

Leprosy in England and Wales

P Van Buynder, J Eccleston, J Leese, DNJ Lockwood

Summary: *This paper reviews cases of leprosy notified in England and Wales to the Central Leprosy Register since its inception in 1951. Leprosy remains a rare condition in England and Wales, with fewer than ten cases notified on average in recent years. No definite case of indigenously acquired leprosy has been reported since the disease became notifiable. Although only a small number of patients present each year, leprosy remains a debilitating disease, and the unfamiliarity of clinicians with this condition can lead to delays in diagnosis and undernotification.*

Key words:

disease notification
epidemiological trends
leprosy
tropical medicine

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Introduction

The apparent global burden of leprosy has diminished since a World Health Assembly resolution in 1991 to make its elimination a priority was adopted¹. The Seventh World Health Organization (WHO) Expert Committee on Leprosy, which met in Geneva in 1997, emphasised the importance of detecting the remaining cases, treating them with multidrug therapy (MDT) via general health facilities, and continuing the process of simplifying diagnosis and treatment^{2,3}.

The apparent dramatic fall from 2.3 million prevalent cases in 1995 to 1.3 million cases in 1996⁴, was, however, due largely to shortening the recommended duration of drug therapy and the subsequent removal from registers of patients who had completed MDT and been pronounced cured⁵. The global prevalence of leprosy appears now to be levelling off, but this stabilising prevalence is thought to reflect steady case detection, particularly of cases in the 16 countries from the Asian, African, and American continents where the global burden of leprosy is now concentrated.

Five hundred thousand new cases of leprosy are

still reported worldwide each year, but case detection is still hampered by a lack of geographical accessibility as well as the stigma attached to leprosy. Any reassurance derived from declining prevalence needs to be tempered by concerns about lack of data on the extent of any reduction in continuing transmission and disease incidence and by an increase in disability among new cases in many countries where the disease is endemic⁶.

Leprosy surveillance in England and Wales

Leprosy became a notifiable disease in England and Wales in 1951, since when a confidential register of all cases notified in England and Wales has been maintained on behalf of the chief medical officers, latterly by the PHLS Communicable Disease Surveillance Centre. Cases that remain on treatment or under surveillance, either because of complications or their treatment ended recently, are maintained on a central register. The central register is updated each year with information obtained from questionnaires sent to the attending physicians. The central register includes demographic information, data on the type of leprosy (see classification in table 1), the clinical disabilities present, and previous and current antileprotic treatment.

Recent trends

A total of 1358 notifications have been received since the register was set up. The rate of case notification peaked at 467 in the period 1960-69, and has since declined: and average of nine notifications have been made annually in the past five years from 1993 to 1997 (figures 1 and 2).

As the numbers of cases of leprosy notified have declined their ethnicity has changed. Leprosy in whites accounted for over a quarter of notifications in the 1950s, but less than 3% in the 1990s. At the same time the proportion of cases of African

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TABLE 1 Classification of leprosy

Type	Skin lesions	Peripheral nerve involvement	Bacillary load	Treatment classification
intermediate	single, may be anaesthetic	none	-/+	Pauci/multibacillary
tuberculoid	single, anaesthetic macule	single	-	Paucibacillary
borderline tuberculoid	multiple, anaesthetic macules	single or	-/+	Multibacillary
borderline	multiple irregular macules and plaques	multiple	+	Multibacillary
borderline lepromatous	macules, plaques and papules	multiple and symmetrical	++	Multibacillary
lepromatous	papules, nodules and infiltration	late, multiple symmetrical	+++	Multibacillary

ethnicity has risen steadily to around 10%; that of Indian ethnicity has fallen to 20% after peaking at almost 40% in the 1970s, and a more recent marked increase in the proportion of cases of Pakistani and Bangladeshi ethnicity has also been seen, from between 7% to 13% in the 1950s to 1980s to 23% in the 1990s. West Indians accounted for 8% of notifications in the first 30 years of the register but none this decade. These trends reflect both alterations in migration patterns and changes in the global burden of leprosy in the past 50 years (figure 3). Although no new cases have been reported in West Indian patients in this cohort a new lepromatous leprosy patient from St Lucia has recently been seen at the Hospital for Tropical Diseases. This emphasises the point that in a disease with a long incubation period patients may still present from area now considered to be free from leprosy.

