be difficult to organise in the United Kingdom unless a simple serological or salivary assay was available to screen for measles antibody.

As well as the short term problem of measles outbreaks in older cohorts, the longer term problem is whether measles can be eliminated with a single dose strategy[16]. Other countries with elimination programmes have opted for mass re-vaccination, to provide an opportunity to vaccinate those who were not vaccinated in earlier years, and to immunise people who did not respond to the initial vaccination ('primary vaccine failures'). In many European countries[17,18] and the United States[19], a second dose is administered routinely to children of school age. Latin American countries have adopted a different approach; their aim is to interrupt the transmission of measles through mass vaccination of all children aged 9 months to 15 years in a short period of time[20]. In the United Kingdom the introduction of a second dose at a particular age would take several years to have any impact on the incidence of measles in children of secondary school age. Similar social factors are likely to determine compliance at each dose, and the same children may remain unvaccinated each time, so that an overall improvement in coverage is not achieved. A national campaign to vaccinate all schoolchildren within a short period of time, although logistically the most demanding approach, would interrupt transmission immediately and could be highly cost effective, both in the short and long term. The feasibility and cost effectiveness of rapidly interrupting the transmission of measles, through a national immunisation campaign aimed at the whole school age population in the United Kingdom, is being evaluated.

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An outbreak of measles in Trafford

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Summary
In the autumn of 1993 an outbreak of measles occurred in Trafford, Greater Manchester, associated with two junior schools. Thirty-four cases were reported. Twenty-five of the 32 cases whose ages were known were aged between 7 and 11 years. The mean age was 8.6 years, and the median and modal age was 10. Two of the cases had received measles vaccine. Eighteen of the 19 cases who provided samples were confirmed as measles by laboratory tests. The incident showed that extensive resources are needed to investigate such outbreaks and implement control measures, and identified problems with the local child health computer system. The outbreak did, however, provide an opportunity to immunise children within the district who had not previously received measles vaccine. It is important for unprotected siblings of affected children to be vaccinated to prevent the secondary spread of infection, and all cases of measles should be notified promptly so that outbreaks can be identified.

Introduction
Notifications of measles to the Office of Population Censuses and Surveys have fallen progressively since the introduction of measles vaccine in 1968 and measles, mumps, and rubella (MMR) vaccine in 1988. The pattern of notifications in Trafford reflected national trends until 1992.

In 1992 the number of notifications of measles in older children and adults increased nationally. Twenty per cent of notifications in 1992 were of those over 10 years of age, compared with 12% in 1987 (E Miller, personal communication). Reports to PHLS Communicable Disease Surveillance Centre (CDSC) suggested that much of this increase was associated with outbreaks in secondary schools[1]. Moreover, small increases in susceptibility to measles have been observed nationally among 7 to 14 year olds since the introduction of MMR vaccine (E Miller, personal communication).

In 1992, 20 cases of measles were notified to Trafford District Health Authority, the lowest number since 1978. Uptake of MMR vaccine among children aged 18 months was 96% in Trafford in 1992, compared with a national

Table 1 Vaccine efficacy at schools A and B

Vaccination status	School A ill	School A not ill	School A attack rate (%)	School B ill	School B not ill	School B attack rate (%)	Total ill	Total not ill	Total attack rate (%)	Total vaccine efficacy (%) (95% confidence limits)
Vaccinated	1	225	0.4	1	247	0.4	2	472	0.4	
Not vaccinated	15	17	46.9	7	20	25.9	22	37	37.3	
Not known	–	–	–	–	1	–	–	1	–	
Total	16	242	6.2	8	267	2.9	24	510	4.5	99 (95-100)

uptake of 93%[2]. In 1993, however, 95 cases of measles were notified, 25 of which were associated with the outbreak reported here. The ages of 87 of these cases were recorded and 41 were aged 10 years or more.

Investigation

In October 1993 a general practitioner in Trafford district alerted the public health department to three cases of 'classical' measles among 9 and 10 year olds who attended a local junior school (school A). The outbreak investigation sought to determine whether the cases had been vaccinated and to identify other susceptible children and offer them vaccination. Further investigation was undertaken to determine the size of the outbreak and control further spread. The head teacher of the school provided the names and addresses of the children in the class with the most cases. The Information Department in Trafford Community Unit checked the vaccination status of these children but, although the children's records were on the database of the child health computer system, data on measles vaccination for children of this age had not been transferred when the computer system was changed. As a result, vaccination status had to be determined by the laborious method of searching microfiche records.

All general practitioners in the locality were telephoned and asked to report any further cases to the public health department. They were asked to describe the symptoms and signs, indicate the degree of certainty with which the diagnoses of measles had been made, and state which school their cases attended.

CDSC was informed of the outbreak and provided specimen kits so that cases could be tested for evidence of recent infection. This was done by testing for IgM in samples of saliva and, if possible, serum. Samples of serum were obtained using a finger prick technique. Names and addresses of children notified by general practitioners at the end of October and beginning of November (weeks 43 to 45) were passed to health visitors who arranged for specimens to be collected and posted. Testing of saliva and serum samples was carried out by the Enteric and Respiratory Virus Laboratory at the PHLS Central Public Health Laboratory. MMR vaccine was subsequently offered and administered by the school nurse to children in the class affected who had not previously been vaccinated and who were well.

By the end of the first week in November, it was clear that the outbreak was not confined to one class. The vaccination records for all children in the school were checked and the vaccination programme was extended to include all children in the school who had not previously been vaccinated and who were well.

A press release about measles, MMR vaccine, and the benefits of immunisation was issued. Vaccination was recommended for all children under 12 who had not previously been vaccinated, because most of the reported cases were 9 and 10 year olds. A copy of the press release, with an explanatory covering letter, was sent to all general practitioners who work in the area administered by Trafford District Health Authority.