The geographical distribution of leprosy cases in England and Wales reflects the distribution of immigrant populations. Almost half of the notifications occurred in the Thames regions, with the former North Western, Yorkshire, Trent, Mersey, and West Midlands regions together accounting for another third.

Although the numbers of new cases of leprosy in England and Wales has declined, new cases and those who have already been treated continue suffer considerable morbidity. From 1990 to 1997, 40% of cases notified had sufficient anaesthesia to cause functional impairment at the time of presentation.

Central Leprosy Register

One hundred and twenty-eight cases are currently on the Central Leprosy Register, 70% of whom are

TABLE 2 Current WHO guidelines for MDT

Type of leprosy	Drug treatment		Duration of treatment	Duration of follow-up
	Monthly supervised	Daily self administered		
Paucibacillary	Rifampicin 600mg	Dapsone 100mg	6months	2 years
Multibacillary	Rifampicin 600mg Clofazimine 300mg	Clofazimine 50mg Dapsone 100mg	24 months	5 years

male, and half of whom were aged 30 years or under when notified initially. Less than 30% of cases on the central register were first notified in the past ten years; a third were diagnosed over 30 years ago. The ethnicity of patients on the central register is shown in figure 4. Over three quarters of cases who remain on the central register were initially diagnosed with lepromatous or borderline lepromatous leprosy.

A total of 115 (90%) patients were reviewed in 1997. Twenty-five of these are currently being treated, including five with relapsed disease. The remaining cases are evenly spread between those being monitored because treatment ended less than five years ago and those who have completed treatment but need follow up for their complications. Eighty (63%) of those on the register have anaesthesia causing functional impairment, 50 (39%) have a significant deformity, 14 (11%) have loss of vision, and 28 (22%) an amputation; overall 91 (71%) have significant sequelae.

Adherence to MDT treatment guidelines in England and Wales (table 2) has been good since the 1980s. All cases remaining on treatment are on a form of MDT.

Discussion

The presentation of leprosy cases outside endemic areas with signs unfamiliar to most British physicians may result in the diagnosis being overlooked. There is

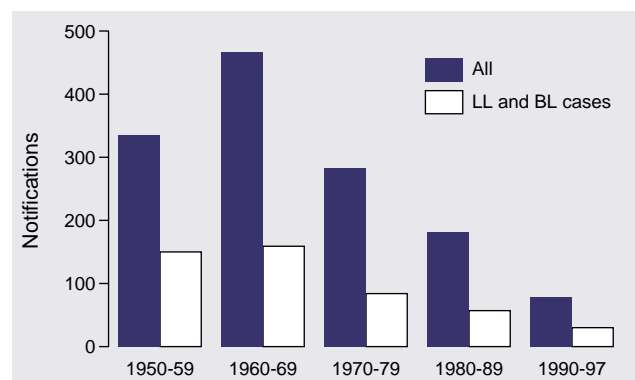
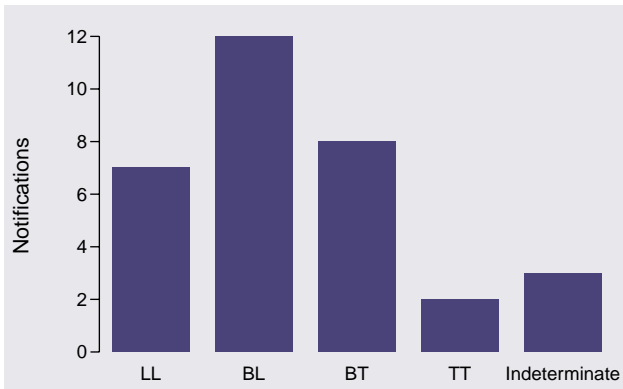
FIGURE 1 Notifications of all leprosy and lepromatous (LL)/borderline lepromatous cases (BL)

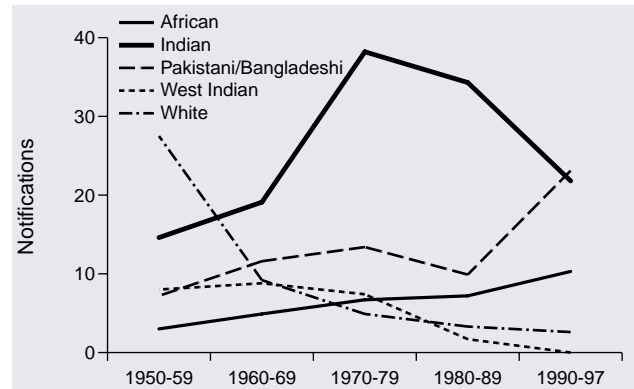
FIGURE 2 Leprosy notifications by type of leprosy: 1990 to 1997 (case numbers)



evidence of delayed recognition of leprosy in England and Wales⁷. The problem of leprosy has not gone away: 28 new cases were seen at the Hospital for Tropical Diseases in London alone in the 42 months from May 1995 to December 1998, compared with 32 cases identified on the register from 1990 to 1997. These figures suggest that undernotification is also a problem.

An updated *Memorandum of Leprosy* was released in 1997 by the Department of Health and the Welsh Office after consultation with the Panel of Leprosy Opinion and the PHLS⁸. This document provides essential information for those who may see or be involved in the management of patients with leprosy and has been circulated to the medical practitioners most likely to be referred patients with leprosy. The Memorandum contains contact details of the experts who constitute the Panel of Leprosy Opinion who are available to advise and consult on the diagnosis and management of individual patients. Copies can be obtained from Department of Health Stores, PO Box 410, Wetherby LS23 7LN. The Hospital for Tropical Diseases, Mortimer Market, Capper Street, London WC1E 6AU, tel 0171 387 9300 ext 5972; fax 0171 380 9761 is the national referral centre for cases of leprosy and suspected leprosy.

FIGURE 3 New cases of leprosy notified in England and Wales by proportions (%) from particular ethnic origin



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The annual review of leprosy patients is undertaken by attending physicians and coordinated at district level by consultants in communicable disease control. The authors are grateful for the continuing key role played by these two groups in maintaining an accurate register.

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Enterovirus infections in England and Wales: laboratory surveillance data: 1975 to 1994

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Summary: *Microbiology laboratories in England and Wales reported 40 366 culture confirmed isolates of echovirus (24 628; 61%) and coxsackievirus (B 11 714; 29%, A 4024; 10%) infections to the PHLS Communicable Disease Surveillance Centre (CDSC) in the 20 years from 1975 to 1994. Nearly half of the organisms were isolated from faeces, and 5741 were isolated from cerebrospinal fluid (75% of them echovirus, 13% coxsackie B, and 12% coxsackie A). Isolation rates for all enteroviruses were highest among infants aged 1 to 2 months. Sixty per cent of patients were aged under 5 years, 10% 5 to 9 years, and only 6% 35 years or over. Predominant serotypes were similar to those reported in other countries including the United States, Finland, and Belgium. Seventy-one per cent of reports were made between July and mid December. Periodicity varied between groups and serotypes: some demonstrated peaks at intervals of two to five years. There was evidence of spread of epidemic serotypes across Europe in certain years. Data collected between March and May each year enabled the strains circulating in the following 'season' to be predicted. Such information might be used to warn clinicians to anticipate particular clinical presentations.*

Key words:

coxsackievirus infections
echovirus infections
enterovirus infections
epidemiological trends

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Introduction

The enteroviruses are members of the family *Picornaviridae*. They consist of five subgroups and a total of 67 different serotypes: 31 echoviruses, 23 coxsackieviruses group A, six coxsackieviruses group B, three polioviruses, and four of the newer enteroviruses types 68-71.

Enteroviruses cause sporadic infections and epidemics worldwide. Peaks occur in summer and early autumn in temperate climates but no such pattern exists in the tropics. Enteroviruses are transmitted from person to person by the faecal oral route, by contact with infected nose and throat discharges, and by droplet spread. Subclinical and inapparent infections far outnumber those that cause clinical illness¹.