In mid-November, cases of measles were reported in children who attended another junior school in the same area (school B). The vaccination status of all pupils in the school was checked and MMR vaccine was offered to all children who were well and had not previously been vaccinated. Laboratory confirmation was not sought.

Results

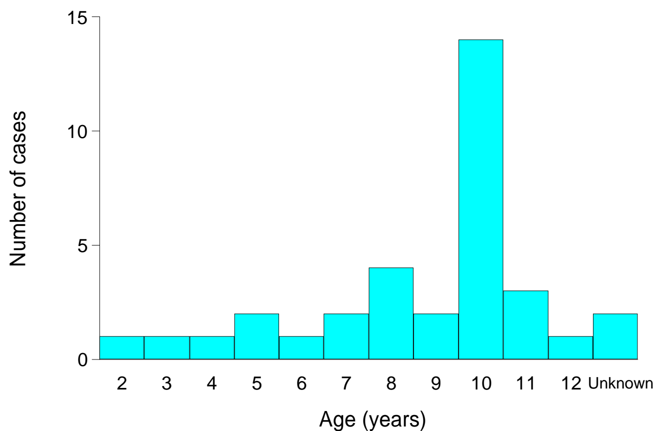
Thirty-four cases of measles were reported during the investigation. Twenty-five of the cases were formally notified by their general practitioners. There were 16 cases in children at school A and a further seven among their siblings. The attack rate in the school was 6% (16 of 258); 46.9% in unvaccinated children and 0.4% in vaccinated children (table 1). The vaccine efficacy was calculated to be 99% (95% confidence limits 95% to 100%)[3]. Nineteen of the 23 cases associated with school A were tested for IgM (table 2). Eighteen provided samples of serum and saliva, and one

Table 2 Laboratory tests (IgM) for cases associated with school A

IgM status: Blood	IgM status: Saliva	Number of cases: School-children	Number of cases: Siblings	Number of cases: Total
Positive	Positive	12	2	14
Positive	Negative	3	–	3
Not available	Positive	–	1	1
Negative	Negative	–	1*	1
Not tested	Not tested	1	3	4
Total		16	7	23

* IgG positive.

Figure Age distribution of cases (n = 34)



provided saliva only. Eighteen were IgM positive. The one case that was negative for IgM had provided samples of serum and saliva. Only one of the cases (a laboratory confirmed case) had received measles vaccine. The schoolchildren were aged 7 to 10 years, and three laboratory confirmed cases occurred in siblings aged 2, 3 and 5 years (figure).

Thirty-two of the 259 pupils at school A had not been vaccinated, and 15 of these were cases (table 1). The 17 susceptible pupils were offered MMR vaccine: 11 were vaccinated and six refused or did not receive parental consent. The general practitioners of these six pupils were informed.

Eight cases of measles were reported at school B, seven of whom were aged 9 to 11 years and one was 5 years old (figure). Only one had previously been vaccinated. When the vaccination records for all pupils at the school were checked, it was found that 20 children who remained well had not been vaccinated. The attack rate was 26% in unvaccinated children and 0.4% in those who had been vaccinated (table 1). The vaccine efficacy was 99% (95% confidence intervals 95% to 100%)[3]. Fifteen of the 20 susceptible children were vaccinated by the school nurse, and one by a general practitioner. The general practitioners of the remaining four, for whom parental consent had not been obtained, were informed.

A further three laboratory confirmed cases of measles –not associated with either school – were identified in children aged 4, 6, and 10 years. These presented to their general practitioners, who reported the cases. None had been vaccinated.

Discussion

The results of this investigation provide evidence to support current concerns about the increased incidence of measles in older children, and the need to explore alternative immunisation strategies.

The administration of MMR vaccine by the school nurse was conducted efficiently and was monitored, but difficulties with ascertainment of vaccination status and the obtaining of consent caused delay, and the control measures may not have affected the secondary spread of infection. Third or fourth wave transmission may, however, have been prevented as there was a notable decline in notifications of measles among older children after week 47 in 1993. Following the press release, three local newspapers published information about measles. It was not possible to show whether this led to a significant increase in uptake of MMR vaccine.

The clinical diagnosis of measles was confirmed in the laboratory for all but one of the 19 cases tested. Other studies have found that 84% of cases associated with outbreaks were confirmed serologically compared with only 17% of sporadic cases[4].

The fact that a large proportion of the cases had not been vaccinated suggests that vaccine efficacy was high – 99%, according to these data. The uptake of measles vaccine by children born in Trafford in 1982, 1983, and 1984, was 70%, 75%, and 80%, respectively. Analysis by electoral ward, however, showed that the north of the district, where the outbreak occurred, had a lower uptake than the district average. The outbreak may, therefore, have been related to greater susceptibility to measles among children in north Trafford.

There was considerable underreporting of cases, although all general practitioners in Trafford were informed about the outbreak. Nine of the 34 cases were not notified formally.

Measles notifications in Trafford have continued to increase in 1994, although there is no clear pattern in age or location of cases. At least two other junior schools have noted the absence of several children reportedly with measles. The feasibilty and cost effectiveness of a national campaign to vaccinate all schoolchildren against measles is currently being evaluated; in Trafford district, therefore, it has been decided not to institute a selective 'catch up' programme of vaccination or to vaccinate all children of school age in the district regardless of their vaccination status. There are several reasons for this: transmission may not be affected, data on vaccination status are not readily available from the computerised database, it would be difficult to mobilise sufficient resources to run an efficient programme, and expectations might be raised among parents in neighbouring districts (Manchester and Salford).

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