Enteroviruses cause numerous diseases including pharyngitis, herpangina, rash with fever, hand foot and mouth disease, meningoencephalitis, myopericarditis, pleurodynia (Bornholm disease), disseminated disease in newborn babies, and epidemic haemorrhagic conjunctivitis. They may play a part in the aetiology of juvenile onset insulin dependent diabetes^{2,3}, congenital

abnormalities⁴, and sporadic motor neurone disease⁵, but seemingly not chronic fatigue syndrome⁶.

Enteroviral infections are diagnosed by isolation of the virus from faeces (the most productive specimen), cerebrospinal fluid (CSF), throat swabs, skin vesicle swabs, or biopsy material using tissue culture or suckling mice inoculation (coxsackieviruses only); serological tests for neutralising, complement fixing, or IgM antibodies; or detection of RNA by the polymerase chain reaction (PCR). Isolation of the virus has been the definitive method of diagnosis for 30 years. Tissue culture and suckling mouse inoculation methods enable strains to be serotyped by neutralisation with type-specific antiserum.

PHLS, NHS, and private laboratories in England and Wales report isolations of enterovirus to the PHLS Communicable Disease Surveillance Centre (CDSC). Data were last reviewed in 1971⁷. We review here the reports of echovirus and coxsackievirus isolations for the 20 years from 1975 to 1994.

Methods

Forty-nine PHLS laboratories and over 250 NHS and private laboratories in England and Wales voluntarily report isolates of enteroviruses to CDSC⁸. The data provided include date of specimen collection, age and sex of patient, clinical details, agent isolated, and the name and region of the reporting laboratory. Data were extracted from the laboratory reporting system at CDSC and analysed using Statistical Packages for the Social Sciences (SPSS). Population denominator data from the Office of Population Censuses and Surveys (OPCS; now the Office for National Statistics) for the mid year 1985 were used to derive estimated annual age specific rates of infection over the

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TABLE 1 Enterovirus isolates, by group and serotype: England and Wales, 1975 to 1994

Echovirus n (%)	Coxsackie B n (%)
E11 5015 (20.4)	B4 2623 (22.4)
E22 3202 (13.0)	B5 2268 (19.4)
E7 2547 (10.3)	B2 2245 (19.2)
E30 2543 (10.3)	B3 1874 (16.0)
E9 2333 (9.5)	B1 1344 (11.5)
E19 1961 (8.0)	B6 524 (4.5)
E6 1382 (5.6)	nk 836 (7.1)
E3 833 (3.4)	Total 11714 (100)
E5 616 (2.5)	
E17 571 (2.3)	
E14 560 (2.3)	
E18 545 (2.2)	
E25 449 (1.8)	
E4 320 (1.3)	
E24 277 (1.1)	
E23 169 (0.7)	
E20 162 (0.7)	
E15 144 (0.6)	
E1 140 (0.6)	
E13 118 (0.5)	
E2 111 (0.5)	
E27 106 (0.4)	
E12 100 (0.4)	
E31 75 (0.3)	
E29 69 (0.3)	
E26 60 (0.2)	
E16 48 (0.2)	
E21 46 (0.2)	
E32 44 (0.2)	
E33 34 (0.1)	
E34 5 (-)	
E28 4 (-)	
E8 2 (-)	
nk 37 (0.2)	
Total 24628 (100)	

TABLE 2 Echovirus, coxsackie B, and coxsackie A virus isolates, by specimen site: England and Wales, 1975 to 1994

Site of specimen	Echovirus n (%)	Coxsackie B n (%)	Coxsackie A n (%)
Faeces*	12213 (49.5)	4996 (42.6)	1899 (47.2)
Respiratory tract†	7702 (31.3)	3873 (33.1)	1125 (28.6)
CSF	4278 (17.4)	790 (6.7)	673 (16.7)
Skin	22 (-)	13 (-)	158 (3.9)
Eye	39 (-)	15 (-)	10 (-)
Mouth	26 (-)	10 (-)	60 (1.5)
Vesicle	- (-)	- (-)	1 (-)
Urine	127 (-)	31 (-)	16 (-)
Other‡	72 (-)	180 (-)	12 (-)
Not known	149 (-)	1806 (15.4)	70 (1.7)
Total	24628 (100)	11714 (100)	4024 (100)

* 'faeces' includes rectal swabs and reports indicating a gastrointestinal origin (for example 'ileostomy' or 'large intestine')
 † 'respiratory tract' includes nasopharyngeal or throat swabs and reports described as 'lungs', 'bronch', 'middle ear'
 ‡ 'other sites' includes 'ascitic fluid', 'brain', 'bone marrow', 'genital', 'lymph gland', 'pericardial', 'placenta', 'umbilicus'

2). The most commonly reported echoviruses were types 11 (20%), 22 (13%), 7 (10%), and 30 (10%) (table 1). The commonest coxsackie B viruses were B4 (22%), B5 (19%), and B2 (19%). The commonest coxsackie A viruses were A9 (62%), A16 (15%), and A7 (7%).

Isolates from males outnumbered those from females by 1.4:1 for echoviruses, 1.3:1 for coxsackie B, and 1.2:1 for coxsackie A. Sixty per cent of patients with any enterovirus were under 5 years of age (29% under 1 year), 10% were 5 to 9 years, 24% 10 to 34 years, and only 6% 35 or over (figure 2). The estimated annual isolation rate was 3.8 per 100 000 population overall and 140/100 000 among those aged 1 to 2 months. Enteroviruses were isolated from CSF at an estimated annual rate of 2/100 000 in children under 1 year of age, peaking at 23/100 000 in the first month of life.

Nine enteroviruses each accounted for over 5% of the total in the 20 year period: echoviruses 11, 22, 7, 30, and 9; coxsackie B4, B5, and B2; and coxsackie A9 (table 3). The table also shows the comparable frequency of isolation of particular enteroviruses in the United States

whole period. A Medline search (1996-present; enterovirus infections; epidemiology) was carried out to identify published reports of comparable international data.

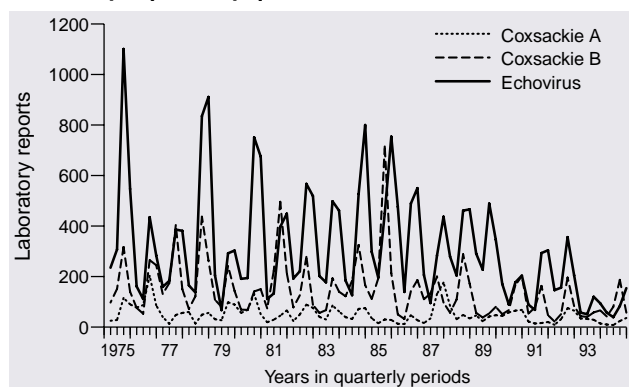
Results

A total of 40 366 echovirus and coxsackievirus isolates were reported to CDSC from 1975 to 1994. Sixty-one per cent of these were echoviruses, 29% coxsackie B viruses, and 10% coxsackie A viruses (figure 1 and table 1). Nearly half of the reports were of faecal isolates (table

TABLE 3 Commonest enteroviruses isolated from clinical specimens (percentages) in England and Wales 1975 to 1994, the US 1970 to 1983⁷, Finland 1971 to 1992 (excluding 1975 and 1984)⁸, and Belgium 1980 to 1994⁹

	England and Wales	US	Finland	Belgium
Enterovirus				
E11	12.4	12.2	12.1	8.5
E22	7.9	<1.6	8.0	5.1
E7	6.3	6.8	6.7	5.3
E30	6.3	3.0	1.4	11.7
E9	5.8	11.3	3.9	<2.8
E6	3.4	5.5	4.5	6.8
E4	0.8	6.3	0.8	<2.8
Coxsackie B				
B4	6.5	4.6	6.2	3.6
B5	5.6	8.7	14.9	6.0
B2	5.6	4.8	4.6	4.0
B3	4.6	4.5	7.3	5.0
Coxsackie A				
A9	6.2	4.5	8.6	<2.8
Total	40366	23481	1681	3333

FIGURE 1 Coxsackievirus types A and B, and echovirus laboratory reports, by quarter: 1975 to 1994



(US) from 1970 to 1983⁹, in Finland from 1971 to 1992¹⁰, and in Belgium from 1980 to 1994¹¹.

Between 322 and 2190 echovirus infections were reported in each of the 20 years in England and Wales, 207 to 1231 coxsackie B viruses, and 72 to 453 coxsackie A viruses (figure 1). There was marked seasonality: 71% of reports had specimen dates between July and mid December. Among the main enteroviruses, several (for example, echovirus 11, coxsackieviruses B4, B5, B2, A9, and A16) appeared at intervals of two to five years, while others (echovirus 22 and coxsackie A7) were identified in most years (figure 3).

Nine per cent of the 24 628 echoviruses were reported in 1975 and 8% in 1978, with further peaks (7% of reports) in 1980, 1984, 1985, and 1986. These peaks were accounted for by large epidemics of echovirus type 19 in 1975 (constituting 47% of all echovirus and coxsackievirus isolates in that year), type 11 in 1978, 30 in 1980, 7 in 1984, and 11 again in 1985, and combined epidemics of echovirus types 11, 22, and 30 in 1986 (figure 3). The 1484 of echovirus type 19 in 1975 was three times the total number of reports of this echovirus (477) in the remaining 19 years.

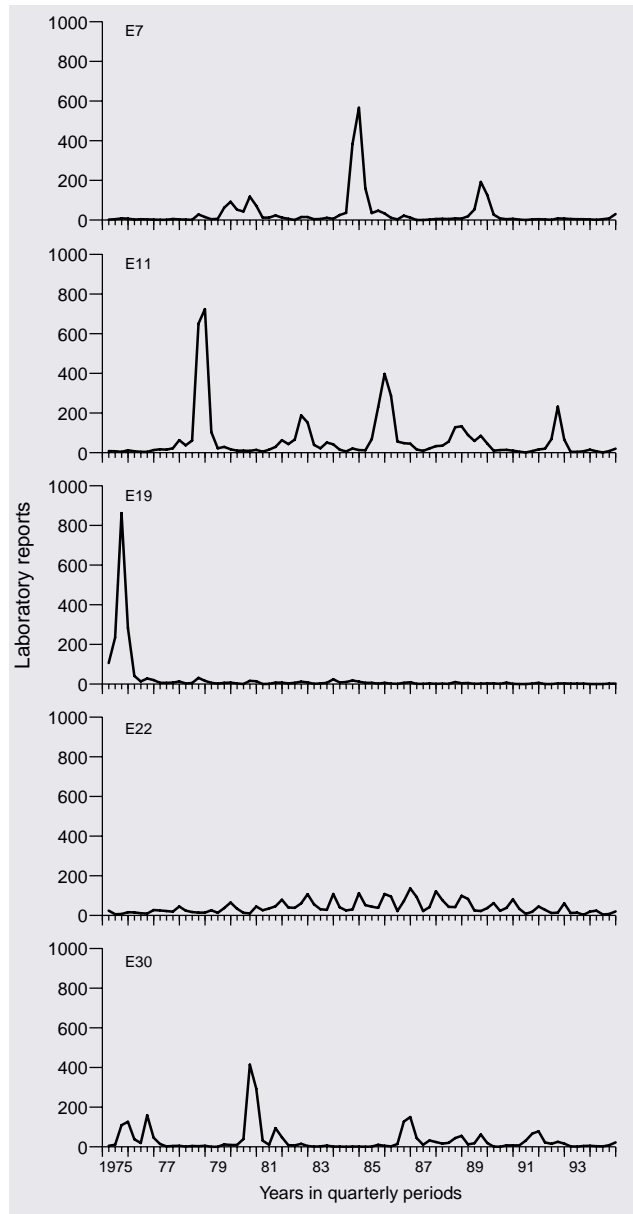
Ten per cent of the 11 714 reports of coxsackie B virus were made in 1985 and 9% in 1981, accounted for by epidemics of B4 and B5 in 1985 (the same year echovirus 11 was increased) and of B2 and B5 in 1981. Epidemics of A9 occurred in 1976 and 1987 and A16 was epidemic in 1980. Transmission was swift and widespread in epidemic years. For example, in the echovirus 11 outbreak of 1978 we traced the pattern of progression of the virus. The first reports, in February and March, were mainly in Merseyside and Gloucester with just a few isolates elsewhere. By mid July all parts of England and Wales were affected.

Using data from these 20 years we identified the top six reported enteroviruses in March to May each year and compared them with the commonest serotypes reported in July to December of the same year. The top six predicted an average 67.5% (range 33% -84%) of all reports during the July to December 'season' in any given year.

Discussion

The laboratory reporting system in England and Wales is voluntary and not all laboratories contribute. The decrease in reports of enteroviruses over the 20 year period (figure 1) may represent the effect of fewer laboratories testing and/or reporting or a true reduction in disease. Laboratories do not always confirm the group and serotype and reports to CDSC are of isolates whose group at least is known. Laboratory isolation rates underrepresent true rates of infection as most enteroviral infections are asymptomatic¹, not all specimens collected are appropriate, and some clinical groups may be more vigorously investigated (for example, those with meningitis). A drawback of tissue culture is that only a few of the 23 coxsackie A serotypes (types A9, A7, A21, A24, and occasionally A16) are recoverable by standard cell culture systems. Most A serotypes require suckling mouse inoculation but very few laboratories offer this

FIGURE 2 Laboratory reports of echovirus 7, 11, 19, 22, and 30 by quarter: England and Wales, 1975 to 1994



method of diagnosis. Thus coxsackie infections in general and especially serotypes other than A9, A7, A21, and A24 are likely to be underdiagnosed, and laboratory data are likely to overemphasise easily cultured serotypes. Nevertheless these laboratory data provide useful information about common enteroviruses isolated in England and Wales.

The age distribution of patients in England and Wales from whom enteroviruses were isolated showed a large peak at 1 to 2 months of age. A ten year summary of surveillance in the US showed that 56% of isolations were from children under 10 years of age and 26% from babies under 1 year of age¹². In Sweden a 25 year study of isolates of echovirus 22 revealed that 92% of 109 patients were under 2 years of age¹³. In New York City a prospective study of over 600 neonates showed 12.8% acquired enteroviral infection (79% asymptomatic) in the first month of life¹⁴. Most studies and textbooks say simply that the incidence of enterovirus infection is high in young children¹⁵. Our study emphasises the

preponderance of laboratory confirmed enteroviral infections in very young infants. If vaccines were to become available they would need to be given to very young babies for maximum impact.

Usually serum raised against one serotype does not cross neutralise others, but serotypes can undergo some antigenic variation, and limited neutralisation is thought to occur between several serotypes¹⁶. In addition, reinfection with the same serotype is thought to occur despite neutralising antibody status¹⁷. Thus laboratory confirmed infections may simply reflect the prevailing serotypes that infect large numbers of the population, but young infants are more likely to have symptoms and to be investigated. Studies in Scotland in 1985 showed that 23% of people in their mid 30s attending general practitioners had anti-coxsackie B IgM and 55% anti-coxsackie B IgG¹⁸.

The predominant serotypes we found were similar to those most frequently reported in studies in the US, Finland, and Belgium^{9,10,11}, although the preponderance of echovirus 22 was not seen in the US, where echoviruses 9 and 4 were commoner.

It has been suggested that when a particular enterovirus is present in large numbers the others tend to be excluded^{19,20}, but we found that at least two can cocirculate in large numbers. Our data suggest that it is possible to predict from data for March to May each year in England and Wales the majority of serotypes likely to circulate in the following 'season' of the same year. This might be used to alert clinicians of likely clinical presentations. In 1996 an outbreak of coxsackie B5 in England and Wales²¹ could have been predicted using data collected early in the year. Coxsackie B 5 was easily the commonest enterovirus isolated from March to May (62 isolates; 31% of all enteroviruses isolated) and from July to December (27 isolated; yy%). This serotype was also circulating at epidemic levels in Cyprus in 1996. Further evidence of spread of virus across Europe was provided in 1980 when echovirus 30 peaked in Belgium and in England and Wales, and in 1988 when its activity increased in the Netherlands and in Belgium¹¹. There was little evidence in our laboratory data set of any consistent pattern of transmission of enteroviruses across England and Wales but more recent clinical data on hand

foot and mouth disease (coxsackie A 16) showed that the incidence in the north of England was lower than elsewhere²² in the last three epidemic years (1988, 1990, and 1994).

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FIGURE 3 Laboratory reports of coxsackievirus A and B and echovirus in England and Wales (rate per 100 000 population, by age): 1975 to 1994

